ANALYTICAL CHEMISTRY DIVISION COMMISSION ON SOLUBILITY DATA

# **SOLUBILITY DATA SERIES**

Volume 36

### **4-AMINOBENZENESULFONAMIDES**

Part III

6-Membered Heterocyclic Substituents and Miscellaneous Systems

## SOLUBILITY DATA SERIES

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*Editor-in-Chief* A.S. KERTES

Volume 36

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Part III

6-Membered Heterocyclic Substituents and Miscellaneous Systems

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# FOREWORD

#### If the knowledge is undigested or simply wrong, more is not better

How to communicate and disseminate numerical data effectively in chemical science and technology has been a problem of serious and growing concern to IUPAC, the International Union of Pure and Applied Chemistry, for the last two decades. The steadily expanding volume of numerical information, the formulation of new interdisciplinary areas in which chemistry is a partner, and the links between these and existing traditional subdisciplines in chemistry, along with an increasing number of users, have been considered as urgent aspects of the information problem in general, and of the numerical data problem in particular.

Among the several numerical data projects initiated and operated by various IUPAC commissions, the Solubility Data Project is probably one of the most ambitious ones. It is concerned with preparing a comprehensive critical compilation of data on solubilities in all physical systems, of gases, liquids and solids. Both the basic and applied branches of almost all scientific disciplines require a knowledge of solubilities as a function of solvent, temperature and pressure. Solubility data are basic to the fundamental understanding of processes relevant to agronomy, biology, chemistry, geology and oceanography, medicine and pharmacology, and metallurgy and materials science. Knowledge of solubility is very frequently of great importance to such diverse practical applications as drug dosage and drug solubility in biological fluids, anesthesiology, corrosion by dissolution of metals, properties of glasses, ceramics, concretes and coatings, phase relations in the formation of minerals and alloys, the deposits of minerals and radioactive fission products from ocean waters, the composition of ground waters, and the requirements of oxygen and other gases in life support systems.

The widespread relevance of solubility data to many branches and disciplines of science, medicine, technology and engineering, and the difficulty of recovering solubility data from the literature, lead to the proliferation of published data in an ever increasing number of scientific and technical primary sources. The sheer volume of data has overcome the capacity of the classical secondary and tertiary services to respond effectively.

While the proportion of secondary services of the review article type is generally increasing due to the rapid growth of all forms of primary literature, the review articles become more limited in scope, more specialized. The disturbing phenomenon is that in some disciplines, certainly in chemistry, authors are reluctant to treat even those limited-in-scope reviews exhaustively. There is a trend to preselect the literature, sometimes under the pretext of reducing it to manageable size. The crucial problem with such preselection - as far as numerical data are concerned - is that there is no indication as to whether the material was excluded by design or by a less than thorough literature search. We are equally concerned that most current secondary sources, critical in character as they may be, give scant attention to numerical data.

On the other hand, tertiary sources - handbooks, reference books and other tabulated and graphical compilations - as they exist today are comprehensive but, as a rule, uncritical. They usually attempt to cover whole disciplines, and thus obviously are superficial in treatment. Since they command a wide market, we believe that their service to the advancement of science is at least questionable. Additionally, the change which is taking place in the generation of new and diversified numerical data, and the rate at which this is done, is not reflected in an increased third-level service. The emergence of new tertiary literature sources does not parallel the shift that has occurred in the primary literature. Foreword

With the status of current secondary and tertiary services being as briefly stated above, the innovative approach of the *Solubility Data Project* is that its compilation and critical evaluation work involve consolidation and reprocessing services when both activities are based on intellectual and scholarly reworking of information from primary sources. It comprises compact compilation, rationalization and simplification, and the fitting of isolated numerical data into a critically evaluated general framework.

The Solubility Data Project has developed a mechanism which involves a number of innovations in exploiting the literature fully, and which contains new elements of a more imaginative approach for transfer of reliable information from primary to secondary/tertiary sources. The fundamental trend of the Solubility Data Project is toward integration of secondary and tertiary services with the objective of producing in-depth critical analysis and evaluation which are characteristic to secondary services, in a scope as broad as conventional tertiary services.

Fundamental to the philosophy of the project is the recognition that the basic element of strength is the active participation of career scientists in it. Consolidating primary data, producing a truly critically-evaluated set of numerical data, and synthesizing data in a meaningful relationship are demands considered worthy of the efforts of top scientists. Career scientists, who themselves contribute to science by their involvement in active scientific research, are the backbone of the project. The scholarly work is commissioned to recognized authorities, involving a process of careful selection in the best tradition of IUPAC. This selection in turn is the key to the quality of the output. These top experts are expected to view their specific topics dispassionately, paying equal attention to their own contributions and to those of their peers. They digest literature data into a coherent story by weeding out what is wrong from what is believed to be right. To fulfill this task, the evaluator must cover all relevant open literature. No reference is excluded by design and every effort is made to detect every bit of relevant primary source. Poor quality or wrong data are mentioned and explicitly disqualified as such. In fact, it is only when the reliable data are presented alongside the unreliable data that proper justice can be done. The user is bound to have incomparably more confidence in a succinct evaluative commentary and a comprehensive review with a complete bibliography to both good and poor data.

It is the standard practice that the treatment of any given solute-solvent system consists of two essential parts: I. Critical Evaluation and Recommended Values, and II. Compiled Data Sheets.

The Critical Evaluation part gives the following information:

- (i) a verbal text of evaluation which discusses the numerical solubility information appearing in the primary sources located in the literature. The evaluation text concerns primarily the quality of data after consideration of the purity of the materials and their characterization, the experimental method employed and the uncertainties in control of physical parameters, the reproducibility of the data, the agreement of the worker's results on accepted test systems with standard values, and finally, the fitting of data, with suitable statistical tests, to mathematical functions;
- (ii) a set of recommended numerical data. Whenever possible, the set of recommended data includes weighted average and standard deviations, and a set of smoothing equations derived from the experimental data endorsed by the evaluator;
- (iii) a graphical plot of recommended data.

The Compilation part consists of data sheets of the best experimental data in the primary literature. Generally speaking, such independent data sheets are given only to the best and endorsed data covering the known range of experimental parameters. Data sheets based on primary sources where the data are of a lower precision are given only when no better data are available. Experimental data with a precision poorer than considered acceptable are reproduced in the form of data sheets when they are the only known data for a particular system. Such data are considered to be still suitable for some applications, and their presence in the compilation should alert researchers to areas that need more work. The typical data sheet carries the following information:

- (i) components definition of the system their names, formulas and Chemical Abstracts registry numbers;
- (ii) reference to the primary source where the numerical information is reported. In cases when the primary source is a less common periodical or a report document, published though of limited availability, abstract references are also given;
- (iii) experimental variables;
- (iv) identification of the compiler;
  - (v) experimental values as they appear in the primary source. Whenever available, the data may be given both in tabular and graphical form. If auxiliary information is available, the experimental data are converted also to SI units by the compiler.

Under the general heading of Auxiliary Information, the essential experimental details are summarized:

- (vi) experimental method used for the generation of data;
- (vii) type of apparatus and procedure employed; (viii) source and purity of materials;

  - (ix) estimated error;
    - (x) references relevant to the generation of experimental data as cited in the primary source.

This new approach to numerical data presentation, formulated at the initiation of the project and perfected as experience has accumulated, has been strongly influenced by the diversity of background of those whom we are supposed to serve. We thus deemed it right to preface the evaluation/compilation sheets in each volume with a detailed discussion of the principles of the accurate determination of relevant solubility data and related thermodynamic information.

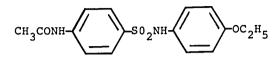
Finally, the role of education is more than corollary to the efforts we are seeking. The scientific standards advocated here are necessary to strengthen science and technology, and should be regarded as a major effort in the training and formation of the next generation of scientists and engineers. Specifically, we believe that there is going to be an impact of our project on scientific-communication practices. The quality of consolidation adopted by this program offers down-to-earth guidelines, concrete examples which are bound to make primary publication services more responsive than ever before to the needs of users. The self-regulatory message to scientists of the early 1970s to refrain from unnecessary publication has not achieved much. A good fraction of the literature is still cluttered with poor-quality articles. The Weinberg report (in 'Reader in Science Information', ed. J. Sherrod and A. Hodina, Microcard Editions Books, Indian Head, Inc., 1973, p. 292) states that 'admonition to authors to restrain themselves from premature, unnecessary publication can have little effect unless the climate of the entire technical and scholarly community encourages restraint ... ' We think that projects of this kind translate the climate into operational terms by exerting pressure on authors to avoid submitting low-grade material. The type of our output, we hope, will encourage attention to quality as authors will increasingly realize that their work will not be suited for permanent retrievability unless it meets the standards adopted in this project. It should help to dispel confusion in the minds of many authors of what represents a permanently useful bit of information of an archival value, and what does not.

If we succeed in that aim, even partially, we  $^{\prime}$  have then done our share in protecting the scientific community from unwanted and irrelevant, wrong numerical information.

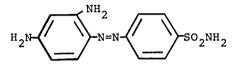
A. S. Kertes

## PREFACE

With few exceptions, these volumes of the solubility data series deal with solubilities of the derivatives of 4-aminobenzenesulfonamide, usually referred to as "sulfanilamide" (sulfanilic acid amide), a name coined in 1937 (1). The history of sulfanilamide begins in 1906, when Schroeter (2) synthesized the molecule containing a 4-acetylaminosulfanilamide portion.



In 1908, Gelmo (3) described sulfanilamide and 13 of its derivatives and gave solubility values for these compounds. In 1935, Domagk (4) detected antibacterial activity of a synthetic azo dye, prontosil, with the structure.



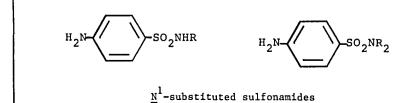
This compound had been tested for antibacterial activity (5), the "sulfanilamide" portion being responsible for its activity. This was confirmed (6) by isolation of sulfanilamide in the urine of patients. Fildes (7) and Wood (8), in 1940, demonstrated that the derivatives of sulfanilamide were antimetabolites of p-aminobenzoic acid (PABA) which is a step in the folic acid synthesis of bacteria. Thus, the structural similarity of PABA and sulfonamides caused interference by competitive antagonism and resulted in a bacteriostatic effect. The discoveries of antibacterial activity led to an exciting flood of research, and thousands of sulfanilamide derivatives have been synthesized. As early as 1948, the number of sulfonamide derivatives (9) was estimated to be several thousand. In the two decades after that, the number of synthesized sulfonamides have gone past 10,000(10)

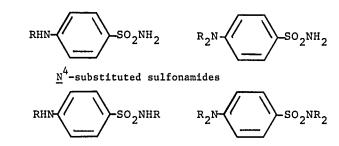
Clinical trials of these sulfonamides and derivatives have been associated with low solubilities and some renal crystalluria. The low solubility, and its sensitivity to pH, could cause crystalline precipitation in the renal tubules in the filtration of blood into acidic urine. Some of the problems of limited solubility were overcome by complexation or salt formation, and solid state manipulations which in turn have stimulated investigations into solubility of the drugs in water, buffers and some binary solvent system. Analytical methodologies span a wide spectrum of techniques and the relevant references are in pharmaceutical, medical and chemical literature.

In all volumes the chemical structures, registry number and the molecular weight of the compounds considered are collected in the front of each volume. The compounds as they occur on the data sheets are given successively in each volume. In the first volume of this series there are 35 compounds. The second and third volumes have 58 compounds and 108 compounds, respectively.

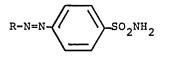
#### NOMENCLATURE:

The nomenclature of sulfanilamide derivatives has conventionally been based on the following numbering system: substituents at the nitrogen atom of the amide group  $(-SO_2NH_2)$  are called  $N^1$ -substituents, whereas substitutents at the 4-amino nitrogen  $(4-H_2N-)$  are called  $N^4$ -substituents. Substitution in either or both of the two positions lead to compounds referred to as "sulfonamides" (sometimes "sulfanilamides" or even "sulfamides"). Here are illustrative examples of this nomenclature.





 $\underline{N}^1$ ,  $\underline{N}^4$ -substituted sulfonamides The 4-amino group can be diazotized to give derivatives of the formula



As the sulfonamide molecule carries a basic  $4-NH_2$  group and an acid  $-SO_2NH_2$  one, it is capable of formation the respective salts or complexes, e.g.



where HX stands for an acid and M is a univalent metal atom.

In common use by health practitioners are nonproprietary names of sulfonamides which are brief and reflect the chemical nature of their molecules. Examples are: sulfacetamide, sulfapyridine, sulfathiazole, sulfadiazine, sulfaguanidine, etc. There are numerous trivial names; for example, sulfanilamide has as many as 140 synonyms, and sulfathiazole has 113. Negwer (11) has compiled an excellent guide to this nomenclature. In chemical literature, systematic names in line either with IUPAC (12) or Chemical Abstract rules (13) are used. The latter has been adopted in these volumes and the systematic name is, where appropriate, followed by the nonproprietary or trivial name.

#### ORGANIZATION OF THE VOLUMES:

The numerical data on the solubility of 2-aminobenzenesulfonamide, 3-aminobenzenesulfonamide, and 4-aminobenzenesulfonamide and its  $\underline{N}^1$  and  $\underline{N}^4$ - derivatives, salts and complexes, compiled up to 1985 inclusive, have been divided into three volumes on the basis of chemical structure of the compounds.

The first volume includes the solubility of 2-aminobenzenesulfonamide, 3-aminobenzenesulfonamide, 4-aminobenzenesulfonamide and the derivatives of the last-named compound substituted at either of the nitrogen atoms, or both, with non-cyclic substituents (see System Index at the end of the first volume). The aroyl substituted the control of the second volume includes sulfanilamide derivatives substituted with 5-membered heterocyclic rings at either of the nitrogen atoms, and their derivatives. The third volume covers the solubilities of the derivatives substituted with 6-membered rings, mixtures of sulfonamides, and miscellanea. The compilations do not include compounds devoid of the  $-NH_2$ , -NHR or  $-NR_2$  group in the benzene ring.

The solvent systems include all solvents with the exception of body fluids. The order of solvents for a particular solute are as follows: water; water-mineral acid; watermineral base; water-mineral salt; water-miscellaneous mineral components; water-mineral and organic compounds; water-organic components; organic solvents; carboxylic acid and their salts; aliphatic acids; aromatic acids; other acids; alcohols, phenols (mono-, di-, polyhydric); amides; amines; aliphatic amines (primary, secondary, tertiary); aromatic amines (primary, secondary, tertiary); other amines; aminoalcohols; carboxylic acid esters; ethers (excluding tensides); hydrocarbons; aliphatic hydrocarbons; aromatic hydrocarbons; miscellaneous hydrocarbons; halogenated hydrocarbons (flouro-, chloro-, bromo-, iodo-); aliphatic halogenated hydrocarbons; aromatic halogenated hydrocarbons; ketones; tensides (surface-active agents); miscellaneous organic solvents.

#### SIGNIFICANT FIGURES AND GRAPHICAL DATA:

In most cases, solubility values given in the primary source by various workers are overstated with respect to significant figures. Since the author(s) original values are given on the data sheets, it is difficult to consider significant figures and analytical limitations in a completely consistant fashion. Therefore, the reader should be aware that in most cases the number of significant figures used for calculations was not that given by the original author(s). This was done to maintain coherence and consistency as data were given to varying significant figures. In many cases graphic data of sufficient size and clarity are reproduced. The data can be regarded of sufficient accuracy to serve as a starting point for more precise determinations. In many instances, the effect of additive concentration, pH, temperature, etc. can be depicted.

#### POLYMORPHISM:

Many sulfonamides exhibit several cyrstalline forms or polymorphs. There are several studies referenced in these volumes that specifically deal with the solubility difference between polymorphic modifications of the same compound. The solubility differences between polymorphs have been found to vary over a large range of values.

#### AMPHOLYTES:

Solubility of ampholytic sulfonamides as a function of pH varies enormously, sometimes by several orders of magnitude. Unless the pH is known experimentally, the solubility value may be suspect especially at low (1-3) and high pH (10-12) values. In these cases, the solubility is a rapidly changing value, frequently with small incremental changes of pH. The abrupt change of solubility with pH is usually associated with the formation of water soluble anionic and cationic species. Buffers, especially at higher concentrations may alter solubility by salting effect and the pH is also affected by ionic strength.

#### EQUILIBRATION TIME:

In general, it appears that many of these determined solubilities may not have been under equilibrium conditions. Unfortunately, in too many instances the equilibration time appears too low. Typically, solutes possess low aqueous solubilities and require long dissolution time to reach saturation. Saturation time should be experimentally determined in each case and for each compound. In many cases up to 24 hours may be required.

The editors consider the vast majority of the solubility values given in these volumes as tentative. It should be stressed, however, that they represent a useful starting point for more accurate determinations of a vast array of substituted 4-aminobenzene-sulfonamides with many structurally and chemically related compound of various types. They amply illustrate the many factors and parameters affecting solubility and the direction and magnitude of these effects.

This compilation and evaluation is not only the result of the joint efforts of the compiler and evaluator, but also of all those who read the manuscripts, expressed their criticism, who procured copies of hard-to-get journals, who translated texts from Japanese as well as of those who in any other way assisted in the compilation and evaluation. We would like to express our gratitude in particular to the following colleagues: Prof. S. Kertes, Dr. M. Salomon, Prof. S. Yalkowsky, Prof. H. Akaiwa, Prof. C. Kalidas, Prof. W. Riess, Prof. A. Guerrero-Laverat, Prof. P. Rohdewald, Prof. J. Putter, Dr.K. L. Loening, Dr. A. Brodin, Dr. D. Zimma, Mr. K. Hazelton, Dr. R. Fernandez-Prini, and Mr. E. MacMullan.

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# INTRODUCTION TO THE SERIES ON SOLUBILITY OF SOLIDS IN LIQUIDS: SUBSERIES ON PHARMACEUTICALS

Nature of the Project

The Solubility Data Project (SDP) has as its aim a comprehensive search of the literature for solubilities of gases, liquids, and solids in liquids or solids. Data of suitable precision are compiled on data sheets in a uniform format. The data for each system are evaluated, and where data from different sources agree sufficiently, recommended values are proposed. The evaluation sheets, recommended values, and compiled data sheets are published on consecutive pages.

For phamaceuticals, the definitions, thermodynamics and methods of analysis are the same as those for the study of solubility of solids in liquids in general. For this subseries, special sections deal with matters of interest for pharmaceuticals, including discussions of polymorphism, factors influencing the rate of dissolution of drugs, and methods used to inhibit or enhance the rate of dissolution.

#### Definitions

A mixture (1, 2) describes a gaseous, liquid, or solid phase containing more than one substance, when the substances are all treated in the same way.

A solution (1, 2) describes a liquid or solid phase containing more than one substance, when for convenience one of the substances, which is called the solvent, and may itself be a mixture, is treated differently than the other substances, which are called solutes. If the sum of the mole fractions of the solutes is small compared to unity, the solution is called a dilute solution.

The solubility of a substance B is the relative proportion of B (or a substance related chemically to B) in a mixture which is saturated with respect to solid B at a specified temperature and pressure. Saturated implies the existence of equilibrium with respect to the processes of dissolution and precipitation; the equilibrium may be stable or metastable. The solubility of a substance in metastable equilibrium is usually greater than that of the corresponding substance in stable equilibrium. (Strictly speaking, it is the activity of the substance in metastable equilibrium that is greater.) Care must be taken to distinguish true metastability from supersaturation, where equilibrium does not exist.

Either point of view, mixture or solution, may be taken in describing solubility. The two points of view find their expression in the quantities used as measures of solubility and in the reference states used for definition of activities, activity coefficients and osmotic coefficients.

The qualifying phrase "substance related chemically to B" requires comment. The composition of the saturated mixture (or solution) can be described in terms of any suitable set of thermodynamic components. Thus, the solubility of a salt hydrate in water is usually given as the relative proportion of anhydrous salt in solution, rather than the relative proportions of hydrated salt and water.

For pharmaceuticals, the solubility of a drug substance in a given medium is of special importance in designing a suitable dosage form for a drug or in determination of a regimen for its administration. The solubility and rate of dissolution will determine the rate of appearance of the drug in various body fluids and at various sites of action. Therefore, the bioavailability of a drug is often determined by its solubility and rate of dissolution.

The solubility is a constant for a given substance in a given medium at constant temperature and pressure. Frequently it is possible to alter the solubility and rate of dissolution dramatically through changes in structure, degree of crystallinity or morphology, or by the addition of a solubilizing agent (cosolvent) to the dissolution medium. The appearance of a drug in adequate concentration at its site of action is a requirement for testing clinical efficiency; thus, enhancement of solubility may be required to render a substance clinically useful.

For reviews of recent literature on solubility and solubilization of

drug substances, see (3, 4).

Quantities Used as Measures of Solubility

1. Mole fraction of substance B, x<sub>B</sub>:

$$x_B = n_B / \sum_{s=1}^{C} n_s$$
 [1]

where  $n_{\rm S}$  is the amount of substance of s, and c is the number of distinct substances present (often the number of thermodynamic components in the system). Mole per cent of B is 100  $x_{\rm B}$ .

2. Mass fraction of substance B, w<sub>B</sub>:

$$w_{\rm B} = m_{\rm B}' / \sum_{{\rm s}=1}^{L} m_{\rm s}'$$
 [2]

where  $m_{\rm g}$  is the mass of substance s. Mass per cent is 100 w<sub>B</sub>. The equivalent terms weight fraction and weight per cent are not used.

3. Solute mole (mass) fraction of solute B (5, 6):

$$x_{s,B} - n_B / \sum_{s=1}^{C} n_s = x_B / \sum_{s=1}^{C} x_s$$
 [3]

$$w_{s,B} = m_{B'} / \sum_{s=1}^{C'} m_{s'} = w_{B} / \sum_{s=1}^{C'} w_{s}$$
 [3a]

where the summation is over the solutes only. For the solvent A,  $x_{S,A} = x_A/(1 - x_A)$ ,  $w_{S,A} = w_A/(1 - w_A)$ . These quantities are called Jänecke mole (mass) fractions in many papers.

4. Molality of solute B (1, 2) in a solvent A:

 $m_B = n_B/n_A M_A$  SI base units: mol kg<sup>-1</sup> [4]

where  $M_A$  is the molar mass of the solvent.

5. Concentration of solute B (1, 2) in a solution of volume V:

$$c_B = [B] = n_B/V \qquad SI \text{ base units: mol m}^3 \qquad [5]$$

The symbol  $c_B$  is preferred to [B], but both are used. The terms molarity and molar are not used.

Mole and mass fractions are appropriate to either the mixture or the solution point of view. The other quantities are appropriate to the solution point of view only. Conversions among these quantities can be carried out using the equations given in Table 1-1 following this introduction. Other useful quantities will be defined in the prefaces to individual volumes or on specific data sheets.

In addition to the quantities defined above, the following are useful in conversions between concentrations and other quantities.

5. Density: 
$$\rho = m/V$$
 SI base units: kg m<sup>-3</sup> [6]

7. Relative density: d; the ratio of the density of a mixture to the density of a reference substance under conditions which must be specified for both (1). The symbol  $d_{t}$  will be used for the density of a mixture at t°C, 1 bar divided by the density of water at t °C, 1 bar. (In some cases, 1 atm ~ 101.325 kPa is used instead of 1 bar ~ 100 kPa.)

8. A note on nomenclature. The above definitions use the nomenclature of the IUPAC Green Book (1), in which a solute is called B and a solvent A In compilations and evaluations, the first-named component (component 1) is the solute, and the second (component 2 for a two-component system) is the solvent. The reader should bear these distinctions in nomenclature in mind when comparing nomenclature and theoretical equations given in this Introduction with equations and nomenclature used on the evaluation and compilation sheets.

#### Thermodynamics of Solubility

The principal aims of the Solubility Data Project are the tabulation and evaluation of: (a) solubilities as defined above; (b) the nature of the saturating phase. Thermodynamic analysis of solubility phenomena has two aims: (a) to provide a rational basis for the construction of functions to represent solubility data; (b) to enable thermodynamic Introduction

quantities to be extracted from solubility data. Both these are difficult to achieve in many cases because of a lack of experimental or

theoretical information concerning activity coefficients. Where

thermodynamic quantities can be found, they are not evaluated critically, since this task would involve critical evaluation of a large body of data that is not directly relevant to solubility. The following is an outline of the principal thermodynamic relations encountered in discussions of solubility. For more extensive discussions and references, see books on thermodynamics, e.g., (7-14). Activity Coefficients (1) (a) Mixtures. The activity coefficient  $f_H$  of a substance B is given by RT in  $(f_B x_B) \sim \mu_B - \mu_B^*$ [7] where  $\mu_B^*$  is the chemical potential of pure B at the same temperature and pressure. For any substance B in the mixture,  $\lim_{X_H \to 1} f_B = 1$ [8] (b) Solutions. (1) Solute B. The molal activity coefficient  $\gamma_B$  is given by RT  $\ln(\gamma_B m_B) = \mu_B - (\mu_B - RT \ln m_B)^{\infty}$ [9] where the superscript " indicates an infinitely dilute solution. For any solute B,  $\gamma_B^{\infty} = 1$ [10] Activity coefficients  $y_B$  connected with concentrations  $c_B$ , and  $f_{X,B}$ (called the rational activity coefficient) connected with mole fractions  $x_B$ , are defined in analogous ways. The relations among them (1, 9) are, where  $\rho^*$  is the density of the pure solvent:  $f_B = (1 + M_A \sum_{g} m_g) \gamma_B = [\rho + \sum_{g} (M_A - M_g) c_g] y_B / \rho^*$ [11] $\gamma_B = (1 - \sum_{a} x_s) f_{X,B} = (\rho - \sum_{a} M_s c_s) y_B / \rho^*$ [12]  $y_{B} = \rho^{*} f_{x,B} [1 + \sum_{a} (M_{s}/M_{A} - 1)x_{B}] / \rho = \rho^{*} (1 + \sum_{a} M_{s}m_{s})y_{B} / \rho$ [13]For an electrolyte solute  $B = C_{\nu+}A_{\nu-}$ , the activity on the molality scale is replaced by (11):  $\gamma_B m_B - \gamma_{\pm}^{\nu} m_B^{\nu} Q^{\nu}$ [14] where  $\nu = \nu_{+} + \nu_{-}$ ,  $Q = (\nu_{+}^{\nu_{+}}\nu_{-}^{\nu_{-}})^{1/\nu}$ , and  $\nu_{\pm}$  is the mean ionic activity coefficient on the molality scale. A similar relation holds for the concentration activity,  $y_Bc_B$ . For the mole fractional activity,  $f_{\mathbf{X},\mathbf{B}}\mathbf{x}_{\mathbf{B}} = Q^{\nu}f_{\pm}^{\nu}x_{\pm}^{\nu}$ [15] where  $x_{\pm} = (x_{\pm}x_{\pm})^{1/\nu}$ . The quantities  $x_{\pm}$  and  $x_{\pm}$  are the ionic mole fractions (11), which are:  $x_{+} = v_{+}x_{B}/[1 + \sum_{s}(v_{s} - 1)x_{s}]; \quad x_{-} = v_{-}x_{B}[1 + \sum_{s}(v_{s} - 1)x_{s}]$ [16] where  $\nu_{S}$  is the sum of the stoichiometric coefficients for the ions in a salt with mole fraction  $x_s$ . Note that the mole fraction of solvent is now  $x_{A}' = (1 - \sum_{s} \nu_{s} x_{s}) / [1 + \sum_{s} (\nu_{s} - 1) x_{s}]$ [17] so that  $x_A' + \sum \nu_s x_s - 1$ [18] The relations among the various mean ionic activity coefficients are:  $f_{\pm} = (1 + M_{A}\sum_{\alpha} v_{s} ms) \gamma_{\pm} \sim [\rho + \sum_{\alpha} (v_{s} M_{A} - M_{s}) c_{s}] y_{\pm} / \rho^{*}$ [19]

 $\gamma_{\pm} = \frac{(1 - \sum_{s} x_{s})f_{\pm}}{1 + \sum_{s} (\nu_{s} - 1)x_{s}} = (\rho - \sum_{s} M_{s}c_{s})y_{\pm}/\rho^{*}$ [20]

$$y_{\pm} = \frac{\rho^{*}[1 + \sum_{g}(M_{g}/M_{A} - 1)x_{g}]f_{\pm}}{\rho[1 + \sum_{g}(\nu_{g} - 1)x_{g}]} = \rho^{*}(1 + \sum_{g}M_{g}m_{g})\gamma_{\pm}/\rho$$
[21]

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The osmotic coefficient,  $\phi$ , of a solvent A is defined as (1):

The rational osmotic coefficient,  $\phi_X$ , is defined as (1):

where  $\mu_A^*$  is the chemical potential of the pure solvent.

 $\phi - (\mu_A^* - \mu_A)/RT M_A \sum m_s$ 

$$\sum_{i=1}^{C} x_i (S_i dT - V_i dp + d\mu_i') + \sum_{i=C+1}^{C} x_i (S_i dT - V_i dp + d\mu_i) = 0 \quad [27]$$

Subtract [26] from [27] and use the equation

$$d\mu_i = (d\mu_i)_{T,p} - S_i dT + V_i dp \qquad [28]$$

and the Gibbs-Duhem equation at constant temperature and pressure:

$$\sum_{i=1}^{C} x_i (d\mu_i')_{T,p} + \sum_{i=C+1}^{C} x_i (d\mu_i)_{T,p} = 0$$
 [29]

The resulting equation is:

(ii) Solvent, A:

$$RT\sum_{i=1}^{C} x_{i}'(dlna_{i})T_{i}p = \sum_{i=1}^{C} x_{i}'(H_{i} - H_{i}')dT/T - \sum_{i=1}^{C} x_{i}'(V_{i} - V_{i}')dp \quad [30]$$

where

w.

$$H_1 - H_1' - T(S_1 - S_1')$$
 [31]

is the enthalpy of transfer of component 1 from the solid to the liquid phase at a given temperature, pressure and composition, with  $H_1$  and  $S_1$ the partial molar enthalpy and entropy of component i.

Use of the equations

$$H_i - H_i^0 - -RT^2(\partial \ln a_i / \partial T)_{x,p}$$
[32]

and

$$V_i - V_i^0 = RT(\partial \ln a_i / \partial p)_{\mathbf{X}, T}$$
[33]

where superscript o indicates an arbitrary reference state gives:

$$RT\sum_{i=1}^{C} x_{i}'dlna_{1} = \sum_{i=1}^{C} x_{i}'(H_{1}^{0} - H_{i}')dT/T - \sum_{i=1}^{C} x_{i}'(V_{1}^{0} - V_{i}')dp \quad [34]$$

s replaced

[24]

[25]

[26]

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[22]

[23]

where

$$dlna_{1} = (dlna_{1})_{T,p} + (\partial lna_{i}/\partial T)_{x,p} + (\partial lna_{i}/\partial p)_{x,T}$$
[35]

The terms involving enthalpies and volumes in the solid phase can be written as:

$$\sum_{i=1}^{C} x_{i}' H_{i}' = H_{s}^{*} \qquad \sum_{i=1}^{C} x_{i}' V_{i}' = V_{s}^{*} \qquad [36]$$

With eqn [36], the final general solubility equation may then be written:

$$R\sum_{i=1}^{C} x_{i}' dlna_{i} = (H_{s}^{*} - \sum_{i=1}^{C} x_{i}' H_{i}^{0})d(1/T) - (V_{s}^{*} - \sum_{i=1}^{C} x_{i}' V_{i}^{0})dp/T$$
[37]

Note that those components which are not present in both phases do not appear in the solubility equation. However, they do affect the solubility through their effect on the activities of the solutes.

Several applications of eqn [37] (all with pressure held constant) will be discussed below. Other cases will be discussed in individual evaluations.

#### (a) Solubility as a function of temperature.

Consider a binary solid compound  $A_n B$  in a single solvent A. There is no fundamental thermodynamic distinction between a binary compound of A and B which dissociates completely or partially on melting and a solid mixture of A and B; the binary compound can be regarded as a solid mixture of constant composition. Thus, with c = 2,  $x_A' = n/(n + 1)$ ,

$$x_B' = 1/(n + 1)$$
, eqn [37] becomes:

$$dln(a_A^n a_B) = -\Delta H_{AB}^{0} d(1/RT)$$
[38]

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where

$$\Delta H_{AB}^{0} = nH_{A} + H_{B} - (n+1)H_{S}^{*}$$
<sup>[39]</sup>

is the molar enthalpy of melting and dissociation of pure solid  $A_{\Pi}B$  to form A and B in their reference states. Integration between T and  $T_{0}$ , the melting point of the pure binary compound  $A_{\Pi}B$ , gives:

$$\ln(a_A^n a_B) = \ln(a_A^n a_B)_{T=T_0} - \int_{\Delta}^{T} \Delta H_{AB} d(1/RT)$$
 [40]

(1) Non-electrolytes

In eqn [32], introduce the pure liquids as reference states. Then, using a simple first-order dependence of  $\Delta H_{AB}^*$  on temperature, and assuming that the activitity coefficients conform to those for a simple mixture (8):

$$RT \ln f_A = w x_B^2 \qquad RT \ln f_B = w x_A^2 \qquad [41]$$

then, if w is independent of temperature, eqn [32] and [33] give:

$$\ln\{x_B(1-x_B)^n\} + \ln\left\{\frac{n^n}{(1+n)^{n+1}}\right\} = G(T)$$
[42]

where

$$G(T) = -\left\{\frac{\Delta H_{AB}^{*} - T^{*} \Delta C_{p}^{*}}{R}\right\} \left\{\frac{1}{T} - \frac{1}{T^{*}}\right\} + \frac{\Delta C_{p}^{*}}{R} \ln(T/T^{*}) - \frac{w}{R} \left\{\frac{xA^{2} + nxB^{2}}{T} - \frac{n}{(n+1)T^{*}}\right\}$$
[43]

where  $\Delta C_p^*$  is the change in molar heat capacity accompanying fusion plus decomposition of the pure compound to pure liquid A and B at temperature  $T^*$ , (assumed here to be independent of temperature and composition), and  $\Delta H_{AB}^*$  is the corresponding change in enthalpy at  $T = T^*$ . Equation [42] has the general form:

$$\ln\{x_{\rm B}(1-x_{\rm B})^n\} = A_1 + A_2/(T/K) + A_3\ln(T/K) + A_4(x_{\rm A}^2 + nx_{\rm B}^2)/(T/K)$$
[44]

If the solid contains only component B, then n = 0 in eqn [42] to [44].

If the infinite dilution reference state is used, then:

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RT  $\ln f_{x,B} = w(x_A^2 - 1)$  [45]

and [39] becomes

 $\Delta H_{AB}^{\infty} = nH_{A}^{*} + H_{B}^{\infty} - (n+1)H_{B}^{*}$ [46]

where  $\Delta H_{AB}^{\infty}$  is the enthalpy of melting and dissociation of solid compound  $A_{\Pi}B$  to the infinitely dilute reference state of solute B in solvent A;  $H_A^*$  and  $H_B^{\infty}$  are the partial molar enthalpies of the solute and solvent at infinite dilution. Clearly, the integral of eqn [32] will have the same form as eqn [35], with  $\Delta H_{AB}^{\infty}$  replacing  $\Delta H_{AB}^*$ ,  $\Delta C_p^{\infty}$  replacing  $\Delta Cp^*$ , and  $x_A^2$  - 1 replacing  $x_A^2$  in the last term.

See (7) and (13) for applications of these equations to experimental data.

(11) Electrolytes

(a) Mole fraction scale

If the liquid phase is an aqueous electrolyte solution, and the solid is a salt hydrate, the above treatment needs slight modification. Using rational mean activity coefficients, eqn [34] becomes:

$$\ln\left\{\frac{x_{B}^{\nu}(1-x_{B})^{n}}{(1+(\nu-1)x_{B})^{n+\nu}}\right\} - \ln\left\{\frac{n^{n}}{(n+\nu)^{n+\nu}}\right\} + \ln\left\{\left[\frac{f_{B}}{f_{B}^{*}}\right]^{\nu}\left[\frac{f_{A}}{f_{A}}\right]^{n}\right\}$$

$$= -\left\{\frac{\Delta H_{AB}^{*} - T^{*}\Delta C_{P}^{*}}{R}\right\}\left\{\frac{1}{T} - \frac{1}{T^{*}}\right\} + \frac{\Delta C_{P}^{*}}{R} - \ln(T/T^{*})$$

$$(47)$$

where superscript \* indicates the pure salt hydrate. If it is assumed that the activity coefficients follow the same temperature dependence as the right-hand side of eqn [47] (15-17), the thermochemical quantities on the right-hand side of eqn [47] are not rigorous thermodynamic enthalpies and heat capacities, but are apparent quantities only. Data on activity coefficients (11) in concentrated solutions indicate that the terms involving these quantities are not negligible, and their dependence on temperature and composition along the solubility-temperature curve is a subject of current research.

A similar equation (with  $\nu = 2$  and without the heat capacity terms) or activity coefficients) has been used to fit solubility data for some MOH-H<sub>2</sub>O systems, where M is an alkali metal (15); enthalpy values obtained agreed well with known values. The full equation has been deduced by another method in (16) and applied to MCl<sub>2</sub>-H<sub>2</sub>O systems in (16) and (17). For a summary of the use of equation [47] and similar equations, see (18).

(2) Molality scale Substitution of the mean activities on the molality scale in eqn [40] gives:

$$\nu \ln \left\{ -\frac{\gamma_{\pm} m_{\rm B}}{\gamma_{\pm} m_{\rm B}^{\star}} \right\} - \nu (m_{\rm B}/m_{\rm B}^{\star} - 1) - \nu \{m_{\rm B}(\phi - 1)/m_{\rm B}^{\star} - \phi^{\star} + 1\}$$

$$= G(T)$$
[48]

where G(T) is the same as in eqn [47],  $m_B^* = 1/nM_A$  is the molality of the anhydrous salt in the pure salt hydrate and  $\gamma_\pm$  and  $\phi$  are the mean activity coefficient and the osmotic coefficient, respectively. Use of the osmotic coefficient for the activity of the solvent leads, therefore, to an equation that has a different appearance to [47]; the content is identical. However, while eqn [47] can be used over the whole range of composition ( $0 \le x_B \le 1$ ), the molality in eqn [48] becomes infinite at  $x_B$  -1; use of eqn [48] is therefore confined to solutions sufficiently dilute that the molality is a useful measure of composition. The essentials of eqn [48] were deduced by Williamson (19); however, the form used here appears first in the Solubility Data Series. For typical applications (where activity and osmotic coefficients are not considered explicitly, so that the enthalpies and heat capacities are apparent values, as explained above), see (20).

The above analysis shows clearly that a rational thermodynamic basis exists for functional representation of solubility-temperature curves in two-component systems, but may be difficult to apply because of lack of experimental or theoretical knowledge of activity coefficients and partial molar enthalpies. Other phenomena which are related ultimately to the stoichiometric activity coefficients and which complicate interpretation

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Introduction

include ion pairing, formation of complex ions, and hydrolysis. Similar considerations hold for the variation of solubility with pressure, except that the effects are relatively smaller at the pressures used in many investigations of solubility (7).

(b) Solubility as a function of composition.

At constant temperature and pressure, the chemical potential of a saturating solid phase is constant:

$$\mu_{A_{n}B}^{*} = \mu_{A_{n}B}(sln) = n\mu_{A} + \mu_{B}$$
[49]

$$= (n\mu_A^* + \nu_+\mu_+^\infty + \nu_-\mu_-^\infty) + nRT \ln f_A x_A$$
$$+ \nu RT \ln (\gamma_+m_+O)$$

for a salt hydrate  $A_{\Pi}B$  which dissociates to water (A), and a salt (B), one mole of which ionizes to give  $\nu_+$  cations and  $\nu_-$  anions in a solution in which other substances (ionized or not) may be present. If the saturated solution is sufficiently dilute,  $f_A = x_A = 1$ , and the quantity  $K_B$  in

 $\Delta G^{\infty} = (\nu_{+}\mu_{+}^{\infty} + \nu_{-}\mu_{-}^{\infty} + n\mu_{A}^{*} - \mu_{AB}^{*})$ 

[50]

is called the solubility product of the salt. (It should be noted that it is not customary to extend this definition to hydrated salts, but there is no reason why they should be excluded.) Values of the solubility product are often given on mole fraction or concentration scales. In dilute solutions, the theoretical behavior of the activity coefficients as a function of ionic strength is often sufficiently well known that reliable extrapolations to infinite dilution can be made, and values of  $K_S$  can be determined. In more concentrated solutions, the same problems with activity coefficients that were outlined in the section on variation of solubility with temperature still occur. If these complications do not arise, the solubility of a hydrate salt  $C_{\nu}A_{\nu} \cdot nH_2O$  in the presence of other solutes is given by eqn [50] as

$$\nu \ln\{m_B/m_B(0)\} = -\nu \ln\{\gamma_{\pm}/\gamma_{\pm}(0)\} - n \ln\{a_A/a_A(0)\}$$
[51]

where  $a_A$  is the activity of water in the saturated solution,  $m_B$  is the molality of the salt in the saturated solution, and (0) indicates absence of other solutes. Similar considerations hold for non-electrolytes.

Consideration of complex mixed ligand equilibria in the solution phase is also frequently of importance in the interpretation of solubility equilibria. For nomenclature connected with these equilibria (and solubility equilibria as well) see (21, 22).

(c) Alteration of the dissolution medium for pharmaceuticals

Many substances which are only slightly soluble in water may be made more soluble by the addition of a cosolvent, surface-active agents, or complexing agents.

(i) Addition of a cosolvent. It is frequently necessary to dissolve a quantity of drug in a small volume of liquid so that it may be administered parenterally by injection. If the drug is not sufficiently soluble in water because of its hydrophobicity, the addition of a quantity of water-miscible, but less polar solvent may render the drug soluble in a small quantity of the mixed solvent. Solvents used for this purpose have included propylene glycol, glycerol, ethanol, polyethylene glycol and glycofural. Solubilities of many drug substances in water-organic solvent mixtures have been tabulated by Yalkowsky and Roseman (23).

(11) Surface-active agents. Another approach to increasing the solubility and rate of dissolution of drug substances is to add a surface-active agent. There is an extensive literature on the application of surfactants and micellar dissolution, which has been summarized recently by Florence (24). Cationic, anionic or neutral surfactants are available. In choosing a surfactant, the possibility of charge-charge interactions between the drug and the surfactant must be considered, as well as the degree of ionization of each species as a function of pH. Micellar dissolution of drugs or additives may protect the dissolved species from hydrolytic degradation by the aqueous solvent. The stability of drugs may therefore be enhanced considerably by the addition of a surfactant.

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membranes. Examples of substantially improved bioavailability of drugs under the influence of micellar dissolution have been reported (24).

(111) Other modifications of the dissolution medium. The solubility of weak acid and weak base drugs will usually depend on the pH of the medium. Within reasonable limits for pharmaceutical preparations, pH may be adjusted to obtain the drug in the charged (and usually more soluble) form. The addition of complexing agents such as chelating agents, organic salts, cyclodextrins, or ion-pairing agents may be used to enhance solubility and rate of dissolution. Examples are given in the chapter by A.J. Repta in (3).

#### The Solid Phase

The definition of solubility permits the occurrence of a single solid phase which may be a pure anhydrous compound, a salt hydrate, a nonstoichiometric compound, or a solid mixture (or solid solution, or "mixed crystals"), and may be stable or metastable. As well, any number of solid phases consistent with the requirements of the phase rule may be present. Metastable solid phases are of widespread occurrence, and may appear as polymorphic (or allotropic) forms or crystal solvates whose rate of transition to more stable forms is very slow. Surface heterogeneity may also give rise to metastability, either when one solid precipitates on the surface of another, or if the size of the solid particles is sufficiently small that surface effects become important. In either case, the solid is not in stable equilibrium with the solution. See (25) for the modern formulation of the effect of particle size on solubility. The stability of a solid may also be affected by the atmosphere in which the system is equilibrated.

Many of these phenomena require very careful, and often prolonged, equilibration for their investigation and elimination. A very general analytical method, the "wet residues" method of Schreinemakers (26), is often used to investigate the composition of solid phases in equilibrium with salt solutions. This method has been reviewed in (27), where [see also (28)] least-squares methods for evaluating the composition of the solid phase from wet residue data (or initial composition data) and solubilities are described. In principle, the same method can be used with systems of other types. Many other techniques for examination of solids, in particular X-ray, optical, and thermal analysis methods, are used in conjunction with chemical analyses (including the wet residues method).

#### Solid State Manipulation in Pharmaceuticals

(1) Polymorphism. Many drug substances may crystallize in more than one form, a phenomenon called polymorphism. The different modifications (polymorphs) arise because of the relative positions and bonding of the molecules in their crystal lattices; true polymorphs do not differ in chemical composition. Polymorphs of the same substance frequently have different physical properties such as solubility and rate of dissolution. Ultimately, the solubility of all forms will revert to that of the form with the lowest Gibbs energy; the solubility of a less-stable form will thus be an initial solubility. The rate of reversion to the most stable form is often very slow, and a form with higher Gibbs energy may exhibit its higher solubility for hours. This phenomenon may be used to advantage by choosing the polymorph with the desired solubility or rate of dissolution. Examples of polymorphism and methods of characterization have been reviewed by Haleblian (29) and Burger (30).

(ii) Crystallinity. In many cases, drug substances may occur in the solid state as amorphous or partly crystalline forms. This is a special case of polymorphism, and may result from rapid precipitation or from freeze-drying. These amorphous or partly crystalline materials are unstable relative to the crystalline form. However, reversion to the crystalline form may be slow, and the less stable forms may be used to enhance solubility and rate of dissolution (31).
(111) Choice of salt form. Many drug substances are organic salts.

(111) Choice of salt form. Many drug substances are organic salts. In most cases the drug molety is the organic cation or anion, such as a quaternary ammonium cation or a carboxylate or sulfonate anion. The counterion is frequently an inorganic ion such as sodium or chloride. It is possible to obtain large variations in initial solubility depending on the choice of the salt form of the drug.

#### COMPILATIONS AND EVALUATIONS

The formats for the compilations and critical evaluations have been standardized for all volumes. A brief description of the data sheets has been given in the FOREWORD; additional explanation is given below. Guide to the Compilations

The format used for the compilations is, for the most part, selfexplanatory. The details presented below are those which are not found in the FOREWORD or which are not self-evident.

Components. Each component is listed according to IUPAC or Chemical Abstracts (CA) name and CA Registry Number. The formula is given either in terms of the IUPAC or Hill (32) system and the choice of formula is governed by what is usual for most current users: i.e., IUPAC for inorganic compounds, and Hill system for organic compounds. Components are ordered according to:

(a) saturating components;

(b) non-saturating components in alphanumerical order;(c) solvents in alphanumerical order.

The saturating components are arranged in order according to a 18-column periodic table with two additional rows:

Columns 1 and 2: H, alkalı elements, ammonium, alkaline earth elements 3 to 12: transition elements

- 13 to 17: boron, carbon, nitrogen groups; chalcogenides, halogens 18: noble gases

Row 1: Ce to Lu Row 2: Th to the end of the known elements, in order of atomic number.

Salt hydrates are generally not considered to be saturating components since most solubilities are expressed in terms of the anhydrous salt. The existence of hydrates or solvates is carefully noted in the text, and CA Registry Numbers are given where available, usually in the critical evaluation. Mineralogical names are also quoted, along with their CA Registry Numbers, again usually in the critical evaluation.

Original Measurements. References are abbreviated in the forms given by Chemical Abstracts Service Source Index (CASSI). Names originally in other than Roman alphabets are given as transliterated by Chemical Abstracts.

Experimental Values. Data are reported in the units used in the original publication, with the exception that modern names for units and quantities are used; e.g., mass per cent for weight per cent; mol dm<sup>-3</sup> for molar; etc. Both mass and molar values are given. Usually, only one type of value (e.g., mass per cent) is found in the original paper, and the compiler has added the other type of value (e.g., mole per cent) from computer calculations based on 1983 atomic weights (33).

Errors in calculations and fitting equations in original papers have been noted and corrected, by computer calculations where necessary.

Source and Purity of Materials. Abbreviations used in Method. Chemical Abstracts are often used here to save space.

Estimated Error. If these data were omitted by the original authors, and if relevant information is available, the compilers have attempted to estimate errors from the internal consistency of data and type of apparatus used. Methods used by the compilers for estimating and and reporting errors are based on the papers by Ku and Eisenhart (34).

Comments and/or Additional Data. Many compilations include this section which provides short comments relevant to the general nature of the work or additional experimental and thermodynamic data which are judged by the compiler to be of value to the reader.

References. See the above description for Original Measurements.

Guide to the Evaluations

The evaluator's task is to check whether the compiled data are correct, to assess the reliability and quality of the data, to estimate errors where necessary, and to recommend "best" values. The evaluation takes the form of a summary in which all the data supplied by the compiler have been critically reviewed. A brief description of the evaluation sheets is given below.

Components. See the description for the Compilations.

Evaluator. Name and date up to which the literature was checked.

Critical Evaluation

(a) Critical text. The evaluator produces text evaluating all the published data for each given system. Thus, in this section the evaluator reviews the merits or shortcomings of the various data. Only published data are considered; even published data can be considered only if the experimental data permit an assessment of reliability.

(b) Fitting equations. If the use of a smoothing equation is justifiable the evaluator may provide an equation representing the solubility as a function of the variables reported on all the compilation sheets.

(c) Graphical summary. In addition to (b) above, graphical summaries are often given.

(d) Recommended values. Data are recommended if the results of at least two independent groups are available and they are in good agreement, and if the evaluator has no doubt as to the adequacy and reliability of the applied experimental and computational procedures. Data are considered as tentative if only one set of measurements is available, or if the evaluator considers some aspect of the computational or experimental method as mildly undesirable but estimates that it should cause only minor errors. Data are considered as doubtful if the evaluator considers some aspect of the computational or experimental method as undesirable but still considers the data to have some value in those instances where the order of magnitude of the solubility is needed. Data determined by an inadequate method or under ill-defined conditions are rejected. However references to these data are included in the evaluation together with a comment by the evaluator as to the reason for their rejection.

(e) References. All pertinent references are given here. Refeto those data which, by virtue of their poor precision, have been References rejected and not compiled are also listed in this section. (f) Units. While the original data may be reported in the units

used by the investigators, the final recommended values are reported in S.I. units (1, 35) when the data can be accurately converted.

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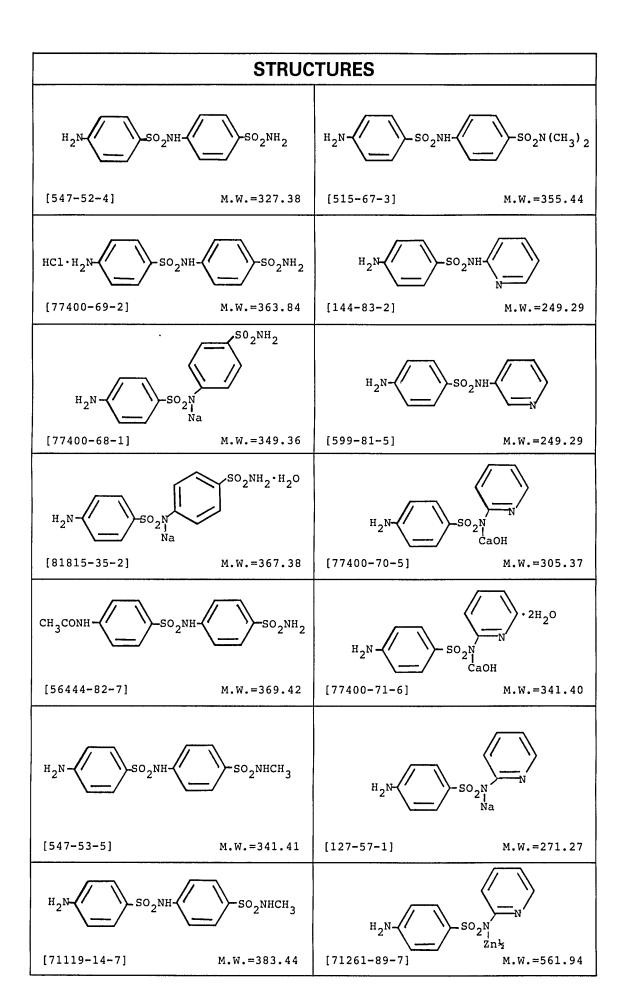
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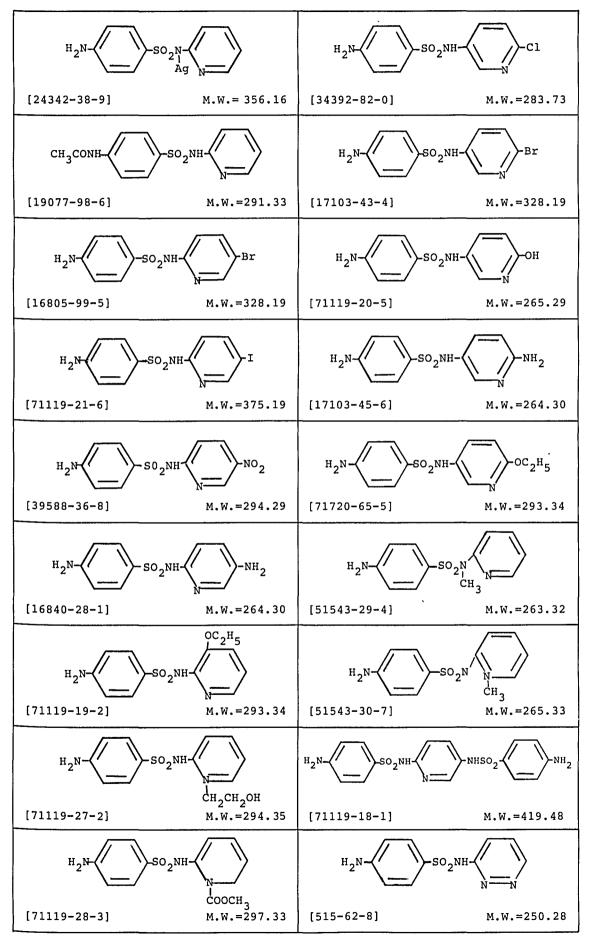
September, 1986

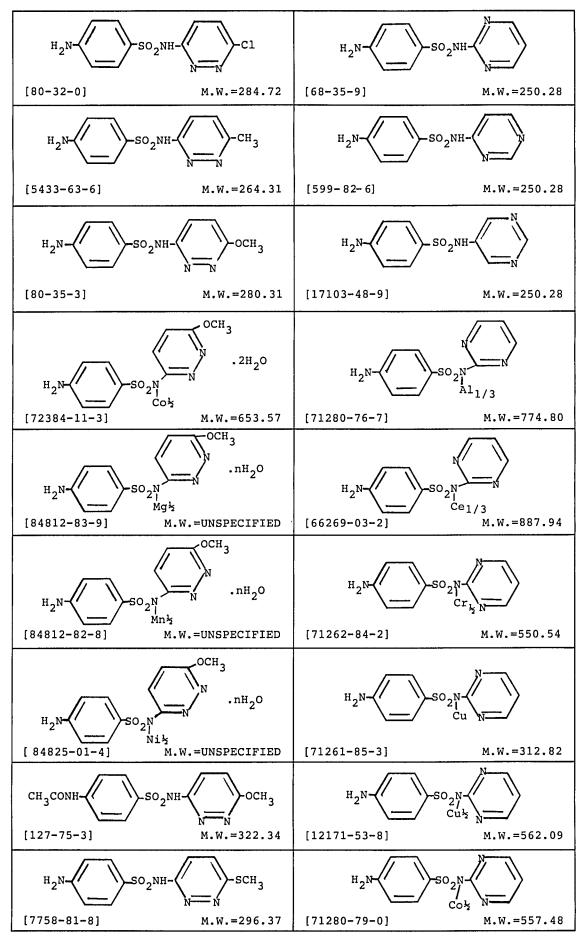
- R. Cohen-Adad,
  - Villeurbanne, France
- S. Lindenbaum, Lawrence, Kansas, U.S.A.
- J.W. Lorimer, London, Ontario, Canada
- A.N. Paruta, Kingston, R.I., U.S.A.
- R. Piekos, Gdansk, Poland
- M. Salomon, Fair Haven, New Jersey, U.S.A.

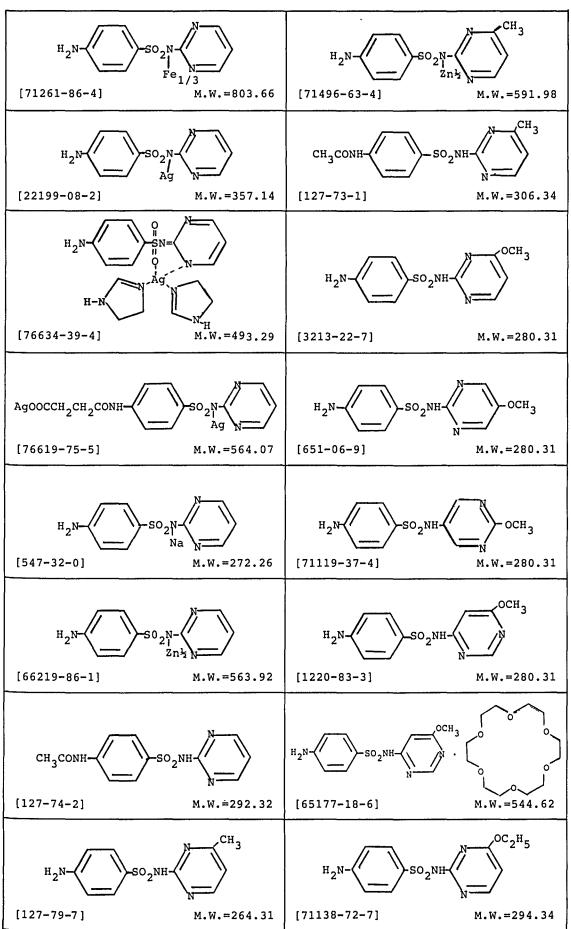
|    | Čonv                              | Table :<br>ities Used as Mea<br>ersion Table for<br>ontaining Solven | asures of Solub<br>2-Component Sys | stems                                     |
|----|-----------------------------------|--|------------------------------------|---|
|    | mole fraction<br>XB =             | mass fraction<br>wg =  | molality<br>m <sub>B</sub> =       | concentration<br>c <sub>B</sub> =         |
| хB | ×B 1-M                            | $\frac{1}{A(1 - 1/x_B)/M_B}$   | $\frac{1}{M_A(1/x_B - 1)}$         | $\frac{\rho}{M_{B} + M_{A}(1/x_{B} - 1)}$ |
| wB | $\frac{1}{1 + M_B(1/w_B - 1)}$    | wB   | $\frac{1}{M_B(1/w_B - 1)}$         | pw <sub>B</sub> /M <sub>B</sub>           |
| mB | $\frac{1}{1 + 1/m_B M_A}$         | $\frac{1}{1 + 1/M_B m_B}$  | mB                                 | $\frac{\rho}{M_B + 1/m_B}$                |
| cB | $\frac{1}{1 + (\rho/c_B - M_B)/}$ | M <sub>A</sub> M <sub>B</sub> c <sub>B</sub> ∕p                      | $\frac{1}{\rho/c_B - M_B}$         | c <sub>B</sub>                            |
|    | l                                 |  |                                    |   |

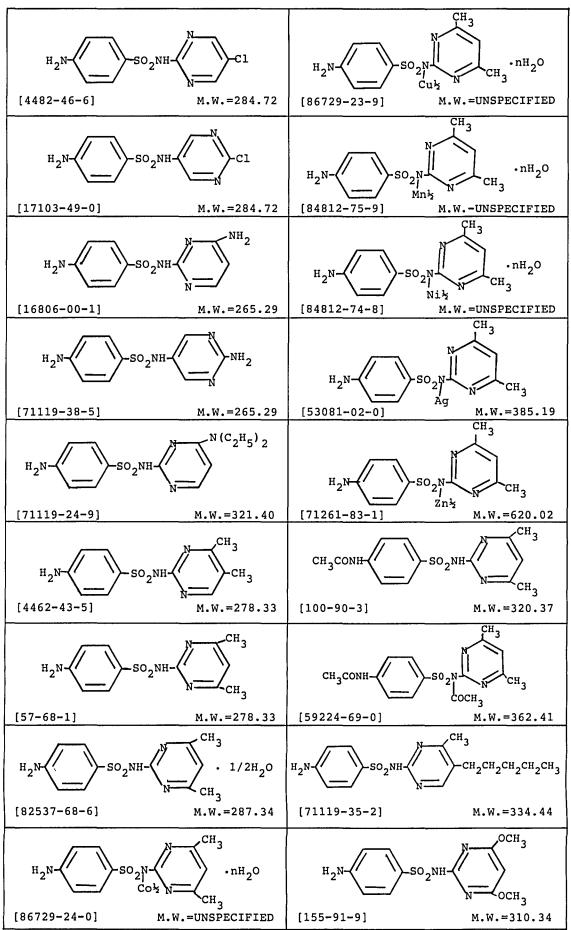
 $\rho$  = density of solution  $M_A$ ,  $M_B$  = molar masses of solvent, solute Formulas are given in forms suitable for rapid computation; all calculations should be made using SI base units. xxiii

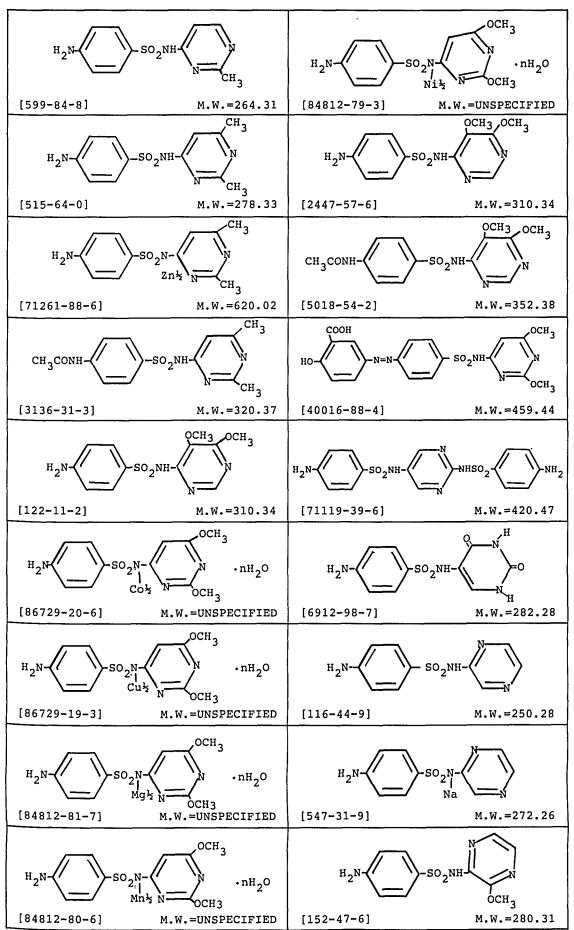


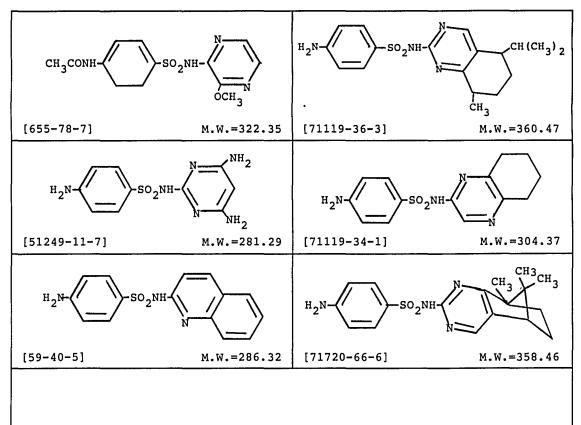












| COMPONENTS:   | ORIGINAL MEASUREMENTS:                            |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-4-  | Becher, R. ; Leya, S. Experientia                 |
| [(aminosulfony1)pheny1]-; (disulfan)  | 1946, 2, 459-60.                                  |
| C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> ; [547-52-4] | <u></u>   |
|   |   |
| (2) Water; H <sub>2</sub> O; [7732-18-5]  |   |
|   |   |
| VARIABLES:  | PREPARED BY:                                      |
| One temperature: 18-19 <sup>0</sup> C   | R. Piekos   |
|   |   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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|   | '   |
| Solubility of 4-amino-N-4-[(aminosulf   | onvi)nhenvi]henzeneeulfonemide in                 |
|   |   |
| water at room temperature (18-19 <sup>0</sup> C) i  | s 30 mg% ( 9.2 x $10^{-4}$ mol dm <sup>-3</sup> , |
| compiler ).   |   |
| compiler ):   |   |
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| AUXILIARY   | INFORMATION                                       |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                   |
| After standing for more than two days the   | Nothing specified.                                |
| soln of the sulfonamide in water was filtered   |   |
| soin of the sufformide in water was fiftered  |   |
| and the sulfonamide was assayed in the fil-   |   |
|   |   |
| trate colorimetrically by the method of Druey   |   |
| and Oesterheld (1).   |   |
|   |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                                  |
|   | Nothing specified.                                |
|   |   |
|   |   |
|   | REFERENCES:                                       |
|   | 1. Druey, J.; Oesterheld, G.                      |
|   | Helv. Chim. Acta. <u>1942</u> , 25, 753.          |
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| CONDONEDITC -   | ORIGINAL MEASUREMENTS:                         |
|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-4-                                       |  |
| [(aminosulfonyl)phenyl]-;(disulfan)   | Becher, R.; Leya, S. Experientia               |
| C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> ; [547-52-4] | <u>1946,</u> 2, 459-60.                        |
| (2) Sodium chloride; NaCl; [7647-14-5]  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
|   |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 18-19 <sup>0</sup> C   | R. Piekos                                      |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-4-[(aminosulfo  | nyl)phenyl]benzenesulfonamide in a             |
| 5% NaCl solution at room temperature (  | $18-19^{\circ}C$ ) is 28 mg% ( 8.6 x $10^{-4}$ |
| mol dm <sup>-3</sup> , compiler ).  |  |
| mol dm <sup>°</sup> , compiler ).   |  |
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| AUXILIARY   | INFORMATION                                    |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                |
|   |  |
| After standing for more than two days the   | Nothing specified.                             |
| soln of the sulfonamide was filtered and  |  |
| the sulfonamide was assayed in the filtrate   |  |
| colorimetrically by the method of Druey   |  |
| and Oesterheld (1).   |  |
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|   | ESTIMATED ERROR:                               |
|   | Nothing specified.                             |
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|   | REFERENCES:                                    |
|   | 1. Druey, J.; Oesterheld, G.                   |
|   | Helv. Chim. Acta <u>1942</u> , 25, 753.        |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                  |
|--|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-4-<br/>[(aminosulfony1)pheny1]- (disulfan);<br/>C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>0<sub>4</sub>S<sub>2</sub>; [547-52-4]</pre> | Becher, R.; Leya, S. Experientia<br>1946, 2, 459-60.    |
| (2) Pectin; (C <sub>13</sub> H <sub>18</sub> O <sub>12</sub> ) <sub>n</sub> ; [9000-69-5]  | <u>1940</u> ; 23 499 000                                |
| (3) Water; $H_20$ ; [7732-18-5]  |   |
| (3) water, 1120, [7732-10-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 18-19 <sup>0</sup> C  | R. Piekos   |
| EXPERIMENTAL VALUES:   | L   |
|  |   |
| Solubility of disulfan in a 2.5% pect  |   |
| mol kg <sup>-1</sup> , compiler ), of pH about 2.6   | at room temperature ( 18-19 <sup>0</sup> C ) is         |
| 41 mg% ( 1.3 x $10^{-3}$ mol dm <sup>-3</sup> , compile  | er ).   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                         |
| The soln was allowed to stand at room temp   | A high quality apple pectin was used: the               |
| for more than 2 days. The soln was then  | rel viscosity of a 0.5% soln was 6.2, and               |
| filtered, and disulfan assayed in the fil-   | for neutralization of 1 g of the pectin,                |
| trate colorimetrically by the method of  | 1.67 cm <sup>3</sup> of a 1 mol $dm^{-3}$ NaOH soln was |
| Druey and Oesterheld (1).  | used. The source and purity of disulfan                 |
|  | and water were not specified.                           |
|  |   |
|  |   |
|  | ESTIMATED ERROR:  |
|  | Nothing specified.                                      |
|  |   |
|  | REFERENCES :  |
| 1  | 1. Druey, J.; Oesterheld, G.                            |
|  | Helv. Chim. Acta 1942, 25, 753.                         |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-4-</li> <li>[(aminosulfonyl)phenyl]-, (disulfan);</li> </ol> | Becher, R.; Leya, S. Experientia                      |
| $C_{12}H_{13}N_{3}O_{4}S_{2};$ [547-52-4]   | <u>1946</u> , 2, 459-60.                              |
| (2) Pectinic acid, sodium salt;   |   |
| $(C_{13}H_{17}NaO_{12})_n; [9049-37-0]$   |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 18-19 <sup>0</sup> C   | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| Solubility of disulfan in a 2.6% neut   | ral sodium pectinate solution                         |
|   |   |
| ( [sodium pectinate] = $6.7 \times 10^{-2}$ mol   |   |
| at room temperature ( 18—19 <sup>0</sup> C ) is 41  | . mg% ( 1.3 x 10 <sup>-3</sup> mol dm <sup>-3</sup> - |
| compiler ).   |   |
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| AUXILIARY   | INFORMATION   |
|   |   |
| METHOD/APPARATUS/PROCEDURE:<br>The soln was allowed to stand for more                               | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |
| than 2 days at room temp. The soln was then   |   |
| filtered, and sulfonamide assayed in the  |   |
|   |   |
| filtrate colorimetrically by the method of  |   |
| Druey and Oesterheld (1).   |   |
|   |   |
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|   | ESTIMATED ERROR:                                      |
|   | Nothing specified.                                    |
|   |   |
|   |   |
|   | REFERENCES:   |
|   | 1. Druey, J.; Oesterheld, G.                          |
| 1   | Helv. Chim. Acta <u>1942</u> , 25, 753.               |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                  |
|--|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-4-<br/>[(aminosulfony1)pheny1]-; (disulfan)</pre> | Becher, R.; Leya, S. Experientia        |
| $C_{12}H_{13}N_{3}O_{4}S_{2};$ [547-52-4]  | 1946, 2, 459-60.                        |
| (2) D-Glucose; $C_6H_{12}O_6$ ; [50-99-7]  |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| -  |   |
| VARIABLES:   | PREPARED BY:                            |
| 0  | R. Piekos                               |
| One temperature: 18-19 <sup>°</sup> C  | R. Flekos                               |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-4-[(aminosul   | fonyl)phenyl]benzenesulfonamide         |
| in a 10% D-glucose solution at room t  |   |
|  | emperature ( 10-13 C ) 18 30 mg%        |
| $(9.2 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler}).$                            |   |
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| AUXILIARY  | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |
| After standing for more than two days the  | Nothing specified.                      |
| soln of 4-amino-N-4-[(aminosulfonyl)phenyl]-   |   |
|  |   |
| benzenesulfonamide was filtered and the  |   |
| sulfonamide was assayed in the filtrate co-  |   |
| lorimetrically by the method of Druey and  |   |
|  |   |
| Oesterheld (1).  |   |
|  | ESTIMATED ERROR:                        |
|  |   |
|  | Nothing specified.                      |
|  |   |
|  | REFERENCES :                            |
|  |   |
|  | 1. Druey, J.; Oesterheld, G.            |
|  | Helv. Chim. Acta <u>1942</u> , 25, 753. |
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| 1  | 1                                       |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-4-<br>[(aminosulfony1)pheny1]- (disulfan);<br>C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> 0 <sub>4</sub> S <sub>2</sub> ; [547-52-4]<br>(2) 2-Propanone (acetone); C <sub>3</sub> H <sub>6</sub> 0;<br>[67-64-1]<br>VARIABLES: |                              |                        | ORIGINAL MEAS                  | ORIGINAL MEASUREMENTS:<br>Gutierrez, F. H.<br>Anales fis. quim. (Madrid) <u>1945</u> , 41<br>537-60. |                     |       |                                |
|--|------------------------------|------------------------|--------------------------------|--|---------------------|-------|--------------------------------|
|  |                              |                        | n); Anales fis                 |  |                     |       |                                |
|  |                              | mperature              |                                |  | R. Piekos           |       |                                |
| t/°C   | ÆNTAL VALU<br>G <sup>a</sup> | JES:<br>E <sup>b</sup> | x <sub>g</sub> /1 <sup>c</sup> | mol/l <sup>d</sup> acetone   | mmol/mol<br>acetone | 1:Xge | 1+X <sup>f</sup> <sub>cc</sub> |
| 0  | 49.983                       | 33.325                 | 407.161                        | 1243   | 88.7                | 2.00  | 2.46                           |
| 5  | 50.500                       | 33.554                 | 408.444                        | 1248   | 89.6                | 1.98  | 2.45                           |
| 10   | 50.998                       | 33.772                 | 409.514                        | 1251   | 90.5                | 1.96  | 2.44                           |
| 15   | 52.271                       | 34.327                 | 416.652                        | 1272   | 92.7                | 1.91  | 2.40                           |
| 20   | 53.312                       | 34.735                 | 421.805                        | 1288   | 94.6                | 1.88  | 2.37                           |
| 25   | 54.024                       | 35.076                 | 424.196                        | 1295   | 95.8                | 1.85  | 2.36                           |
| 30   | 55.934                       | 35.742                 | 435.894                        | 1331   | 99.2                | 1.81  | 2.29                           |
| 35   | 57.800                       | 36.629                 | 446.967                        | 1365   | 102.5               | 1.73  | 2.24                           |
| 40   | 60.198                       | 37.577                 | 461.959                        | 1411   | 106.8               | 1.66  | 2.16                           |
| 45   | 64.817                       | 39.326                 | 493.517                        | 1507   | 114.9               | 1.54  | 2.03                           |
| 50   | 69.244                       | 40.914                 | 523.139                        | 1597   | 122.8               | 1.47  | 1.91                           |

 ${}^{a}_{G} = \frac{p + 100}{P - p}$ , where p and P are the weights of solute and solution, resp.

 $^{b}E = \frac{G\ 100}{G\ +\ 100}$ ;  $^{c}g/1$  acetone;  $^{d}$ should be mmol/1 acetone (compiler);

 $e_g$  of acetone required to dissolve 1 g of solute; <sup>f</sup>volume (cm<sup>3</sup>) of acetone required to dissolve 1 g of solute.

| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |  |  |
|---|---|--|--|
| A special all-glass app was contructed ena-   | The source of the materials was not speci-  |  |  |
| bling the prepn of satd solns, agitation by   | fied. Pure, anhyd acetone was used. The   |  |  |
| bubbling a stream of acetone-satd N, filtra-  | absence of impurities and water was confirmed   |  |  |
| tion, and distn off the solvent without con-  | by procedures of the German Pharmacopeia VI   |  |  |
| tact with air. Two exchangeable dissoln ves-  | and Spanish Pharmacopeia VIII.  |  |  |
| sels of 15 and 8 $\mathrm{cm}^3$ working capacity were  | The purity of disulfan was not specified.   |  |  |
| used depending on the soly of solute. The   |   |  |  |
| app was immersed in a thermostat. The vols  |   |  |  |
| of acetone used were 15 or 5 cm <sup>3</sup> , and the<br>equilibration time was 2-2.5 h. The satd<br>solns were filtered, weighed and the solvent<br>was distd off, the residues were dried at<br>105°C, weighed, examd for the presence of<br>solvated acetone. | ESTIMATED ERROR:<br>Soly: measurements were repeated until 2<br>values not differing in the second<br>decimal were obtained (authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES: |  |  |

AUXILIARY INFORMATION

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|   |  |                                  |  |                               |  |   |  | -   |  |
|---|--|----------------------------------|--|-------------------------------|--|---|--|---|--|
| COMPONENTS  | S:   |                                  |  |                               | ORIGINAL MEASURE   | MENTS:  |  |   |  |
| [(am<br>ride<br>C <sub>12</sub> H<br>(2) 2-Pr   | inosulfor<br>(disulfa<br>13 <sup>N</sup> 3 <sup>0</sup> 4 <sup>S</sup> 2 | ny1)pheny<br>an-HC1);<br>HC1; [7 | -amino-N-4<br>1]-, monob<br>7400-69-2]<br>; C <sub>3</sub> H <sub>6</sub> 0; | 4-<br>nydrochlo-              |  |   |  |   |  |
| VARIABLES   |  |                                  |  |                               |  |   |  |   |  |
| Temperature   |  |                                  |  |                               | PREPARED BY:   | . Piekos  |  |   |  |
| EXPERIMEN   | TAL VALUE  | S:                               |  |                               |  |   | <u></u>  |   |  |
| t/ <sup>o</sup> C   | G <sup>a</sup>   | Ep                               | Xg/1 <sup>c</sup>  | mol/1 <sup>d</sup><br>acetone | mmol/mol<br>acetone  | 1:xg  | $1 + x_{cc}^{f}$   |   |  |
| 15  | 0.406  | 0.404                            | 3.236  | 8.89                          | 0.65   | 246.31  | 309.02   |   |  |
| 20  | 0.420  | 0.418                            | 3.323  | 9.13                          | 0.67   | 238.09  | 300.93   |   |  |
| 25  | 0.433  | 0.431                            | 3.400  | 9.34                          | 0.69   | 230.95  | 294.12   |   |  |
|   |  |                                  |  |                               |  |   | 11 · · · · · · · · · · · · · · · · · ·   |   |  |
|   |  |                                  |  | AUXILIARY                     | INFORMATION  |   |  |   |  |
| METHOD/APPARATUS/PROCEDURE:<br>A special all-glass app was constructed ena-<br>bling the prepn of satd solns, agitation by<br>bubbling a stream of acetone-satd N, filtra-<br>tion, and distn off the solvent without con-<br>tact with air. Two exchangeable dissoln ves-<br>sels of 15 and 8 cm <sup>3</sup> working capacity were<br>used depending on the soly of solute. The<br>app was immersed in a thermostat. The vols<br>of acetone used were 15 or 5 cm <sup>3</sup> , and the<br>equilibration time was 2-2.5 h. the satd<br>solns were filtered, weighed, the solvent<br>was distd off, the residues were dried at<br>$105^{\circ}$ C, weighed, and examd for the presence<br>of solvated acetone. |  |                                  |  |                               | The purity of d<br>ESTIMATED ERROR:<br>Soly: measuren<br>values m<br>decimal | he material<br>yd acetone w<br>ties and wa<br>dures of the<br>nish Pharmad<br>isulfan-HCl | s was not sy<br>was used. The<br>ter in it was<br>e German Pha<br>copeia VIII<br>was not spa<br>was not spa<br>epeated unt<br>g in the sea | he ab-<br>as con-<br>armaco-<br>ecified<br>i1 2<br>cond |  |
|   |  |                                  |  |                               |  |   |  |   |  |

| [(am:<br>salt<br>[774)  | Inosulfon<br>(Na disu<br>D0-68-1]<br>Opanone (<br>54-1]<br>Temper | lfan); C <sub>1</sub><br>acetone);<br>ature | -, monosod<br>2 <sup>H</sup> 12 <sup>N</sup> 3 <sup>NaO</sup> 4 <sup>S</sup> | ium Gut<br>2; And<br>537      | NAL MEASUREMENT<br>tierrez, F. H.<br>Ules fis. quin<br>7-60.<br>RED BY:<br>R. Pie   | n. (Madrid   | ?) <u>1945</u> , 41,   |
|---|---|---|--|-------------------------------|---|--|--|
| t/ <sup>o</sup> C   | G <sup>a</sup>  | Ep  | x <sub>g</sub> /1 <sup>c</sup>   | mol/l <sup>d</sup><br>acetone | mmol/mol<br>acetone   | 1:xg   | $1 + x_{cc}^{f}$   |
| 0   | 0.144   | 0.144                                       | 1.173  | 3.3                           | 0.24  | 694.44   | 852.52   |
| 10  | 0.161   | 0.161                                       | 1.293  | 3.7                           | 0.26  | 621.12   | 773.39   |
| 20  | 0.174   | 0.174                                       | 1.377  | 3.9                           | 0.29  | 574.71   | 726.21   |
| 30  | 0.191   | 0.190                                       | 1.488  | 4.2                           | 0.32  | 523.56   | 672.04   |
| 40  | 0.206   | 0.205                                       | 1.581  | 4.5                           | 0.34  | 485.43   | 632.51   |
| 50  | 0.220   | 0.219                                       | 1.655  | 4.7                           | 0.36  | 454.54   | 604.24   |
| <sup>e</sup> g of   | acetone   | required t                                  |  | l g of solut                  | nol/l acetone (d<br>re; <sup>f</sup> volume (d  |  | tone   |
|   |   |   | AUXI   | LIARY INFOR                   | MATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:<br>A special all-glass app was contructed ena-<br>bling the prepn of satd solns, agitation by<br>bubbling a stream of acetone-satd N, filtra-<br>tion, and distn off the solvent without con-<br>tact with air. Two exchangeable dissoln ves<br>sels of 15 and 8 cm <sup>3</sup> working capacity were<br>used depending on the soly of solute. The<br>app was immersed in a thermostat. The vols<br>of acetone used were 15 or 5 cm <sup>3</sup> , and the<br>equilibration time was 2-2.5 h. The satd<br>solns were filtered, weighed, the solvent<br>was distd off, the residues were dried at<br>105°C, weighed, and examd for the presence<br>of solvated acetone. |   |   |  |                               | E AND PURITY OF<br>source of the m<br>l. Pure, anhyd<br>ence of impurit:<br>hed by procedure<br>a VI and Spanish<br>purity of Na di<br>MATED ERROR:<br>: measurements<br>values not d | acetone wa<br>acetone wa<br>ies and wat<br>es of the G<br>n Pharmacop<br>Isulfan was<br>were repea | as not speci-<br>s used. The<br>ser was con-<br>serman Pharmacc<br>beia VIII.<br>a not specified<br>ated until 2 |

,

| AVD AVENUMA  |   |  |  |  |  |
|--|---|--|--|--|--|
| <pre>COMPONENTS: 1) Benzenesulfonamide, 4-amino-N-[4-    (aminosulfonyl)phenyl]-,monosodium salt    monohydrate (Na disulfan monohydrate);    C<sub>12</sub>H<sub>12</sub>N<sub>3</sub>Na0<sub>4</sub>S<sub>2</sub>·H<sub>2</sub>0; [81815-35-2]</pre> | ORIGINAL MEASUREMENTS:<br>Crossley, M. L.; Northey, E. H.;<br>Hultquist, M. E.<br>J. Am. Chem. Soc. <u>1938</u> , 60, 2222-4. |  |  |  |  |
| 2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |  |  |  |
| VARIABLES:   | PREPARED BY:  |  |  |  |  |
| Temperature  | R. Piekos   |  |  |  |  |
| EXPERIMENTAL VALUES:   |   |  |  |  |  |
|  |   |  |  |  |  |
| 6-1-1  | 414   |  |  |  |  |
| + / <sup>0</sup> C   | mol dm <sup>-3 a</sup>  |  |  |  |  |
| 10 9.6   | 0.26  |  |  |  |  |
| 37 20.0  | 0.54  |  |  |  |  |
|  |   |  |  |  |  |
| <sup>a</sup> Calculated by compi   | ler   |  |  |  |  |
|  |   |  |  |  |  |
|  |   |  |  |  |  |
|  |   |  |  |  |  |
|  | Y INFORMATION   |  |  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |  |  |  |  |
| Nothing specified.   | The Na disulfan monohydrate was prepd by  |  |  |  |  |
| ofference  | the authors and purified by recrystn from   |  |  |  |  |
|  | concd aq soln with use of activated char-   |  |  |  |  |
|  | coal. Analysis - calcd 6.28% Na, found  |  |  |  |  |
|  | 6.35% Na. Assay by nitrite 100.2%   |  |  |  |  |
|  | Purity of the water was not specified.  |  |  |  |  |
|  | ESTIMATED ERROR:  |  |  |  |  |
|  | Nothing specified.  |  |  |  |  |
|  | REFERENCES :  |  |  |  |  |
|  |   |  |  |  |  |
|  |   |  |  |  |  |
|  |   |  |  |  |  |

| <pre>COMPONENTS:<br/>(1) Acetamide, [4-[[[4-(aminosulfony1)pheny1]<br/>-amino]sulfony1]pheny1]- (acety1 disulf-<br/>anilamide); C<sub>14</sub>H<sub>14</sub>N<sub>3</sub>0<sub>5</sub>S<sub>2</sub>; [56444-82-7]<br/>(2) 2-Propanone (acetone); C<sub>3</sub>H<sub>6</sub>0;<br/>[67-64-1]</pre> |   |                        |   |             |         | L MEASUREMENT<br>rrez, F. H.<br>s fis. quim.<br>0.    |                | ) <u>1945</u> , <i>41</i> ,                   |  |
|---|---|------------------------|---|-------------|---------|---|----------------|---|--|
| VARIABLES   | :   |                        |   |             | PREPARI | ED BY:  |                | · · · · · · · · · · · · · · · · · · ·         |  |
|   | Temp  | erature                |   |             |         | R. Piel   | kos            |   |  |
| EXPERIMEN<br>t/ <sup>o</sup> C  | TAL VALUE   |                        | x <sub>g</sub> /1 <sup>c</sup>                | mol<br>acet |         | mmol/mol<br>acetone                                   | 1:Xg           | $1 + X_{cc}^{f}$                              |  |
|   |   |                        |   |             |         |   |                |   |  |
| 0   | 1.271   | 1.255                  | 10.354  | 28.         |         | 2.0   | 78.52          | 96.58   |  |
| 5   | 1.402   | 1.382                  | 11.339  | 30.         |         | 2.2   | 71.32          | 88.19   |  |
| 10  | 1.608   | 1.563                  | 12.912  | 34.         |         | 2.5   | 62.19          | 77.45   |  |
| 15  | 1.687   | 1.659                  | 13.457  | 36.         |         | 2.7   | 59.28          | 74.32<br>72.26                                |  |
| 20  | 1.749   | 1.719                  | 13.838  | 37.         |         | 2.8   | 55.75          |   |  |
| 25  | 1.984   | 1.945                  | 15.578  | 42.         |         | 3.1   | 50.40          | 64.19<br>57.44                                |  |
| 30  | 2.234   | 2.185                  | 17.410  | 47.         |         | 3.5   | 44.76<br>39.76 | 51.36   |  |
| 35  | 2.515   | 2.453                  | 19.448  | 52.<br>59.  |         | 3.9<br>4.5  | 35.03          | 45.65   |  |
| 40  | 2.854   | 2.775                  | 21.902  | 59.<br>66.  |         | 4.J<br>5.1  | 30.77          | 40.41   |  |
| 45  | 3.250   | 3.138                  | 24.746<br>27.795                              | 75.         |         | 5.8   | 25.55          | 39.13   |  |
| 50  | 3.679   | 3.548                  | 21.195  | 13.         | 2       | 5.0   | 23.33          | 57.15   |  |
| <sup>e</sup> g of a   | cetone re   |                        | tone; <sup>d</sup> shou<br>dissolve l<br>ute. |             |         | (compiler).<br><sup>f</sup> volume (cm <sup>3</sup> ) | of aceton      | e required                                    |  |
|   |   |                        | AUX   | (ILIARY     | INFORMA | TION  | <del>.</del>   |   |  |
| METHOD /AP  | PARATUS /   | PROCEDURE :            |   |             | SOURCE  | AND PURITY OF   | MATERIALS      |   |  |
|   |   |                        | as construct                                  | ed ena-     |         |   |                |   |  |
| •   | -   |                        | olns, agita                                   |             |         |   |                |   |  |
|   |   |                        | one-satd N,                                   |             |         |   |                |   |  |
|   | -   |                        | olvent with                                   |             |         | ocedures of th  | e German F     | harmacopeia VI                                |  |
| tact wi   | th air.   | Two excha              | ngeable dis                                   | soln        | and Sp  | anish Pharmac   | opeia VIII     | •   |  |
| vessels   | of 15 ar  | nd 8 cm <sup>3</sup> w | orking capa                                   | city        | The pu  | irity of the s  | olute was      | not specified.                                |  |
| were us   | ed depend   | ling on th             | e soly of s                                   | olute.      |         |   |                |   |  |
| The app   | was imm   | nersed in              | a thermosta                                   | t. The      |         |   |                |   |  |
| the equ   | vols of acetone used were 15 or 5 cm <sup>3</sup> , and<br>the equilibration time was 2-2.5 h. The<br>satd solns were filtered, weighed, the sol- |                        |   |             |         |   | ering in t     | ated until 2 va-<br>the second deci-<br>nor). |  |
| vent wa   | s distd c   | off, the r             | esidues wer                                   | e dried     |         | ±0.1°C (auth  | or).           |   |  |
| at 105 <sup>0</sup>   | C, weighe   | d, and ex              | amd for the                                   | pre-        | REFERE  | NCES:   |                |   |  |
| sence o   | f solvate   | ed acetone             | •   |             |         |   |                |   |  |
|   |   |                        |   |             |         |   |                |   |  |
|   |   |                        |   |             |         |   |                |   |  |
|   |   |                        |   |             |         |   |                |   |  |
|   |   |                        |   |             |         |   |                |   |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-[4-<br>[(methylamino)sulfonyl]phenyl]- (Neo-                        | Krüger- Thiemer, E.                                   |
| uliron); $C_{13}H_{15}N_{3}O_{4}S_{2}$ ; [547-53-5]   | Arch. Dermatol. Syphilis 1942, 183,                   |
| (2) Phosphoric acid, monopotassium salt;  | 90-116.   |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   | <i>yo</i> 1101  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: ca 20°C; one pH: 4.37  | R. Piekos   |
| one temperature: ca 20 C; one pr: 4.57  | R. FIEROS   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
|   |   |
|   |   |
|   |   |
|   |   |
|   |   |
| Solubility of Neo-uliron in a 0.735M (1   | <b>- -</b>  |
| room temperature (about 20 <sup>0</sup> C), is 0.015  | 7 g% (4.60 x $10^{-4}$ mol dm <sup>-3</sup> solution, |
| compiler).  |   |
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|   |   |
| AUXILIARY   | INFORMATION   |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                       |
| Neo-uliron (0.5 g) was dissolved in 10 cm <sup>3</sup>  | Neo-uliron was the product manufd by "Bayer".         |
|   | The source and purity of the remaining ma-            |
| of the 0.735N (10%) $KH_2PO_4$ soln, shaken for 2 h, and filtered. A 1-cm <sup>3</sup> aliquot of the |   |
|   | terials were not specified.                           |
| filtrate was then withdrawn, cooled, acidi-   |   |
| fied with 2N HCl, and the sulfonamide con-  |   |
| tent was detd colorimetrically by the method  |   |
| of Marshall modified by Kimmig (1) using an   |   |
| Authenrieth colorimeter. The pH was mea-  |   |
| sured on an ultraionograph using a glass  | ESTIMATED ERROR:<br>Soly: precision ±5% (author).     |
| electrode.  | Temp: not specified.                                  |
|   | pH : ±0.05 pH unit (author).                          |
|   |   |
|   | REFERENCES:   |
|   | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> ,           |
|   | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.            |
|   |   |
|   |   |
|   |   |

| 12   |  |
|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-[4-   | ORIGINAL MEASUREMENTS:                               |
| [(methylamino)sulfonyl]phenyl]- (Neo-  | Krllger-Thiemer, E.                                  |
| uliron); C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> ; [547-53-5]           | Arch. Dermatol. Syphilis <u>1942</u> , 183, 90-116.  |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                        | 90-110.  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: ca 20 <sup>0</sup> C; one pH: 8.74  | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| Solubility of Neo-uliron in a 0.705M (<br>room temperature (about 20 <sup>0</sup> C) is 0.130<br>compiler ). |  |
|  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                      |
| Neo-uliron (0.5 g) was dissolved in 10 cm <sup>3</sup>   | Neo-uliron was the product manufd by "Bayer".        |
| of the 0.705M (10%) $Na_2HPO_4$ soln, shaken for   | The source and purity of the remaining ma-           |
| 2 h, and filtered. A 1-cm <sup>3</sup> aliquot of the  | terials were not specified.                          |
| filtrate was then withdrawn, cooled, acidi-  |  |
| fied with 2N HCl, and the sulfonamide con-   |  |
| tent was detd colorimetrically by the method   |  |
| of Marshall modified by Kimmig (1) using an  |  |
| Authenrieth colorimeter. The pH was measur-  |  |
| ed on an ultraionograph using a glass elec-  | ESTIMATED ERROR:                                     |
| trode.   | Soly: precision ±5% (author).                        |
|  | Temp: not specified.<br>pH : ±0.05 pH unit (author). |
|  | REFERENCES :   |
|  | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> ,          |
|  | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.           |

| OMPONENTS:   |        | ORIGINAL  | MEASUREMEN  | ITS:            |                        |      |
|--|--------|-----------|---|-----------------|------------------------|------|
| .) Benzenesulfonamide, 4-amino-N-[4-   |        | Krüger    | -Thiemer,   | Е.              |                        |      |
| [(methylamino)sulfonyl]phenyl]-<br>uliron); C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>4</sub> S <sub>2</sub> ; [547-53                   |        |           | Dermatol.   |                 | s 1942.                | 183, |
| <ul> <li>Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>   | 90-116 |           | Syptem  | <u> </u>        | 1009                   |      |
| <ul> <li>B) Phosphoric acid, monopotassium s<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> <li>b) Water; H<sub>2</sub>O; [7732-18-5]</li> </ul> | alt;   |           |   |                 |                        |      |
| ARIABLES:  |        | PREPARED  | BY:   |                 |                        |      |
| Temperature, pH  |        |           | R. Pi   | ekos            |                        |      |
| XPERIMENTAL VALUES:  |        |           |   |                 |                        |      |
|  |        |           |   | A 1 1 1 1 1 1 . |                        |      |
| Composition of 1/15M phosphate   |        |           |   | Solubilit       | У                      |      |
| •  | pH     | Room temp | ) (ca 20 <sup>0</sup> C)  |                 | у<br>37 <sup>0</sup> С |      |
| •  | рН     | g% 10     | o (ca 20 <sup>o</sup> C)<br>,4 mol dm <sup>-3</sup><br>olution <sup>a</sup> |                 |                        |      |

| 1.0  | 99.0 | 0.91               | 4.944 | 0.028 | 8.20  | -     | -     |  |
|------|------|--------------------|-------|-------|-------|-------|-------|--|
| 10.0 | 90.0 | 0.91               | 5.906 | 0.025 | 7.32  | 0.046 | 13.47 |  |
| 61.1 | 38.9 | 0.93               | 7.005 | 0.027 | 7.91  | 0.058 | 16.99 |  |
| 9.5  | 0.5  | 0.733 <sup>b</sup> | 7.51  | 0.032 | 9.37  | -     | -     |  |
| 94.7 | 5.3  | 0.95               | 8.018 | 0.078 | 22.85 | -     | -     |  |
|      |      |                    |       |       |       |       |       |  |

<sup>a</sup>Calculated by compiler

<sup>b</sup>Molar content; 10% buffer solution

### AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: Neo-uliron (0.5 g ) was dissolved in 10 cm<sup>3</sup> Neo-uliron was the product manufd by "Bayer". of a buffer soln, shaken for 2 h at  $20^{\circ}C$ (or left for 48 h at 37°C), and filtered at respective temp. A 1-cm<sup>3</sup> aliquot of the filtrate was then withdrawn, cooled (dild for expts at  $37^{\circ}$ C), acidified with 1 cm<sup>3</sup> of 2N HCl and the sulfonamide content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

| The source and purity of the remaining | ma- |
|--|-----|
| terials were not specified.            |     |
|  |     |
|  |     |
|  |     |
|  |     |
|  |     |
| ESTIMATED ERROR:                       |     |
| Soly: precision: ±5% (author).         |     |
| Temp: not specified.                   |     |
| pH : ±0.05 pH unit (author).           |     |
| REFERENCES:                            |     |
| 1                                      |     |

1. Kimmig, J. Arch. Dermatol. 1938, 176, 722; Erg. Hyg. 1941, 24, 398.

| COMPONENT   | S:<br>enesulfona                                 | mide, 4-am                        | ino-N-[4-                              | ORIGINAL                             | MEASUREMENTS:               |  |                        |                  |
|---|--|-----------------------------------|--|--------------------------------------|-----------------------------|--|------------------------|------------------|
|   | thylamino):                                      |                                   |  | Gutie                                | errez, F. H.                |  |                        |                  |
|   | 15 <sup>N</sup> 3 <sup>0</sup> 4 <sup>S</sup> 2; |                                   |  | Anales fis. quim. (Madrid) 1945, 41, |                             |  |                        |                  |
| (2) 2-Propanone (acetone); C <sub>3</sub> H <sub>6</sub> 0; |  |                                   |  |                                      | 537-6                       |  |                        |                  |
|   | 64-1]  | cetone);                          | C3H60;                                 | !                                    |                             |  |                        |                  |
| ARIABLES  | 5:   | <u> </u>                          |  | PREPAREI                             | D BY:                       |  |                        |                  |
|   | Temper   | ature                             |  |                                      |                             | R. Piek  | os                     |                  |
| XPERIMEN  | TAL VALUES                                       | :                                 |  |                                      |                             |  |                        |                  |
| t/°C  | G <sup>a</sup>                                   | E <sup>b</sup>                    | X <sub>g</sub> /1 <sup>c</sup>         |                                      | o1/1 <sup>d</sup><br>cetone | mmo1/mol<br>acetone  | l:Xg                   | $1 + X_{cc}^{f}$ |
| 0   | 17.565   | 14.940                            | 143,084                                | 41                                   | .9.1                        | 29.80  | 5.79                   | 6.98             |
| 5   | 18.507   | 15.617                            | 149,685                                | 43                                   | 38.4                        | 31.41  | 5.40                   | 6.67             |
| 10  | 19.309   | 16.185                            | 154.530                                | 45                                   | 52.6                        | 32.84  | 5.17                   | 6.47             |
| 15  | 20.062   | 16.709                            | 159.914                                | 46                                   | 58.4                        | 34.12  | 4.98                   | 6.25             |
| 20  | 22.107   | 18.104                            | 174.911                                | 51                                   | 2.3                         | 37.60  | 4.52                   | 5.72             |
| 25  | 23.202   | 18.881                            | 182.182                                | 53                                   | 33.6                        | 39.46  | 4.32                   | 5.49             |
| 30  | 25.474   | 20.302                            | 198.507                                | 58                                   | 30.5                        | 43.33  | 3.92                   | 5.04             |
| 35  | 28.002   | 21.876                            | 216.539                                | 63                                   | 34.3                        | 47.63  | 3.55                   | 4.52             |
| 40  | 30.735   | 23.509                            | 235.887                                | 69                                   | 0.9                         | 52.28  | 3.25                   | 4.24             |
| 45  | 37.109   | 27.065                            | 282.631                                | 82                                   | 27.8                        | 63.12  | 2.69                   | 3.54             |
| 50  | 47.626   | 32.261                            | 359.814                                | 105                                  | 3.9                         | 82.71  | 2.10                   | 2.78             |
| <sup>b</sup> E =<br>eg                                      | <u>G 100</u><br>G + 100<br>of acetone            | _; <sup>C</sup> g/l a<br>required | cetone; <sup>d</sup> si<br>to dissolve | hould<br>lgc                         | be mmol/                    | olute and solut<br>1 (compiler).<br>e; <sup>f</sup> volume (cm |                        |                  |
|   | required to                                      | o dissolve                        | 1 g of solu                            | ute.                                 |                             | <u></u>  |                        |                  |
|   |  |                                   | AUXII                                  | LIARY                                | INFORMAT                    |  |                        |                  |
|   | PARATUS/PR<br>al all-gla                         |                                   | contructed                             | ena-                                 | SOURCE A                    | AND PURITY OF M<br>irce of the mat                             | ATERIALS:<br>erials wa | s not speci-     |
| -   | -  |                                   |  |                                      | •                           | Pure, anhyd ac   |                        | -                |
| bubblin   | g a stream                                       | of aceton                         | e-satd N, f:                           | itra-                                | absence                     | of impurities  | and wate               | r was confirm    |
| tion, a   | nd distn o                                       | ff the sol                        | vent withou                            | t con-                               | ed by p                     | procedures of t  | he German              | Pharmacopeia     |
| tact wi   | th air. To                                       | wo exhange                        | able dissol                            | n                                    | VI and                      | Spanish Pharma   | copeia VI              | II.              |
| vessels   | of 15 and  | 8 cm <sup>3</sup> wor             | king capacit                           | ty                                   | The pur                     | ity of the sol   | ute was n              | ot specified.    |
| were us   | ed dependi                                       | ng on the                         | soly of solu                           | ute.                                 |                             |  |                        |                  |
| The app   | was imme   | rsed in a                         | thermostat.                            | The                                  |                             |  |                        |                  |
| vols of   | acetone u  | sed were 1                        | 5 or 5 cm <sup>3</sup> ,               | and                                  | FSTIMAT                     | ED ERROR:  |                        |                  |
| -   | ilibration                                       |                                   |  | The                                  | Soly:                       | measurements w<br>values not dif                               |                        |                  |
|   |  |                                   | eighed, the<br>idues were o            |                                      |                             | decimal were o   |                        |                  |
|   |  |                                   | d for the p                            |                                      | Temp:<br>REFEREN            | ±0.1°C (autho  | r).                    |                  |
|   | f solvated                                       |                                   | a for the h                            |                                      | NEFEREN                     | -L3;   |                        |                  |
| 20100 0   |  |                                   |  |                                      |                             |  |                        |                  |
|   |  |                                   |  |                                      |                             |  |                        |                  |
|   |  |                                   |  |                                      |                             |  |                        |                  |

|  | 1  |
|--|--|
| <pre>COMPONENTS:<br/>(1) Acetamide, N-[4-[[[4-[(methylamino)-<br/>sulfonyl]phenyl]animo]sulfonyl]phenyl]-<br/>(acetyl Neo-uliron); C<sub>15</sub>H<sub>17</sub>N<sub>3</sub>O<sub>5</sub>S<sub>2</sub>;<br/>[71119-14-7]<br/>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]<br/>(3) Water; H<sub>2</sub>O; ]7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Krüger-Thiemer, E.<br>Arch. Dermatol. Syphilis <u>1942</u> , 183,<br>90-116. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: ca 20 <sup>0</sup> C; one pH: 8.74  | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| Solubility of acetyl Neo-uliron in a 0.<br>8.74 at room temperature (about 20 <sup>0</sup> C) i<br>solution, compiler).  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;  |
| Acetyl Neo-uliron (0.5 g) was dissolved in   | Acetyl Neo-uliron (source not specified)   |
| 10 $\text{cm}^3$ of the 0.705 M (10%) $\text{Na}_2\text{HPO}_4$ soln of  | gave no coloration upon diazotization of   |
| pH 8.74, shaken for 2 h at room temp (about  | its satd soln, thus showing absence of   |
| $20^{\circ}$ C), and filtered. The filtrate was treat  | - Neo-uliron.  |
| ed with equal vol of 2N HC1, and refluxed  | The source and purity of the remaining   |
| for 15 min. After proper diln, a 1-cm <sup>3</sup> ali-  | materials were not specified.  |
| quot was withdrawn, acidified, cooled, and   |  |
| the sulfonamide content was detd colorimetri   | -  |
| cally (as Neo-uliron) by the Marshall method   | ESTIMATED ERROR:   |
| modified by Kimmig (1) using an Authenrieth  | Soly: precision ±5% (author)   |

pH : ±0.05 pH unit (author) **REFERENCES:** 

Temp: not specified

colorimeter. The pH was detd on an ultra-

ionograph using a glass electrode.

1. Kimmig, J. Arch. Dermatol. <u>1938</u>, 176, 722; Erg. Hyg. <u>1941</u>, 24, 398.

| 16  |   |
|---|---|
| <pre>16<br/>COMPONENTS:<br/>(1) Acetamide, N-[4-[[[4-[(methylamino) -<br/>sulfonyl]phenyl]amino]sulfonyl]phenyl]-<br/>(acetyl Neo-uliron); C<sub>15</sub>H<sub>17</sub>N<sub>3</sub>O<sub>5</sub>S<sub>2</sub>;<br/>[71119-14-7]<br/>(2) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]<br/>(3) Water; H<sub>2</sub>O; [7732-18-5]<br/>VARIABLES:<br/>One temperature: ca 20<sup>o</sup>; one pH: 4.37<br/>EXPERIMENTAL VALUES:<br/>Solubility of acetyl Neo-uliron in a C<br/>4.37 at room temperature (about 20<sup>o</sup>C)<br/>solution, compiler ).</pre> |   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Acetyl Neo-uliron (0.5 g) was dissolved in<br>10 cm <sup>3</sup> of the 0.735M (10%) KH <sub>2</sub> PO <sub>4</sub> soln of<br>pH 4.37, shaken for 2 h at room temp (about<br>20°C), and filtered. The filtrate was treat<br>ed with equal vol of 2N HCl, and refluxed<br>for 15 min. After proper diln, a 1-cm <sup>3</sup> ali-<br>quot was withdrawn, acidified, cooled, and<br>the sulfonamide content was detd colorimetri  | The source and purity of the remaining<br>materials were not specified.   |
| cally (as Neo-uliron) by the Marshall method<br>modified by Kimmig (1) using an Authenrieth   | ESTIMATED ERROR:<br>Soly: precision ±5% (author).<br>Temp: not specified. |

colorimeter. The pH was detd on an ultraionograph using a glass electrode. Temp: not specified. pH : ±0.05 pH unit (author). REFERENCES:

> Kimmig, J. Arch. Dermatol. <u>1938</u>, 176, 722; Erg. Hyg. <u>1941</u>, 24, 398.

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| <ol> <li>Acetamide, N-[4-[[[4-[(methylamino)-<br/>sulfony1[pheny1]amino]sulfony1]pheny1]-<br/>(acety1 Neo-uliron); C<sub>15</sub>H<sub>17</sub>N<sub>3</sub>O<sub>5</sub>S<sub>2</sub>;<br/>[71119-14-7]</li> <li>Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ol> | Krüger-Thiemer, E.<br><i>Arch. Dermatol Syphilis</i> <u>1942</u> , <i>183</i> ,<br>90-116. |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:   |
| VARIABLES:<br>Temperature, pH   | R. Piekos  |

### EXPERIMENTAL VALUES:

| Composition of 1/15M phosphate<br>buffer solutions |                                 | Composition of 1/15M phosphate |                                  | Solubility |   |        |  |
|--|---------------------------------|--------------------------------|----------------------------------|------------|---|--------|--|
|  |                                 |                                | Room temp (ca 20 <sup>0</sup> C) |            | 37 <sup>0</sup> C                             |        |  |
| Na <sub>2</sub> HPO <sub>4</sub>                   | кн <sub>2</sub> ро <sub>4</sub> | %Content                       | рН                               | g%         | 10 <sup>4</sup> mol dm <sup>-3</sup> solution | g%     | 10 <sup>4</sup> mol dm <sup>-3</sup><br>solution |
| 1.0  | 99.0                            | 0.91                           | 4.944                            | 0.0019     | 0.495   | -      | -  |
| 10.0   | 90.0                            | 0.91                           | 5.906                            | 0.0022     | 0.573   | 0.0024 | 0.625  |
| 61.1   | 38.9                            | 0.93                           | 7.005                            | 0.0038     | 0.991   | 0.0051 | 1.33   |
| 9.5  | 0.5                             | 0.733 <sup>b</sup>             | 7.51                             | 0.0040     | 1.043   | -      | -  |
| 94.7   | 5.3                             | 0.95                           | 8.018                            | 0.0128     | 3.338   | -      | -  |

<sup>a</sup>Calculated by compiler.

<sup>b</sup>Molar content; 10% buffer solution.

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
|---|---|
| Acetyl Neo-uliron (0.5 g) was dissolved in                          | Acetyl Neo-uliron (source not specified)    |
| 10 cm <sup>3</sup> of a buffer soln, shaken for 2 h at              | gave no coloration upon diazotization of    |
| 20 <sup>0</sup> C (or left for 48 h at 37 <sup>0</sup> C), filtered | its satd soln, thus showing absence of      |
| at respective temp. The filtrate was treat-                         | Neo-uliron.                                 |
| ed with equal vol of 2N HCl and refluxed                            | The source and purity of the remaining      |
| for 15 min. After proper diln, a 1 $cm^3$                           | materials were not specified.               |
| aliquot was withdrawn, cooled, and the sul-                         |   |
| fonamide content was detd colorimetrically                          |   |
| (as Neo-uliron) by the Marshall method modi-                        | ESTIMATED ERROR:                            |
| fied by Kimmig (1) using Authenrieth colori-                        | Soly: precision ±5% (author).               |
| meter. the pH was detd on an ultraiono-                             | Temp: not specified.                        |
| graph using a glass electrode.                                      | pH : ±0.05 pH unit (author).                |
|   | REFERENCES:                                 |
|   | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> , |
|   | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.  |
|   |   |
|   |   |
|   |   |

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| COMPONE  | ENTS:  |                         |                                      | -                             | ORIGINA            | L MEASUREMENTS:                    |            |                           |
|--|--|-------------------------|--------------------------------------|-------------------------------|--------------------|------------------------------------|------------|---------------------------|
| (1) Benzenesulfonamide, 4-amino-N-[4-  |  |                         | <u> </u>                             |                               |                    |                                    |            |                           |
| [(dimethylamino)sulfonyl]phenyl]-;   |  |                         |                                      | rrez, F. H.                   | <i>(</i> ), 7 • 7) |                                    |            |                           |
|  |  | 4 <sup>S</sup> 2; [515· |                                      |                               |                    | s Fis. quim.                       | (Maaria)   | <u>1945</u> , <i>41</i> , |
|  |  |                         | e); C <sub>3</sub> H <sub>6</sub> 0; |                               | 537-6              | 0.                                 |            |                           |
|  | -<br>[67-64-1]   |                         | 50                                   |                               |                    |                                    |            |                           |
| VARIAB   |  | ·····                   | <u> </u>                             |                               | PREPARE            | D BY:                              |            |                           |
|  |  | Temperat                | ture                                 |                               |                    | R. Pie                             | kos        |                           |
|  |  |                         |                                      |                               |                    |                                    |            |                           |
| EXPERT   | MENTAL VA  | LUES:                   | <u> </u>                             |                               |                    |                                    |            |                           |
| t/°C   | MENTAL VA<br>G <sup>a</sup>  | Ep                      | x <sub>g</sub> /1 <sup>c</sup>       | mol                           | L/1 <sup>d</sup>   | mmol/mol                           | 1:Xge      | $1 + x_{cc}^{f}$          |
|  |  |                         |                                      | ace                           | tone               | acetone                            |            |                           |
| 0  | 26.007   | 20.639                  | 211.853                              | 509                           | )                  | 42.5                               | 3.84       | 4.72                      |
| 5  | 27.025   | 21.275                  | 218.575                              | 615                           | 5                  | 44.1                               | 3.70       | 4.57                      |
| 10   | 28.036   | 21.897                  | 225.129                              | 633                           | 3                  | 45.8                               | 3.56       | 4.44                      |
| 15   | 29.064   | 22.519                  | 231.669                              | 654                           | ÷                  | 47.5                               | 3.44       | 4.31                      |
| 20   | 30.092   | 23.130                  | 238.072                              | 672                           | 2                  | 49.0                               | 3.32       | 4.20                      |
| 25   | 31.120   | 23.733                  | 244.354                              | 689                           | )                  | 50.9                               | 3.21       | 4.09                      |
| 30   | 31.898   | 24.214                  | 248.581                              | 701                           | L                  | 52.1                               | 3.13       | 4.92                      |
| 35   | 33.500   | 25.093                  | 259.055                              | 733                           | L                  | 54.7                               | 2.98       | 3.86                      |
| 40   | 35.705   | 26.311                  | 274.000                              | 745                           | 5                  | 58.3                               | 2.80       | 3.65                      |
| 45   | 39.169   | 28.144                  | 298.242                              | 841                           | L                  | 64.0                               | 2.55       | 3.35                      |
| 50   | 44.509   | 30.800                  | 336.265                              | 949                           | )                  | 72.7                               | 2.25       | 2.98                      |
| <sup>b</sup> E =<br>eg c   | $a_{G} = \frac{p \ 100}{P - p}$ , where p and P are the weights of<br>$b_{E} = \frac{G \ 100}{G + 100}$ ; $c_{g/1}$ acetone; $d_{should}$ be mm<br>$e_{g}$ of acetone required to dissolve 1 g of so<br>to dissolve 1 g of solute. |                         |                                      | mo1/1                         | (compiler);        |                                    | e required |                           |
|  |  |                         | AUX1                                 | ILIARY                        | INFORMA            | TION                               |            |                           |
| MERLIOD  |  | C /DDOCEDUD             |                                      |                               | · · · ·            |                                    |            |                           |
|  |  | S/PROCEDUR              | was contructed                       | d ona-                        | 1                  | AND PURITY OF M<br>ource of the ma |            |                           |
|  |  |                         | solns, agitati                       |                               |                    | Pure, anhyd a                      |            | -                         |
|  |  |                         | etone-satd N, f                      | -                             |                    | ce of impuritie                    |            |                           |
|  | 0  |                         | vent without co                      |                               |                    | procedures of                      |            |                           |
| · ·  |  |                         |                                      |                               | · ·                | d Spanish Pharm                    |            | -                         |
| with air. Two exchangeable dissoln vessels<br>of 15 and 8 cm <sup>3</sup> working capacity were used |  |                         |                                      | urity of the so               | -                  |                                    |            |                           |
|  |  | •                       |                                      |                               |                    |                                    |            |                           |
| depending on the soly of solute. The app<br>was immersed in a thermostat. The vols of                |  |                         |                                      |                               |                    |                                    |            |                           |
| acetone used were 15 or 5 cm <sup>3</sup> , and the equi-  |  |                         | ESTIMAT                              | ED ERROR:                     |                    | <u> </u>                           |            |                           |
| libration time was 2-2.5 h. The satd solns   |  |                         | Soly:                                | measurements                  | •                  |                                    |            |                           |
| were filtered, weighed, the solvent was  |  |                         |                                      | values not di<br>decimal were | -                  |                                    |            |                           |
| distd  | l off, the   | residues                | were dried at                        | 105°C,                        | Temp:              | ±0.1 <sup>0</sup> C (auth          | or).       |                           |
| weigh  | ned, and e   | examd for t             | he presence of                       | E sol-                        | REFEREN            | ICES:                              |            |                           |
| 1  | l acetone.   |                         |                                      |                               |                    |                                    |            |                           |
|  |  |                         |                                      |                               |                    |                                    |            |                           |
|  |  |                         |                                      |                               |                    |                                    |            |                           |
|  |  |                         |                                      |                               |                    |                                    |            |                           |
| 1  |  |                         |                                      |                               | 1                  |                                    |            |                           |

| COMPONENTS:<br>(1) Benzen<br>pyridi<br>C <sub>11</sub> H <sub>11</sub><br>(2) Water | esulfonamide, 4-amino-N-2-<br>nyl- (sulfapyridine); | EVALUATOR:<br>Anthony N. Paruta<br>Department of Pharmaceutics<br>University of Rhode Island<br>Kingston, Rhode Island, USA and |
|---|---|---|
| or  | s phosphate buffers                                 | Ryszard Piekos<br>Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986  |

#### CRITICAL EVALUATION:

The solubility of sulfapyridine was studied in water mainly at 310K in eleven papers (1-11) as shown in Table I.

Table I: Solubility of sulfapyridine in water at various temperatures

|           | <u> </u> | 10 <sup>3</sup> mol dm | -3 (*indicates_mol_Kg_ |
|-----------|----------|------------------------|------------------------|
| Reference | 298K     | 303K/308K              | 310K                   |
| 1         |          | -                      | 2.2                    |
| 2         | -        | 2.3(308K)              | -                      |
| 3         | -        | -                      | 1.98                   |
| 4         | -        | -                      | 1.8                    |
| 5         | -        | -                      | 8                      |
| 6         | 1.07*    | -                      | 1.95*                  |
| 7         | -        | -                      | 1.89                   |
| 8         | -        | -                      | 2.1                    |
| 9         | -        | -                      | 1.48                   |
| 10        | -        | 2.01(303K)             | -                      |
| 11        | -        | -                      | 2.09 (pH=6)            |

Lebel, Schroeder and Simesen (2) gave a value at 308K and Yamazaki et al. (10) at 303K, both values are about the right order of magnitude and in line with the other results. Kitao et al. (11) appear to have determined the solubility at 310K where the pH value is the natural pH produced by the solute in water. Neish's (9) value of  $1.48 \times 10^{-3}$ mol dm<sup>-3</sup> is too low with respect to the other values probably due to the poor control of temperature. Trefouël's (5) value is about four times greater than the apparent average. Sapozhnikova and Postovskii (7) used a one hour equilibration which is felt to be inadequate. Although the value given (7) is in line it was not taken into account in the determination of the recommended value. The remaining values (1,3,4,6,8) all determined with appropriate methods were used to calculate the simple average. The recommended value for sulfapyridine in water at 310K is 2 x  $10^{-3}$ mol dm<sup>-3</sup>.

Solubilities of sulfapyridine in aqueous buffered solutions at 293K and 310K are shown in Table II.

Table II: Solubility of sulfapyridine at various temperatures and pH values

|           |      | $10^3 \text{ mol } \text{dm}^{-3}$ |       |  |
|-----------|------|------------------------------------|-------|--|
| Reference | pH   | _293K                              | 310K  |  |
| 12        | 5.90 | 2.808                              | 4.252 |  |
| 13        | 6.0  | 2.6                                | -     |  |
| 14        | 5.9  | -                                  | 2.4   |  |
| 12        | 7.0  | 2.848                              | 4.252 |  |
| 13        | 7.0  | 2.7                                | -     |  |
| 14        | 7.0  | -                                  | 2.3   |  |
| 12        | 8.0  | 3.249                              | -     |  |
| 13        | 8.0  | 2.8                                | -     |  |

The values given by Langecker (13) appear to be quite low, it should be noted that the solution was boiled for one hour and then stored for an unspecified period. It is possible that the low value's are due to decomposition. Krüger-Thiermer (11), and Pulver and Suter (12) are in reasonable agreement. Both used 0.067M mol dm<sup>-3</sup> phosphate buffer solutions. At pH 6,7 and 8 the recommended values are at 293K, 2.7 x  $10^{-3}$  mol dm<sup>-3</sup>, 2.8 x  $10^{-3}$  mol dm<sup>-3</sup> and 3.0 x  $10^{-3}$  mol dm<sup>-3</sup> respectively.

It would be of interest to compare these values with those in pure water. Dissolving sulfapyridine in water results in a near neutral solution (pH=7); and enhanced dissolution at a lower temperature, 310K to 293K, may be due to a salting-in effect. It should be noted that the buffer concentration is  $6.6 \times 10^{-3}$  mol dm<sup>-3</sup> and the solute is a fraction ( $\approx 2-3 \times 10^{-3}$  mol dm<sup>-3</sup>) of these highly soluble salts.

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20

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 Yamazaki, M.; Aoki.; Kamada, A.; Yata, N. Yakuzaigaku <u>1967</u>, 27(1), 37-40.
 Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. Chem. Pharm. Bull. <u>1973</u>, 21, 2417-26.
 Krüger-Thiemer, E. Arch. Dermatol. Syphilis <u>1942</u>, 183, 90-116.
 Pulver, R.; Suter, R. Schweiz. Med. Wochenschr. <u>1943</u>, 73(13), 403-8.
 Langecker, H. Arch. Exptl. Path. Pharmakol. <u>1943</u>, 205, 291-301.

| COMPONENTS:                                | ORIGINAL MEASUREMENTS:              |
|--|-------------------------------------|
| (1) Benzenesulfonamide, 4-amino-N-2-       | Hug, E. Rev. soc. Argentina biol.   |
| pyridinyl- (sulfapyridine);                | <u>1940,</u> 16, 662–6.             |
| $C_{11}H_{11}N_3O_2S;$ [144-83-2]          | · · · · · · · · · · · · · · · · ·   |
| (2) Water; $H_20$ ; [7732-18-5]            |                                     |
| (-/ mater, m20; [//32-10-3]                |                                     |
|  |                                     |
| VARIABLES:                                 | PREPARED BY:                        |
| One temperature: 37 <sup>°</sup> C         | R. Piekos                           |
|  |                                     |
| EXPERIMENTAL VALUES:                       |                                     |
|  |                                     |
|  |                                     |
|  |                                     |
| 1  |                                     |
| 1  |                                     |
| Solubility of sulfapyridine in water at    | 37°C te 54 mov ( 2 2 - 10-3 - 1 1-3 |
|  | το το στ μεν ( 2 2 X IV ΠΟΙ απ -    |
| solution, compiler ).                      |                                     |
|  |                                     |
|  |                                     |
|  |                                     |
|  |                                     |
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|  | INFORMATION                         |
| METHOD / APPARATUS / PROCEDURE :           | SOURCE AND PURITY OF MATERIALS:     |
| A satd soln of sulfapyridine was prepd by  | Nothing specified                   |
| heating on a water bath. The soln was then |                                     |
| cooled down to 37°C and maintained at this |                                     |
|  |                                     |
| temp for 7 days.                           |                                     |
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|  | ESTIMATED ERROR:                    |
|  | Nothing specified                   |
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|  | REFERENCES :                        |
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| Components:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-<br>pyridinyl- (sulfapyridine);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | Lebel, H.; Schroeder, E.; Simesen, M.<br><i>M. Acta Med. Scand.</i> <u>1940</u> , <i>105(4)</i> ,<br>395-410. |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 35 <sup>0</sup> C   | R. Piekos   |
| EXPERIMENTAL VALUES:   | ••••••••••••••••••••••••••••••••••••••  |
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|  |   |
| Solubility of sulfapyridine in water a   | $t^{35^{\circ}}$ is 1:1800 corresponding  |
| to 56 mg% ( 2.3 $\times 10^{-3}$ mol dm <sup>-3</sup> solut  |   |
|  | ion, compiler ).  |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| Nothing specified  | Nothing specified   |
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|  | ESTIMATED ERROR:  |
|  | Nothing specified   |
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|  | REFERENCES :  |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                          |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-                           | Roblin, R. O., Jr.; Winnek, P. S.               |
| pyridinyl- (sulfapyridine);                                    | J. Am. Chem. Soc. <u>1940</u> , 62, 1999-2002.  |
| $G_{1}^{H_{11}N_{3}O_{2}S}; [144-83-2]$                        |   |
|  |   |
| (2) Water; [7732-18-5]   |   |
| VARIABLES:   |   |
|  | PREPARED BY:                                    |
| One temperature: 37 <sup>0</sup> C                             | R. Piekos                                       |
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| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfapydridine in water                          | at 37°C is 49.5 mg/100 cm <sup>3</sup> solution |
| $(1.98 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler}).$ |   |
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|  | TNEODWATTON                                     |
|  | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:                                    | SOURCE AND PURITY OF MATERIALS:                 |
| Excess sulfonamide in water was heated and                     | Sulfapyridine, mp 190-1°C, was probably         |
| stirred on a steam bath for 30 min. The                        | prepd by the authors.                           |
| suspension was then agitated for 24 h in a                     | Purity of the water was not specified.          |
| thermostat at 37°C. A sample of the satd                       |   |
| soln was withdrawn through a glass filter,                     |   |
| dild, and analyzed by the modified Marshall                    |   |
| method (1) using a General Electric record-                    |   |
| ing spectrophotometer for comparing the                        |   |
| colors with those of the standards.                            | ESTIMATED ERROR:                                |
|  | Nothing specified                               |
|  |   |
|  | DEFEDENCIE.                                     |
|  | REFERENCES:                                     |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.         |
|  | J. Pharmacol. <u>1939</u> , 66, 4.              |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Durel, M. P.; Allinne, M.                       |
| pyridinyl- (sulfapyridine);   | Bull. Soc. Med. Hop. Paris III                  |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | <u>1941</u> , 251-9.                            |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                    |   |
| $(2)$ water, $n_2^{0}$ , $[7752-10^{-5}]$                                   |   |
| VARIABLES:  | PREPARED BY:                                    |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                       |
|   |   |
| EXPERIMENTAL VALUES:  | L   |
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| Solubility of sulfapyridine in water a                                      | t 37°C is 0.45 g/liter ( 1.8 x 10 <sup>-5</sup> |
| mol dm <sup>-3</sup> , compiler ).  |   |
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| AUXILIARY   | INFORMATION                                     |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:                 |
| A mixt of sulfapyridine and water was                                       | Source and purity of sulfapyridine were         |
| agitated for 24 hours at 37°C.  | not specified.                                  |
|   | Distilled water was used.                       |
|   | piblille water was used.                        |
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|   | ESTIMATED ERROR:                                |
|   | Nothing specified                               |
|   | woening specified                               |
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|   | REFERENCES :                                    |
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| COMPONENTS:   | OBTOTNAT AGUDDUMUMG                                 |
|---|---|
|   | ORIGINAL MEASUREMENTS:                              |
| (1) Benzenesulfonamide, 4-amino-N-2-  | Tréfouël, M.  |
| pyridinyl- (sulfapyridine);   | Bull. Acad. Med. Paris <u>1941</u> , 124,           |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | 546-54.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |   |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  | L <u></u>   |
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| Solubility of sulfapyridine in water a                                      | t 37 <sup>0</sup> C is 0.2 part per 100 parts water |
| $(8 \times 10^{-3} \text{ mol } \text{kg}^{-1} \text{ water, compiler})$    |   |
| ( 8 x 10 - mol kg - water, compiler   | )•  |
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|   | INFORMATION   |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                     |
| Sulfapyridine was diazotized, coupled with                                  | Nothing specified                                   |
| N-naphthy1-1-N-diethy1-3-propylenediamine                                   |   |
| and assayed colorimetrically.   |   |
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|   | ESTIMATED ERROR:                                    |
|   |   |
|   | Nothing specified                                   |
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|   | REFERENCES :  |
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| COMPONENTS :   |   |           | ORIGIN | AL MEASUREMENTS:  |
|  | (1) Benzenesulfonamide, 4-amino-N-2-<br>pyridinyl- (sulfapyridine); |           |        | k, W. G.; Strakosch, E. A.;<br>tan, N. I. <i>J. Lab. Clin. Med.</i><br>, <i>28</i> , 188-9. |
| (2) Water; H <sub>2</sub> 0; [7732                     |   |           |        | ,,  |
| VARIABLES:   |   |           | PREPAR | ED BY:  |
| Temperature  |   |           |        | R. Piekos   |
| EXPERIMENTAL VALUES:                                   |   |           |        | - <u> </u>  |
|  |   |           |        |   |
|  |   |           |        |   |
|  | . 10 a  |           | Solub  | ility   |
|  | t/ <sup>o</sup> C   | g/100 g v | water  | 10 <sup>3</sup> mol kg <sup>-1</sup> water <sup>a</sup>                                     |
|  | 25  | 0.0268    |        | 1.07  |
|  | 37  | 0.0486    |        | 1.95  |
|  |   |           |        |   |
|  |   | AUXILIARY | INFORM | ATION   |
| METHOD/APPARATUS/PROCEDURE:                            |   |           |        | AND PURITY OF MATERIALS:  |
| A small tinted glass cont<br>sulfapyridine in water wa |   |           |        | er source nor purity of sulfapyridine<br>pecified.  |
| ter bath thermostat for 2                              |   |           |        | ree distd water was used.   |
| soln was then filtered by                              | aspirat:  | ion       |        |   |
| through a washed and drie                              | ed asbest   | os filter |        |   |
| stick into a weighed weig                              |   |           |        |   |
| entire app was kept at th                              |   |           |        |   |
| the compd was dissolved.<br>was then detd by the meth  |   |           |        | MED EDDAD.  |
| Marshall (1), using a pho                              |   |           |        | TED ERROR:<br>not specified.  |
| meter.   |   |           | Temp:  | ±0.1 <sup>0</sup> C (authors).  |
|  |   |           | REFER  | ENCES :   |
|  |   |           |        | Bratton, A. C.; Marshall, E. K., Jr.  |
|  |   |           |        | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|  |   |           |        |   |

| COMPONENTS:  |                      |                           | ORIGINAL MEASUREMENTS                                   | •   |
|--|----------------------|---------------------------|---|---|
| (1) Benzenesulfonami   | Lde, 4-amin          | no-N-2-                   |   | •<br>'.; Postovskii, I. Ya.                       |
| pyridinyl- (sul  | -                    |                           |   | 1944, 17, 427-34.                                 |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; |                      |                           |   |   |
| (2) Water; H <sub>2</sub> 0;                                     |                      | 51                        |   |   |
| (-) water, wyo,  | [//32 10             | - 1                       |   |   |
| VARIABLES:   |                      |                           | PREPARED BY:  |   |
| Temperatur   | re                   |                           | R. Pi   | ekos  |
| EXPERIMENTAL VALUES:   |                      |                           |   |   |
|  |                      |                           |   |   |
|  |                      |                           |   |   |
|  |                      |                           | Solubility  |   |
|  | t/ <sup>0</sup> C    | Weight %                  | 10 <sup>3</sup> mol kg <sup>-1</sup> water <sup>a</sup> |   |
|  | 20                   | 0.0194                    | 0.778   |   |
|  | 37                   | 0.0470                    | 1.89  |   |
|  | 50                   | 0.094                     | 3.8   |   |
|  | 75                   | 0.24                      | 9.6   |   |
|  | 99                   | 0.61 <sup>b</sup>         | 25  |   |
| -  | <sup>a</sup> Calcula | ated by compil            | .er   |   |
|  | <sup>b</sup> Calcula | ated from the             | heat of dissolution                                     |   |
|  |                      | 0 cal mol <sup>-1</sup> ) |   |   |
|  |                      |                           |   |   |
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|  |                      | AUXILIARY                 | INFORMATION   |   |
| METHOD/APPARATUS/PROCE   |                      |                           | SOURCE AND PURITY OF                                    |   |
| Sulfapyridine was dis<br>form a satd soln whic                   |                      |                           |   | apyridine was used. Its                           |
| agitated in a glass v  |                      | •                         | ture.   | t reported in the litera                          |
| thermostat. The equi   |                      |                           |   | was not specified.                                |
| tained after 1 h. Fi   |                      |                           | Furity of the water                                     | was not spectified.                               |
| of the satd soln were  |                      | -                         |   |   |
| or dishes and evapd t  | -                    |                           |   |   |
| wer than 110-115°C.  | -                    | -                         |   |   |
| to const wt at 105-11  |                      |                           |   |   |
|  |                      |                           |   | : quite reliable result<br>he temp range 20-75°C. |
|  |                      |                           | At higher temps the                                     | accuracy was poor due to                          |
|  |                      | •                         | evapn of water durin<br>Temp: ±0.05 <sup>o</sup> C (aut | g sampling (authors).<br>hors).                   |
|  |                      |                           | REFERENCES :  |   |
|  |                      |                           |   |   |
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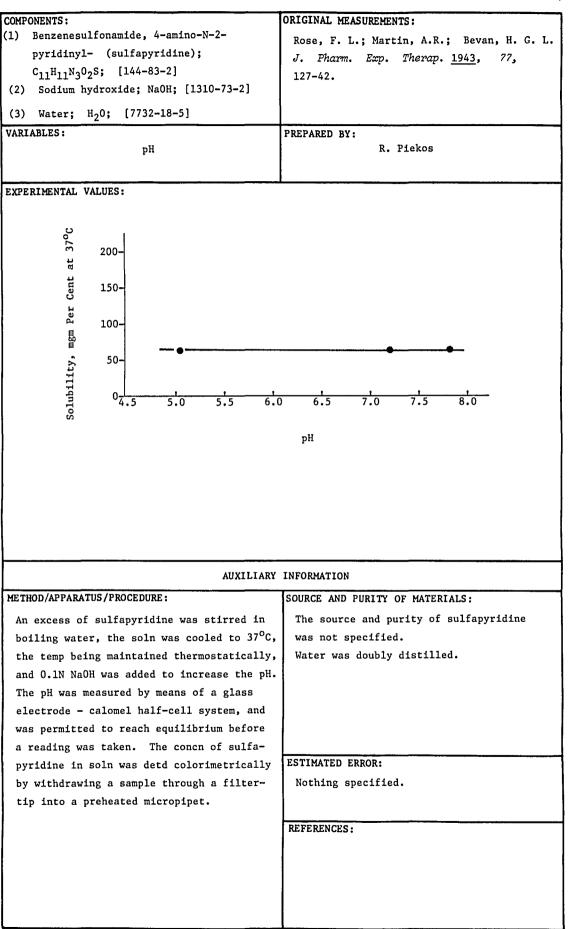
| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Langecker, H.  |
| <pre>pyridinyl- (sulfapyridine);</pre>  | Arch. Exptl. Path. Pharmakol. <u>1948</u> ,  |
| <sup>C</sup> <sub>11</sub> <sup>H</sup> <sub>11</sub> <sup>N</sup> <sub>3</sub> <sup>0</sup> <sub>2</sub> <sup>S</sup> ; [144-83-2] | 205, 291-301.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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|   |  |
| Solubility of sulfapyridine in water  | at $37^{\circ}$ C is 53 mg% ( 2.1 x $10^{-3}$  |
| mol dm <sup>-3</sup> , compiler ).  |  |
| mol dm , compiler ).  |  |
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| AUXILIARY   | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:  |
| An excess of sulfapyridine in water was   | Source and purity of the materials were  |
| boiled and left for 24 h in a vessel protect  | not specified.   |
| ed from access of CO2. The concn of sulfa-  |  |
| pyridine was detd colorimetrically by the   |  |
| method of Bratton and Marshall (1) using  |  |
| a Havemann colorimeter (2), as well as by   |  |
| microanal detn of the solid residue.  |  |
|   | ECTIVATED EDDOD  |
|   | ESTIMATED ERROR:   |
|   | Nothing specified  |
|   |  |
|   | REFERENCES:  |
|   | <ol> <li>Bratton, A. G.; Marshall, E. K.</li> <li>J. Biol. Chem. <u>1939</u>, 128, 537.</li> </ol> |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.<br>2. Havemann, R. Klin. Wochenschr.                        |
|   | <u>1940</u> , p. 503.  |
|   | <u></u> , p. 550.  |
|   |  |

| COMPONENTS:                                | ORIGINAL MEASUREMENTS:                          |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-       | Neish, W. J. P. Rec. trav. chim.                |
| pyridinyl- (sulfapyridine);                | <u>1948,</u> 67, 361-71.                        |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]      |   |
|  |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:                                 | PREPARED BY:                                    |
| One temperature: 37 <sup>0</sup> C         | R. Piekos                                       |
|  |   |
| EXPERIMENTAL VALUES:                       |   |
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| Solubility of sulfapyridine in water a     | t $37^{\circ}$ C is 370 y/ml ( 1.48 x $10^{-3}$ |
| mol dm <sup>-3</sup> , compiler ).         |   |
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| AUXILIARY                                  | INFORMATION                                     |
| METHOD / APPARATUS / PROCEDURE :           | SOURCE AND PURITY OF MATERIALS:                 |
| A suspension of sulfapyridine (10 mg/5 ml) | Sulfapyridine: not specified.                   |
| in water was kept for 5 h at 37°C and 1 h  | Distd water was used.                           |
| at room temp before fitration. Soly was    |   |
| detd by the Westfall's method (1) based on |   |
| diazotization of the sulfonamide, coupling |   |
| with Na 2-napthol-3,6-disulfonate and com- |   |
| paring the color with that of a std soln   |   |
| in a Klett colorimeter.                    |   |
|  | ESTIMATED ERROR:                                |
|  | Nothing specified                               |
|  |   |
|  | REFERENCES:                                     |
|  | 1. Westfall, B. B. J. Nat. Cancer               |
|  | Inst. <u>1945</u> , 6, 23.                      |
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| COMPONENTS:                                  | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-         | Yamazaki, M.; Aoki, M.; Kamada, A.;                           |
| pyridinyl- (sulfapyridine);                  | Yata, N. Yakuzaigaku 1967, 27(1),                             |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]        | 37-40.  |
|  |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]     |   |
| VARIABLES:                                   | PREPARED BY:  |
| One temperature: 30 <sup>0</sup> C           | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:                         | · · · · · · · · · · · · · · · · · · ·                         |
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| Solubility of sulfapyridine in water         | at $30^{\circ}$ C is 2.01 mmol/L ( 0.501 g dm <sup>-3</sup> , |
| compiler ).                                  |   |
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| AUXILIARY                                    | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:                               |
|  |   |
| Sulfapyridine (0.5 g) was placed in an L-    | Nothing specified.  |
| shaped tube together with 20 ml of water.    |   |
| The mixt was shaken in a thermostat until    |   |
| equilibrium was attained. The sulfapyridine  |   |
| was then assayed in the supernatant spectro- |   |
| photometrically at 545 nm on a Beckmann DU   |   |
| spectrophotometer. The results were taken    |   |
| from a calibration graph.                    |   |
|  | ESTIMATED ERROR:  |
|  | Soly: not specified.  |
|  | Temp: ±1 <sup>0</sup> C (authors).                            |
|  | REFERENCES :  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                    |
| (1) Benzenesulfonamide, 4-amino-N-2-  | Kitao, K.; Kubo, K.; Morishita, T.;                       |
| pyridinyl- (sulfapyridine);   | Yata, N.; Kamada, A. Chem. Pharm. Bull.                   |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | <u>1973,</u> 21, 2417-26.                                 |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |   |
| (2) Water, 120, [7752-10-5]   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
| Une temperature: 57 C   | R. FIEROS   |
|   | L   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfapyridine in water  | at $37^{\circ}$ C is 2.09 mmol dm <sup>-3</sup> solution. |
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| AUXILIARY   | INFORMATION   |
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| METHOD /APPARATUS / PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;                           |
| The sulfapyridine concn in the aq soln (pH                                  | Comm available sulfapyridine was used as                  |
| 6) was detd by diazotization. No details                                    | supplied.   |
| were given.   | Deionized water was used.                                 |
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|   | ESTIMATED ERROR:  |
|   | Soly: not specified.                                      |
|   | Temp: ±1 <sup>0</sup> C (authors).                        |
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|   | REFERENCES:   |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4- | amino-N-2-                       | ORIGINAL MEASUREMENTS:                                      |
| pyridinyl- (sulfapyri                     |                                  | Avico, U.; Cavazutti, G.; di Francesco, R.;                 |
| $C_{11}H_{11}N_3O_2S;$ [ 144-83           |                                  | Signoretti Ciranni, E.; Zuccaro, P.                         |
| (2) Sodium chloride; NaCl                 |                                  | Farmaco, Ed. Pratica <u>1975</u> , 30(1),                   |
|   |                                  | 40-6.   |
| (3) Water; H <sub>2</sub> 0; [7732-18     |                                  |   |
| VARIABLES:                                |                                  | PREPARED BY:  |
| Temperature                               |                                  | R. Piekos   |
| EXPERIMENTAL VALUES:                      | ······                           | l   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   | Solubi<br>t/ <sup>0</sup> C in d | lity of amorphous sulfapyridine<br>equimolal NaCl solutions |
|   | g/100 g                          | g water $10^3 \text{ mol kg}^{-1} \text{ water}^a$          |
|   | 25 0.0                           | 51 2.4  |
|   | 35 0.3                           | 75 3.0  |
|   | 40 0.8                           | 3.2   |
|   |                                  |   |
|   | <sup>a</sup> Calculated by       | cound los   |
|   | -Calculated by                   | compiler .  |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   | AUXILIARY                        | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:               |                                  | SOURCE AND PURITY OF MATERIALS:                             |
| A soln of Na salt of sulfa                | pyridine was added               |   |
| to a HCl soln contg stoich                |                                  | not specified. The mp of crystalline sul-                   |
| of the acid to neutralize                 |                                  | fapyridine was 191-3°C.                                     |
| neutralization was carried                |                                  | Purity of the water was not specified.                      |
| stat and the pH of the mix                |                                  |   |
| close to that of a satd su                |                                  |   |
| The procedure was repeated                |                                  |   |
| initial concn of the reage                |                                  |   |
| max concn of sulfapyridine                | at which no                      | ESTIMATED ERROR:  |
| pptn occurred.                            |                                  | Nothing specified.  |
|   |                                  |   |
|   |                                  | REFERENCES:   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |
|   |                                  |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-</li> </ol>  | Krüger-Thiemer, E.  |
| <pre>pyridinyl- (sulfapyridine);</pre>  | Arch. Dermatol. Syphilis 1942, 183,   |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]   | 90-116.   |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:  |
| One temperture: ca 20 <sup>0</sup> C; one pH: 8.74  | R. Piekos   |
| EXPERIMENTAL VALUES:<br>Solubility of sulfapyridine in a 0.70<br>at room temperature (about 20 <sup>o</sup> C), is (<br>solution, compiler ).   |   |
| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |
| Sulfapyridine (0.5 g) was dissolved in the  | Sulfapyridine was the product manufd by   |
| 0.705M (10%) Na <sub>2</sub> HPO <sub>4</sub> soln (pH 8.74), at  | Nordmark under the name Eubasin.  |
| room temp (about $20^{\circ}$ C), shaken for 2 h, and   | The source and purity of the remaining  |
| filtered. A 1-cm <sup>3</sup> aliquot of the filtrate<br>was withdrawn, cooled, acidified with 2N<br>HCl, and the sulfapyridine content was detd<br>colorimetrically by the method of Marshall<br>modified by Kimmig (1) using an Authenrieth |   |
| colorimeter. The pH was detd on an ultra-   | ESTIMATED ERROR:  |
| ionograph using a glass electrode.  | Soly: precision ±5% (author).   |
|   | Temp: not specified.  |
|   | pH : ±0.05 pH unit (author).  |
|   | REFERENCES :  |
|   | <ol> <li>Kimmig, J. Arch. Dermatol.</li> <li>176, 722; Erg. Hyg. <u>1941</u>, 24, 398.</li> </ol> |
|   |   |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                      |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Krüger-Thiemer, E.                          |
| pyridinyl- (sulfapyridine);  | Arch. Dermatol. Syphilis 1942, 183,         |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2]                            | 90-116.                                     |
| <ul> <li>Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> |   |
| (3) Water; H <sub>2</sub> O; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:                                |
| One temperature: ca 20 <sup>0</sup> C; one pH: 4.37  | R. Piekos                                   |
| EXPERIMENTAL VALUES:   |   |
|  |   |
|  |   |
|  |   |
| Solubility of sulfapyridine in a 0.735M  |   |
| at room temperature (about 20 <sup>0</sup> C), is 0.   | 054 g% ( 2.17 mol $dm^{-3}$ solution,       |
| compiler ).  |   |
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| AUXILIARY  | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:             |
| Sulfapyridine was dissolved in a 0.735M  | Sulfapyridine was the product manufd by     |
| (10%) $KH_2PO_4$ soln in amt of 0.5 g/10 cm <sup>3</sup> ,   | Nordmark under the name Eubasin.            |
| shaken for 2 h, and filtered. A 1-cm <sup>3</sup> ali-   | The source and purity of the remaining      |
| quot of the filtrate was withdrawn, cooled,  | materials were not specified.               |
| acidified with 2N HCl, and the sulfapyri-  |   |
| dine content was detd colorimetrically by  |   |
| the method of Marshall modified by Kimmig  |   |
| (1) using Authenrieth colorimeter. The   |   |
|  |   |
| PH was detd on an ultraionograph using a   | ESTIMATED ERROR:                            |
| glass electrode.   | Soly: precision ±5% (author).               |
|  | Temp: not specified.                        |
|  | pH : ±0.05 pH unit (author).                |
|  | REFERENCES:                                 |
|  | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> , |
|  | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.  |
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| 5   |                                 |                    |          |                  |  |                    |                                    |       |
|---|---------------------------------|--------------------|----------|------------------|--|--------------------|------------------------------------|-------|
|   |                                 |                    |          | ORI              | GINAL MEA  | SUREMENTS:         | <u> </u>                           |       |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyridinyl- (sulfapyridine);</li> </ol>  |                                 |                    |          | Kı               | Uger-Thie  | emer, E.           |                                    |       |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]   |                                 |                    |          |                  |  | natol. Syph        | ilis <u>1942</u> ,                 | 183,  |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] |                                 |                    |          | 90               | 0-116.   |                    |                                    |       |
| <ol> <li>Phosphok</li> <li>KH<sub>2</sub>PO<sub>4</sub></li> </ol>                    | oric acid, m<br>; [7778-77      |                    | m salt;  |                  |  |                    |                                    |       |
| 4) Water;   |                                 | 32-18-5]           |          | PRI              | PARED BY   | :                  |                                    |       |
| ARIABLES:   | Temperature                     | ; рН               |          |                  |  | R. Piekos          |                                    |       |
| XPERIMENTA  | L VALUES:                       |                    |          | <u>R</u>         |  |                    |                                    |       |
| Composi   | tion of 1/15                    | M phosphate        | :        |                  |  | Solubil            | ity                                |       |
|   | buffer solut                    |                    |          | Room             | temp (ca   | 20 <sup>0</sup> C) | 37 <sup>0</sup> C                  |       |
| Na <sub>2</sub> HPO <sub>4</sub>  | кн <sub>2</sub> ро <sub>4</sub> | %Content           | рН       | g%               | 10 <sup>3</sup> mol<br>solutio                                       |                    | 10 <sup>3</sup> mol dr<br>solution |       |
| 1.0   | 99.0                            | 0.91               | 4.944    | 0.070            | 2.808  |                    |                                    |       |
| 10.0  | 90.0                            | 0.91               | 5.906    | 0.070            | 2.808  | 0.106              | 4.252                              |       |
| 61,1  | 38.9                            | 0.93               | 7.005    | 0.071            | 2.848  | 0.106              | 4.252                              |       |
| 9.5   | 0.5                             | 0.733 <sup>b</sup> | 7.51     | 0.060            | 2.407  | -                  | -                                  |       |
| 94.7  | 5.3                             | 0.95               | 8.018    | 0.081            | 3.249  | _                  | -                                  |       |
|   |                                 | ed by compi        |          | solutio          | on.  |                    |                                    |       |
|   |                                 |                    |          |                  |  |                    |                                    |       |
|   |                                 |                    | AUXIL    | ARY INI          | ORMATION   |                    |                                    |       |
| ÆTHOD/APPA  | RATUS/PROCEI                    | DURE:              |          | so               | URCE AND   | PURITY OF MA       | TERIALS:                           |       |
| •   | line (0.5 g)                    |                    |          |                  | Sulfapyridine was the product manufd by                              |                    |                                    |       |
|   | ouffer soln,<br>Left for 48     |                    |          |                  | Nordmark under the name Eubasin.                                     |                    |                                    |       |
|   | left for 48<br>respective t     |                    | -        |                  | The source and purity of the remaining materials were not specified. |                    |                                    |       |
|   | ltrate was t                    | -                  | -        |                  |  | nor sh             |                                    |       |
|   | expts at 37                     |                    |          | 1                |  |                    |                                    |       |
| $1 \text{ cm}^3 \text{ of } 2$  | 2N HCl, and                     | the sulfapy        | ridine   |                  |  |                    |                                    |       |
| content wa  | as detd cold                    | rimetricall        | y by the |                  |  |                    |                                    |       |
| method of Marshall modified by Kimmig (1)   |                                 |                    |          | ESTIMATED ERROR: |  |                    |                                    |       |
| -   | luthenrieth                     |                    | -        |                  |  | cision ±%%         | (author).                          |       |
|   | on an ultrai                    | onograph us        | ing a    |                  | Temp: not specified.<br>pH : ±0.05 pH unit (author).                 |                    |                                    |       |
| glass elec  | crode.                          |                    |          |                  | H : ±0.<br>FERENCES :  |                    | \author).                          |       |
|   |                                 |                    |          |                  |  |                    |                                    |       |
|   |                                 |                    |          | 1                | Kimmiş   | g, J. Arch.        | Dermatol.                          | L938, |

| (sulfag  | pyridine);    | e, N-2-pyridiny1-<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> 0 <sub>2</sub> S; | ORIGINAL MEASUREMENTS:<br>Pulver, R.; Suter, R.  |   |
|--|---------------|---|--|---|
| <pre>[144-83-2] (2) Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</pre> |               | disodium salt;<br>94-4]   | Schweiz. Med. Wochenschr. <u>1943</u> ,<br>73(13), 403-8.  |   |
| (3) Phospho  | 4             | monopotassium salt;   |  |   |
| (4) Water;   |               | 732-18-5]   | PREPARED BY:   |   |
| VARIABLES:   | pH            |   | R. Piekos  |   |
| EXPERIMENTAL   |               |   |  |   |
|  |               |   |  |   |
|  |               |   |  |   |
|  |               | Solubility of sulf  | apyridine in M/15 phosphate  |   |
|  | рН            | buffers (according  | to Sørensen) at 20 <sup>0</sup> C  |   |
|  |               | mg%   | $10^3 \text{ mol } dm^{-3} a$  |   |
|  | 6.0           | 64  | 2.6  |   |
|  | 7.0           | 67  | 2.7  |   |
|  | 8.0           | 70  | 2.8  |   |
|  | ·             | Calculated by compile   | r  |   |
|  |               | Calculated by compile   | r  |   |
|  |               |   | r<br>  |   |
| ME THOD / AP PAR.  |               | AUXILIAR  |  |   |
| METHOD/APPAR<br>Nothing  |               | AUXILIAR  | ( INFORMATION  | - |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  | - |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  |   |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  |   |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  |   |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  |   |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS;  |   |
|  | ATUS / PROCEE | AUXILIAR  | Y INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.   |   |
|  | ATUS / PROCEE | AUXILIAR  | X INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.<br>ESTIMATED ERROR:<br>Nothing specified. |   |
|  | ATUS / PROCEE | AUXILIAR  | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.  |   |
|  | ATUS / PROCEE | AUXILIAR  | X INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.<br>ESTIMATED ERROR:<br>Nothing specified. |   |
|  | ATUS / PROCEE | AUXILIAR  | X INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.<br>ESTIMATED ERROR:<br>Nothing specified. |   |

|   | A1171127A  |                |  |  |  |
|---|--|----------------|--|--|--|
| COMPONENTS:<br>(1) Benzenesulfonmaide, 4-amino-N-2- |  | -N-2-          | ORIGINAL MEASUREMENTS:                                 |  |  |
| pyridinyl- (sulfapyridine);                         |  |                | Langecker, H.  |  |  |
| <i>(</i> <b>)</b> )                                 | C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2]<br>) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] |                | Arch. Exptl. Path. Pharmakol. <u>1948</u> ,            |  |  |
|   |  |                | 205, 291-301.  |  |  |
| (3)   | Phosphoric acid, monopotass:<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  | ium salt;      |  |  |  |
| (4)   | Water; H <sub>2</sub> 0; [7732-18-5]   |                | PREPARED BY:   |  |  |
| variables:<br>pH                                    |  |                | R. Piekos  |  |  |
| EXPE  | RIMENTAL VALUES:   |                |  |  |  |
|   |  |                | _  |  |  |
|   | pH of the 1/15M  | Sc             | olubility at 37°C                                      |  |  |
|   | phosphate buffer   | mg%            | $10^3 \text{ mol } dm^{-3} \text{ a}$                  |  |  |
|   | 4.9  | 44             | 1.8  |  |  |
|   | 5.9  | 60             | 2.4  |  |  |
|   | 7.0  | 58             | 2.3  |  |  |
|   | 7,5  | 62             | 2.5  |  |  |
|   |  |                |  |  |  |
|   |  | AUXILIARY      | INFORMATION  |  |  |
| METI  | HOD/APPARATUS/PROCEDURE:   |                | SOURCE AND PURITY OF MATERIALS:                        |  |  |
| An  | excess of sulfapyridine was  | added to the   | Source and purity of the materials were                |  |  |
| buffer soln and boiled for 1 h in a sealed          |  |                | not specified.   |  |  |
| am  | pul followed by keeping the  | ampul at 37°C. |  |  |  |
| Th  | e concn of sulfapyridine was   | detd colori-   |  |  |  |
| metrically by the method of Bratton and             |  |                |  |  |  |
| Ma  | rshall (1) using a Havemann (  | colorimeter    |  |  |  |
| (2  | ), as well as by microanal de  | etn of the     |  |  |  |
| so  | lid residue.   |                |  |  |  |
|   |  |                | ESTIMATED ERROR:                                       |  |  |
|   |  |                | Nothing specified.                                     |  |  |
|   |  |                | DEDERENANG   |  |  |
|   |  |                | REFERENCES:<br>1. Bratton, A. G.; Marshall, E. K., Jr. |  |  |
|   |  |                | J. Biol. Chem. 1939, 128, 537.                         |  |  |
|   |  |                | 2. Havemann, R. Klin. Wochenschr.                      |  |  |
|   |  |                | <u>1940</u> , p. 503.                                  |  |  |
|   |  |                |  |  |  |

| COMPONENTS:  | OPTCINAL MEACUPENERS                       |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-   | ORIGINAL MEASUREMENTS:                     |
| pyridinyl- (sulfapyridine);  | Yamazaki, M.; Aoki, M.; Kamada, A.;        |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]  | Yata, N. Yakuzaigaku, <u>1967</u> , 27(1), |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                  | 37-40.                                     |
| <ul> <li>Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                               |
| VARIABLES:   | R. Piekos                                  |
| One temperature: 30°C; one pH: 7.4   |  |
| EXPERIMENTAL VALUES:   | <b>5</b>                                   |
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|  |  |
| Solubility of sulfapyridine in a pho   | contate huffer colution of all 7 4         |
|  |  |
| ( $\mu$ = 0.17 ) at 30°C is 1.91 mmol/L  | ( 0.476 g dm <sup>-3</sup> , compiler ).   |
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| AUXILIARY  | INFORMATION                                |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:            |
| Sulfapyridine (0.5 g) was placed in an L-  | Nothing specified.                         |
| shaped tube together with 20 ml of the buf-  |  |
| fer soln. The mixt was then shaken in a  |  |
| thermostat until equilibrium was attained.   |  |
|  |  |
| The sulfapyridine was then assayed in the  |  |
| supernatant spectrophotometrically at 545  |  |
| nm on a Beckmann DU spectrophotometer. The   |  |
| results were taken from a calibration graph.   | ,  |
| 1  | ESTIMATED ERROR:                           |
|  | Soly: not specified.                       |
|  | Temp: ±1 <sup>0</sup> C (authors).         |
|  | DEPENDING                                  |
|  | REFERENCES :                               |
|  | 1  |
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|---|---|
| 4 | υ |

| <pre>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyridinyl- (sulfapyridine);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>0<sub>2</sub>S; [144-83-2]</pre> | IGINAL MEASUREMENTS:<br>Hekster, Y. A.; Vree, T. B.; Damsma, J.E.;<br>Friesen, W. T. J. Antimicrob. Chemother. |
|---|--|
|   | <u>1981,</u> 8, 133-44.  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]<br>(3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]             |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5] PF   | EPARED BY:   |
| VARIABLES: pH   | R. Piekos  |

| - 11 | Solubility at 25 <sup>0</sup> C |                               |  |
|------|---------------------------------|-------------------------------|--|
| рН   | mg/l                            | $10^4$ mol dm <sup>-3</sup> a |  |
| 5.5  | 120                             | 4.81                          |  |
| 7.5  | 200                             | 8.02                          |  |

<sup>a</sup>Calculated by compiler.

| AUXILIARY INFORMATION   |  |  |  |
|---|--|--|--|
| ETHOD/APPARATUS/PROCEDURE:                                    | SOURCE AND PURITY OF MATERIALS:  |  |  |
| Satd solns of sulfapyridine were prepd in                     | The source and purity of the materials   |  |  |
| phosphate buffers of pH 5.5 and 7.5 at room                   | were not specified.  |  |  |
| temp (25 <sup>0</sup> C). The concn of the solute was         |  |  |  |
| measured by means of a Spectra Physics 3500B                  |  |  |  |
| high-performance liquid chromatograph equip-                  |  |  |  |
| ped with a column oven (Model 748) and a                      |  |  |  |
| Pye-Unicam LC-UV spectrophotometric detector.                 |  |  |  |
| The detector was connected to a 1-mV record-                  |  |  |  |
| er. A stainless steel column (10 cm x 4.6                     | ESTIMATED ERROR:   |  |  |
| mm i.d.) was packed with Lichrosorb RPS,                      | The detection limit of the solute by HPLC was $0.5 \text{ mg/l}$ (authors). The error in tempe |  |  |
| 5 $\mu\text{m}\text{,}$ obtained from Chrompack. An injection | rature and pH was not specified.   |  |  |
| loop of 100 $\mu 1$ was used. The oven temp was               |  |  |  |
| 40 <sup>0</sup> C. Detection of sulfapyridine was per-        | REFERENCES:  |  |  |
| formed at 260 nm.   |  |  |  |
|   |  |  |  |
|   |  |  |  |

|  |                                      |              | 4  |
|--|--------------------------------------|--------------|--|
| COMPONENTS:  | ·····                                |              | ORIGINAL MEASUREMENTS:                             |
|  | (1) Benzenesulfonamide, 4-amino-N-2- |              | Hawking, F.  |
| pyridinyl- (sulfapyridine);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] |                                      | / >          | Lancet, 1941, 240, 786-8.                          |
| (2) Calcium chloride; CaCl <sub>2</sub> ; [10043-52-4]   |                                      | 0043-52-4]   | <i>Lancev</i> , <u>1941</u> , 210, 700 0.          |
| (3) Potassium chloride; KCl; [7447-40-7]   |                                      | 447-40-7]    |  |
| (4) Sodium chloride; NaCl; [7647-14-5]   |                                      | 7-14-5]      |  |
| (5) Water; H <sub>2</sub> 0;   | [7732-18-5]                          |              | PREPARED BY:                                       |
| VARIABLES:   | -                                    |              | R. Piekos  |
| VARIABLES:<br>Temperature  |                                      |              |  |
| EXPERIMENTAL VALUES  | :                                    |              |  |
|  |                                      |              |  |
|  |                                      |              |  |
|  | t/°C                                 | Solubility c | of bicarbonate-free Locke's solution <sup>a</sup>  |
|  | c, o                                 | mg/10        | 00 ml $10^4 \text{ mol } dm^{-3} a$                |
| -  |                                      |              |  |
|  | 17                                   | 17           | 6.8  |
|  | 36                                   | 41           | 16.5   |
| - 1  |                                      |              |  |
|  | <sup>a</sup> The solution            | contained Na | aCl 9 g, KCl 0.2 g, CaCl <sub>2</sub> 0.2 g,       |
|  |                                      | r, and had a | -  |
|  | <sup>b</sup> Calculated b            |              |  |
|  | -calculated b                        | y complier.  |  |
|  |                                      |              |  |
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|  |                                      | AUXILIARY    | INFORMATION  |
| METHOD/APPARATUS/PR  | OCEDURE .                            |              |  |
|  |                                      |              | SOURCE AND PURITY OF MATERIALS:                    |
| Sulfapyridine was  | -                                    |              | Nothing specified.                                 |
| bonate-free Locke  |                                      | •            |  |
| a tube which was o   |                                      |              |  |
| CO2. The supernat  |                                      |              |  |
| a paper, dild in a   | a hot room to                        | prevent pptn | . 9  |
| and sulfapyridine  | was detd by t                        | he method    |  |
| of Marshall and Li   | itchfield (1).                       |              |  |
|  |                                      |              |  |
|  |                                      |              | ESTIMATED ERROR:                                   |
|  |                                      |              | Soly: average of 3 detns has been given (authors). |
|  |                                      |              | Temp: not specified.                               |
|  |                                      |              | REFERENCES:  |
|  |                                      |              | 1. Marshall, E. K., Jr.; Litchfield, J.            |
|  |                                      |              | T., Jr. Science <u>1938</u> , 88, 85.              |
|  |                                      |              |  |
|  |                                      |              |  |
|  |                                      |              |  |
|  |                                      |              |  |

| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyridiny1- (sulfapyridine);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>S; [144-83-2]<br/>(2) Ethanol; C<sub>2</sub>H<sub>6</sub>O; [64-17-5]<br/>(3) Water; H<sub>2</sub>O; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Sapozhnikova, N. V.; Postovskii, I. Ya.<br>Zh. Prikl. Khim. <u>1944,</u> 17, 427-34. |
|--|--|
| VARIABLES:   | PREPARED BY:   |
| Concentration of ethanol, temperature  | R. Piekos  |

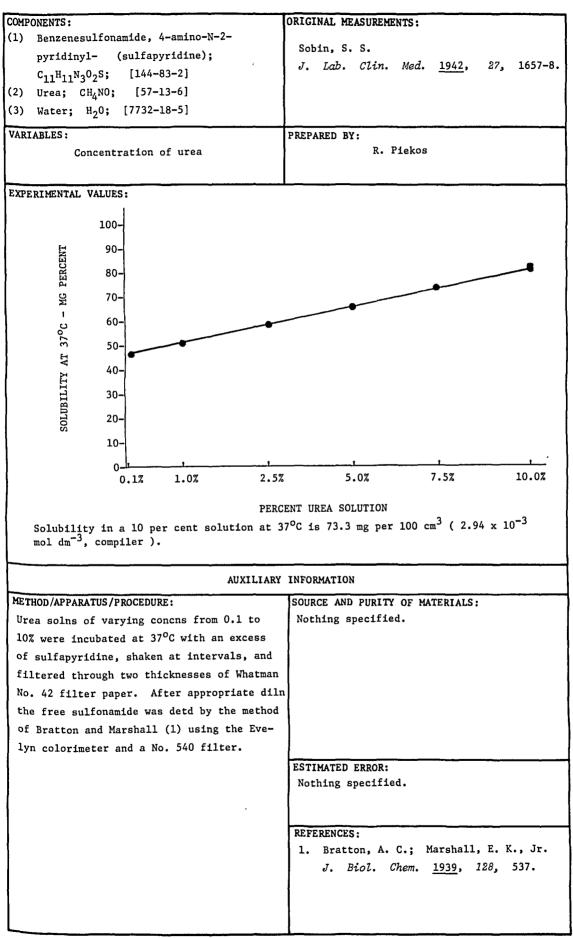
.

## EXPERIMENTAL VALUES:

| Concentration | Solubility   |      |         |  |  |
|---------------|--|------|---------|--|--|
| of ethanol    | at 37°C  |      | at 75°C |  |  |
| Weight%       | Weight% 10 <sup>2</sup> mol kg <sup>-1</sup><br>solvent <sup>a</sup> |      | Weight% | 10 <sup>2</sup> mol kg <sup>-1</sup><br>solvent <sup>a</sup> |  |
| 0.0           | 0.047  | 0.19 | 0.25    | 1.00   |  |
| 19.2          | 0.32   | 1.29 | 0.91    | 3.68   |  |
| 38.3          | 0.37   | 1.49 | 1.57    | 6.40   |  |
| 57.6          | 0.58   | 2.34 | 3.00    | 12.4   |  |
| 67.2          | -  | -    | 3.10    | 12.8   |  |
| 76.4          | 0.54   | 2.18 | 3.0     | 12.4   |  |
| 96.0          | 0.39   | 1.57 | 2.3     | 9.4  |  |

<sup>a</sup>Calculated by compiler

| AUXILIARY  | INFORMATION   |
|--|---|
| METHOD/APPARATUS/PROCEDURE:<br>Sulfapyridine was dissolved in EtOH-water<br>mixts to form satd solns which were occa-<br>sionally agitated in glass vessels immersed<br>in a thermostat. The equilibrium was usual-<br>ly attained after 1 h. Five- to 100-cm <sup>3</sup><br>samples of the satd soln were placed in Pt<br>crucibles or dishes and evapd to dryness at<br>temps lower than 110-115°C. The residue | <pre>INFORMATION SOURCE AND PURITY OF MATERIALS: Pure, recrystd sulfapyridine was used. Its mp conformed to that reported in the literature. The purity of ethanol and water was not specified. ESTIMATED ERROR: Soly: quite reliable results were obtained     (authors). Temp: ±0.05°C (authors). REFERENCES:</pre> |
| crucibles or dishes and evapd to dryness at<br>temps lower than 110-115 <sup>o</sup> C. The residue<br>was dried to const wt at 105-110 <sup>o</sup> C and   | Soly: quite reliable results were obtain<br>(authors).<br>Temp: ±0.05°C (authors).  |



| COMPONENTS:  | ORIGINAL MEASUREMENTS:                       |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Dolique, R.; Foucault, J.                    |
| pyridinyl- (sulfapyridine);  | Trav. soc. pharm. Montpellier <u>1952</u> ,  |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2]<br>(2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [64-17-5] | 12, 145-53.                                  |
| (3) 1,2,3-Propanetriol; C <sub>3</sub> H <sub>8</sub> O; [56-81-5]   | 12, 145 55.                                  |
| (4) Water; $H_20$ ; [7732-18-5]  |  |
|  |  |
| VARIABLES:<br>One temperature: 26-28 <sup>0</sup> C  | PREPARED BY:<br>R. Piekos                    |
| one Lemperature. 20-20 0   |  |
|  | ·····  |
| EXPERIMENTAL VALUES:   |  |
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|  |  |
| Solubility of sulfapyridine in a mixtu   | re of 1,2,3-propanetriol and 95%             |
| ethanol ( 2:1 by wt ) at 26-28 <sup>0</sup> C is 0.  | 575% ( 2.32 x $10^{-2}$ mol kg <sup>-1</sup> |
| solvent, compiler ).   |  |
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|  | INFORMATION                                  |
|  | SOURCE AND PURITY OF MATERIALS:              |
| METHOD/APPARATUS/PROCEDURE:  |  |
| The sulfapyridine content was detd by diazo-   | Nothing specified                            |
| tization of the amine group in a cold acidi-   |  |
| fied 0.1N $\text{KNO}_2$ soln. an excess of $\text{KNO}_2$ was   |  |
| detected by using iodinated starch.  |  |
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|  | ESTIMATED ERROR:                             |
|  | Nothing specified                            |
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|  | REFERENCES :                                 |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                                      |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Dolique, R.; Foucault, J.                                   |
| pyridinyl- (sulfapyridine);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | Trav. soc. pharm. Montpellier <u>1952,</u>                  |
| (2) Ethanol; $C_{2}H_{6}O$ ; [64-17-5]   | 12, 145-53.   |
| (3) 1,2,3-propanetriol; C <sub>3</sub> H <sub>8</sub> O <sub>3</sub> ; [56-81-5]                           |   |
| (4) Urea; $CH_2N_2O$ ; [57-13-6]   |   |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:  |
| VARIABLES:   | R. Piekos   |
| One temperature: 26-28°C   |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfapyridine at 26-28 <sup>0</sup>  | In a saturated solution of urea in                          |
| a mixture of 1,2,3-propanetriol and 95   | <sup>0</sup> ethanol ( 2:1 by wt. ), containing             |
| 54.5 g of urea per 100 g of the mixtur   | ce, is $0.78\%$ ( $3.2 \times 10^{-2}$ mol kg <sup>-1</sup> |
|  |   |
| solvent, compiler ).   |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                             |
| The sulfapyridine content was detd by diazo-   | Nothing specified.  |
| tization of the amine group in a cold aci-   |   |
| dified 0.1N KNO2 soln. An excess of KNO2   |   |
| Was detected by using iodinated starch.  |   |
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|  | ESTIMATED ERROR:  |
|  |   |
|  | Nothing specified.  |
| •  |   |
|  | REFERENCES:   |
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| COMPONENTS:  |  | ORIGINAL MEASUREMENTS:                 |                                       |  |
|--|--|--|---------------------------------------|--|
| (1) Benzenesulfonamide,  |  | Neish, W. J. P. Rec.                   | trav. chim.                           |  |
| pyridinyl- (sulfapy  | pyridinyl- (sulfapyridine);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] |  |                                       |  |
|  |  | <u>1948</u> , <i>67</i> , 361-71.      |                                       |  |
| (2) 1H-Purine-2,6-dione,<br>trimethy1- (caffein                        |  |  |                                       |  |
| C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> ; [58-08- | -2]  |  |                                       |  |
| (3) Water; H <sub>2</sub> 0; [7732-                                    |  |  |                                       |  |
| VARIABLES:   | ······································   | PREPARED BY:                           |                                       |  |
| Concentration of   | caffeine   | R. Piekos                              |                                       |  |
|  | Carronno   |  |                                       |  |
|  |  | I                                      | · · · · · · · · · · · · · · · · · · · |  |
| EXPERIMENTAL VALUES:   |  |  |                                       |  |
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|  |  |  |                                       |  |
| Concentratio   | on Solubility of   | f sulfapyridine at 37 <sup>0</sup> C   |                                       |  |
| of caffeine  | Y/ml   | $10^3 \text{ mol } dm^{-3} a$          |                                       |  |
| g/100 m1   | 1 / 112  | 10 101 64                              |                                       |  |
| -  |  | <u> </u>                               |                                       |  |
| 0.5  | 470  | 1.88                                   |                                       |  |
| 0.75   | 480  | 1.92                                   |                                       |  |
| 0.75   | 400  | 1.92                                   |                                       |  |
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|  | AUXILIARY  | INFORMATION                            |                                       |  |
| METHOD/APPARATUS/PROCEDUR  | E :  | SOURCE AND PURITY OF MAT               | FRIATS.                               |  |
| A suspension of sulfapyr   |  | Sulfapyridine: not spe                 |                                       |  |
| soln was kept for 5 h at   |  | Anhydrous caffeine was                 |                                       |  |
|  |  |  | -                                     |  |
| room temp before filtrat   |  |  | ecified).                             |  |
| by the Westfall's method   | l (1) based on diazo-  | Distd water was used.                  |                                       |  |
| tization of the sulfonam   | ide, coupling with   |  |                                       |  |
| Na 2-napthol-3,6-disulfo   | onate and comparing  |  |                                       |  |
| the color with that of a   |  |  |                                       |  |
|  | , otu obin in u  |  |                                       |  |
| Klett colorimeter.   |  |  |                                       |  |
|  |  | ESTIMATED ERROR:                       |                                       |  |
|  |  |  |                                       |  |
| ]  |  | Nothing specified.                     |                                       |  |
| 1  |  |  |                                       |  |
|  |  | REFERENCES :                           |                                       |  |
|  |  |  |                                       |  |
|  |  | 1. Westfall, B. B. J                   | . Nat. Cancer                         |  |
| ł  |  | Inst. 1945, 6, 23.                     |                                       |  |
|  |  |  |                                       |  |
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| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyridinyl- (sulfapyridine);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>S; [144-83-2]<br/>(2) Methane, trichloro- (chloroform);<br/>CHCl<sub>3</sub>; [67-66-3]</pre>  | ORIGINAL MEASUREMENTS:<br>Yamazaki, M.; Aoki, M.; Kamada, A.;<br>Yata, N. Yakuzaigaku, <u>1967</u> , 27(1),<br>37-40. |
| VARIABLES:<br>One temperature: 30 <sup>0</sup> C   | PREPARED BY:<br>R. Piekos   |
| EXPERIMENTAL VALUES:<br>Solubility of sulfapyridine in chlor<br>( 0.815 g dm <sup>-3</sup> , compiler ).   | oform at 30 <sup>0</sup> C is 3.27 mmol/L   |
|  |   |
|  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>Sulfapyridine (0.5 g) was placed in an L-<br>shaped tube together with 20 ml of chloro-<br>form. The mixt was shaken in a thermostat<br>until equilibrium was attained. The sulfa-<br>pyridine was then assayed in the supernatant<br>spectrophotometrically at 545 nm on a Beck-<br>mann DU spectrophotometer. The results were<br>taken from a calibration graph. | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.   |
|  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±1 <sup>0</sup> C (authors).  |
|  | REFERENCES :  |

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                             |  |  |  |
| (1) Benzenesulfonamide, 4-amino-N-2-  | Kitao, K.; Kubo, K.; Morishita, T.;                |  |  |  |
| <pre>pyridinyl- (sulfapyridine);</pre>                                      | Yata, N.; Kamada, A.                               |  |  |  |
| C <sub>11</sub> N <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | <u>1973</u> , <i>21</i> , 2417-26.                 |  |  |  |
| (2) Methane, trichloro-; CHCl <sub>3</sub> ;                                |  |  |  |  |
| [67-66-3]   |  |  |  |  |
| VARIABLES:  | PREPARED BY:                                       |  |  |  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |  |  |  |
|   |  |  |  |  |
| EXPERIMENTAL VALUES:  |  |  |  |  |
| Solubility of sulfapyridine in CHCl <sub>3</sub>                            | at 37°C is 2.86 mmol dm <sup>-3</sup> solution.    |  |  |  |
| AUXILIARY   | INFORMATION  |  |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                    |  |  |  |
| One ml of the sulfapyridine soln in CHCl <sub>3</sub>                       | Comm available sulfapyridine was used as           |  |  |  |
| at equilibrium was taken into a test tube.                                  | supplied.  |  |  |  |
| After evapn of the solvent, the residue was                                 | Neither source nor purity of CHCl <sub>3</sub> was |  |  |  |
| dissolved in 1N NaOH, the soln was properly                                 | specified.   |  |  |  |
| dild with deionized water and the concn of                                  |  |  |  |  |
| sulfapyridine was detd by diazotization.                                    |  |  |  |  |
|   |  |  |  |  |
|   |  |  |  |  |
|   | ESTIMATED ERROR:                                   |  |  |  |
|   | Soly: not specified.                               |  |  |  |
|   | Temp: ±1 <sup>o</sup> C (authors).                 |  |  |  |
|   |  |  |  |  |
|   | REFERENCES:  |  |  |  |
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                                     |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                        | Burlage, H. M. J. Am. Pharm. Assoc.,                       |
| pyridinyl- (sulfapyridine);                                 | <i>Sci. Ed.</i> <u>1948</u> , <i>37</i> , 345.             |
| $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]                       |  |
| (2) 2-Propanol; C <sub>3</sub> H <sub>8</sub> O; [67-63-0]  |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 25°C                                       | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfapyridine in 2-prop                       | panol at 25 <sup>°</sup> C is 0.1750 g/100 cm <sup>3</sup> |
| solution ( $7.020 \times 10^{-3} \text{ mol dm}^{-3}$ , com |  |
|   | upiiel ).  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:                                 | SOURCE AND PURITY OF MATERIALS:                            |
| Satd solns of sulfapyridine in 2-propanol                   | The sulfapyridine was manufd by Merck and                  |
| were prepd at 25 <sup>o</sup> C and definite vols of the    | was of the U.S.P. purity. The source and                   |
| solns were measured into tared dishes by                    | purity of 2-propanol were not specified.                   |
| means of standard pipets. The alcohol was                   |  |
| allowed to evap at room temp and the residue                |  |
| was dried at 105 <sup>0</sup> C. In the case of losses      |  |
| due to apparent decompn, the residue was                    |  |
| dried in a desiccator (1).                                  |  |
|   | ESTIMATED ERROR:   |
|   | Nothing specified.   |
|   |  |
|   |  |
|   | REFERENCES:<br>1. Burlage, H. M. J. Am. Pharm. Assoc.      |
|   | Sci. Ed. 1947, 36(1), 16.                                  |
|   |  |
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| COMPONENTS:           |  |             | ORIG                                    | ORIGINAL MEASUREMENTS:              |  |           |                  |      |
|-----------------------|--|-------------|---|-------------------------------------|--|-----------|------------------|------|
| (1) Benz              | enesulfon  | amide, 4-a  | mino-N-2-                               | Gut                                 | ierrez, F. H.                                |           |                  |      |
| pyri                  | dinyl-   | (sulfapyri  | dine);                                  | And                                 | les fis. quim.                               | (Madrid)  | <u>1945</u> ,    | 41,  |
| С11н                  | $C_{11}H_{11}N_{3}O_{2}S;$ [144-83-2]                              |             |   | 53                                  | 7-60.  |           |                  |      |
|                       |  | (acetone);  |   |                                     |  |           |                  |      |
| [67-                  | 64-1]  |             |   |                                     |  |           |                  |      |
| VARIABLES:            |  |             |   | PREP                                | ARED BY:                                     |           |                  |      |
|                       | Temper   | ature       |   |                                     | R. Pie                                       | kos       |                  |      |
| EXPERIMENT            | AL VALUES  | :           |   | I                                   |  |           |                  |      |
| t/ <sup>o</sup> C     | G <sup>a</sup>   | Ep          | Xg/1 <sup>c</sup>                       | mol/1<br>aceton                     |  | 1:Xg      | $1 + x_{co}^{f}$ | 2    |
| 0                     | 0.791  | 0.785       | 6.443                                   | 26                                  | 1.8  | 126.42    | 155.28           |      |
| 5                     | 0.825  | 0.818       | 6.663                                   | 27                                  | 1.9  | 121.21    | 150.15           |      |
| 10                    | 1.058  | 1.047       | 8.496                                   | 34                                  | 2.2  | 94.52     | 117.79           |      |
| 15                    | 1.447  | 1.426       | 11.534                                  | 46                                  | 3.4  | 69.11     | 86.73            |      |
| 20                    | 1.613  | 1.587       | 12.762                                  | 51                                  | 3.8  | 62.00     | 78.37            |      |
| 25                    | 1.902  | 1.866       | 14.935                                  | 60                                  | 4.4  | 52.63     | 66.93            |      |
| 30                    | 2.416  | 2.359       | 18.828                                  | 76                                  | 5.6  | 41.39     | 53.11            |      |
| 35                    | 2.999  | 2.717       | 23.191                                  | 91                                  | 7.0  | 33.44     | 43.12            |      |
| 40                    | 3.552  | 3.430       | 27.238                                  | 109                                 | 8.3  | 28.15     | 36.34            |      |
| 45                    | 4.310  | 4.132       | 32.816                                  | 132                                 | 10.0   | 23.20     | 30.47            |      |
| 50                    | 5.180  | 4.924       | 39.135                                  | 156                                 | 12.1   | 19.30     | 25.55            |      |
| $a_{G} = \frac{p}{p}$ | $a_{\rm G} = \frac{p \ 100}{P - p}$ , where p and P are weights of |             | s of solu                               | te and solution,                    | resp.  |           |                  |      |
| 1 .                   | P  | next page   |   |                                     |  | -         |                  |      |
|                       |  | f -0-       | - · · · · · · · · · · · · · · · · · · · | IARY INFO                           |  |           |                  |      |
| METHOD/API            | ADATIIS /DI  | OCEDURE .   | AUXIL:                                  |                                     | CE AND PURITY OF                             | MATERIALC |                  |      |
|                       | -  |             | contructed                              |                                     | e source of the m                            |           | as not sp        | eci- |
| 1 .                   | -  | ••          | ns, agitatio                            |                                     | fied. Pure, anhyd acetone was used. The      |           |                  |      |
| -                     |  |             | tone-satd N,                            |                                     | absence of impurities and water was confirm- |           |                  |      |
|                       | 0  |             | he solvent w                            |                                     |  |           |                  |      |
|                       | -  |             | exchangeable                            |                                     |  |           |                  |      |
|                       |  |             | <sup>3</sup> working ca                 |                                     | -  |           |                  |      |
|                       | ty were used depending on the soly of sol-                         |             |   |                                     | ed.  |           |                  |      |
| ute. Th               |  |             |   | tat.                                |  |           |                  |      |
| The vola              | The vols of acetone used were 15 or 5 cm <sup>3</sup> ,            |             |   | ESTIMATED ERROR:                    |  |           |                  |      |
| and the               | and the equilibration time was 2-2.5 h. The                        |             |   | The Sol                             |  |           |                  |      |
| satd sol              | satd solns were filtered, weighed, the sol-                        |             | sol-                                    | values not differenng in the second |  |           |                  |      |
| vent was              | distd of   | f, the res  | sidues were d                           |                                     |  | or).      |                  |      |
| at 105°C              | C, weighed   | l, and exam | nd for the pr                           | e-                                  | RENCES:                                      |           |                  |      |
| sence of              | solvated   | l acetone.  |   |                                     |  |           |                  |      |
|                       |  |             |   |                                     |  |           |                  |      |
|                       |  |             |   |                                     |  |           |                  |      |
|                       |  |             |   |                                     |  |           |                  |      |
|                       |  |             |   |                                     |  |           |                  |      |

## Continued from previous page.

 $b_E = \frac{G \ 100}{G + 100}$ ; c g/l acetone; d should be mmol/l acetone ( compiler ); eg of acetone required to dissolve 1 g of solute; fvolume ( cm<sup>3</sup>) of acetone required to dissolve 1 g of solute.

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Barber, H. J.; Wilkinson, J. H.           |
| pyridinyl- (sulfapyridine);   | Quart. J. Pharm. Pharmacol. <u>1946</u> , |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [144-83-2] | 19, 248-55.                               |
| (2) Methylcyclohexanone; C <sub>7</sub> H <sub>12</sub> O;<br>[1331-22-2]   |   |
| VARIABLES:  | PREPARED BY:                              |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                 |
| EXPERIMENTAL VALUES:  |   |
|   |   |
|   |   |
| Approximate solubility of sulfapyridin                                      |   |
| is 3.5 per cent w/v ( 0.14 mol $dm^{-3}$ s                                  | solution, compiler ).                     |
|   |   |
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|   | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:           |
| Nothing specified.  | Nothing specified.                        |
|   |   |
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|   |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                          |
|   | Nothing specified.                        |
|   | REFERENCES :                              |
|   |   |
|   |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:            |
|---|-----------------------------------|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Barber, H. J.; Wilkinson, J. H.   |
| pyridinyl- (sulfapyridine);   | Pharm. J. <u>1946</u> , 105-6.    |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S; [114-83-2] |                                   |
| (2) Methylcyclohexanone; C <sub>7</sub> H <sub>12</sub> O;                  |                                   |
| [1331-22-2]   |                                   |
|   |                                   |
| VARIABLES:  | PREPARED BY:<br>R. Piekos         |
| One temperature: 25°C   | R. FIERDS                         |
|   |                                   |
| EXPERIMENTAL VALUES:  |                                   |
|   |                                   |
|   |                                   |
|   |                                   |
|   |                                   |
|   |                                   |
|   | a=0-                              |
| Approximate solubility of sulfapyridi                                       | ne in methylcyclohexanone at 25°C |
| is 3.5 per cent w/v ( 0.14 mol dm <sup>-3</sup>                             | solution, compiler ).             |
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| AUXILIARY   | INFORMATION                       |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |
|   |                                   |
| Nothing specified.  | Nothing specified.                |
|   |                                   |
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|   |                                   |
|   | ESTIMATED ERROR:                  |
|   |                                   |
|   | Nothing specified.                |
|   |                                   |
|   | REFERENCES :                      |
|   |                                   |
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|   |                                   |

**F** 4

| 54   |   |
|--|---|
| COMPONENTS:  | ORIGINAL MEASUREMENTS:                              |
| (1) Benzenesulfonamide, 4-amino-N-3-   | Roblin, R. O., Jr.; Winnek, P. S.                   |
| pyridiny1-; C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> 0 <sub>2</sub> S; | J. Am. Chem. Soc. <u>1940</u> , 62, 1999–2002.      |
| [599-81-5 ]  |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                     |   |
|  |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
|  |   |
|  |   |
|  |   |
|  |   |
| Solubility of 4-amino-N-3-pyridinylbenz                                      | enesulfonamide in water at 37 <sup>0</sup> C        |
| is 3.3 mg/100 cm <sup>3</sup> solution (1.3 x 10 <sup>-</sup>                | $4 \text{ mol } dm^{-3}$ , compiler)                |
|  | moi dm , compiler).                                 |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                     |
| Excess sulfonamide in water was heated and                                   | The sulfonamide, mp 258-9 <sup>0</sup> C (dec), was |
| stirred on a steam bath for 30 min. The                                      | probably prepd by the authors by reacting           |
| suspension was then agitated for 24 h in a                                   | 3-aminopyridine with acetylsulfanilyl chlo-         |
| thermostat at 37 <sup>0</sup> C. A sample of the satd                        | ride followed by hydrolysis. Purity of the          |
| soln was withdrawn through a glass filter,                                   | water was not specified.                            |
| dild, and analyzed by the modified Marshall                                  |   |
| method (1) using a General Electric record-                                  |   |
| ing spectrophotometer for comparing the                                      |   |
| colors with those of the standards.  | ESTIMATED ERROR:                                    |
|  | Nothing specified.                                  |
|  | worning observed.                                   |
|  |   |
|  | REFERENCES :  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.             |

J. Pharmacol. <u>1939</u>, 66, 4.

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| COMPONENTS        | COMPONENTS: ORIGINAL MEASUREMENTS:  |             |                                |                               |  |             |                                  |  |
|-------------------|---|-------------|--------------------------------|-------------------------------|--|-------------|----------------------------------|--|
|                   |   | n, (4-amino | -N-2-pyridi                    | ny1- Gutie                    | rrez, F. H.                              |             |                                  |  |
| =                 | <ol> <li>Hydroxycalcium, (4-amino-N-2-pyridinyl-<br/>benzenesulfonamidato)-;</li> </ol>   |             |                                |                               | s fis. quim.                             | (Madrid)    | 1945, <i>41</i> ,                |  |
|                   | C <sub>11</sub> H <sub>11</sub> CaN <sub>3</sub> O <sub>3</sub> S; [77400-70-5]   |             |                                | 537-6                         | 0.                                       |             |                                  |  |
|                   | copanone (<br>-64-1]  | (acetone);  | с <sub>3<sup>H</sup>6</sub> 0; |                               |  |             |                                  |  |
| VARIABLES         |   |             |                                | PREPARE                       | D BY:                                    |             |                                  |  |
|                   | Temper  | ature       |                                |                               | R. Pie                                   | kos         |                                  |  |
|                   | remper  | ature       |                                |                               |  |             |                                  |  |
|                   | TAL VALUES  |             | _                              |                               | <u> </u>                                 |             | £                                |  |
| t/ <sup>0</sup> C | G <sup>a</sup>  | Ep          | X <sub>g</sub> /1 <sup>c</sup> | mol/1 <sup>d</sup><br>acetone | mmol/mol<br>acetone                      | 1:Xg        | 1 + X <sup>f</sup> <sub>cc</sub> |  |
| 0                 | 1.554   | 1.526       | 12.659                         | 41.5                          | 2.9                                      | 64.35       | 78.99                            |  |
| 5                 | 1.256   | 1.244       | 10.159                         | 33.0                          | 2.4                                      | 79.62       | 98.45                            |  |
| 10                | 0.843   | 0.841       | 6.809                          | 22.6                          | 1.6                                      | 117.92      | 146.86                           |  |
| 15                | 0.754   | 0.748       | 6.010                          | 19.7                          | 1.4                                      | 132.63      | 166.39                           |  |
| 20                | 0.654   | 0.649       | 5.264                          | 17.2                          | 1.2                                      | 152.91      | 189.96                           |  |
| 25                | 0.559   | 0.555       | 4.389                          | 14.4                          | 1.05                                     | 179.61      | 227.84                           |  |
| 30                | 0.543   | 0.540       | 4.232                          | 13.9                          | 1.03                                     | 184.16      | 236.29                           |  |
| 35                | 0.480   | 0.478       | 3.712                          | 12.2                          | 0.91                                     | 208.25      | 269.39                           |  |
| 40                | 0.455   | 0.453       | 3.492                          | 11.4                          | 0.86                                     | 229.80      | 286.36                           |  |
| 45                | 0.420   | 0.418       | 3.198                          | 10.5                          | 0.79                                     | 238.09      | 312.69                           |  |
| 50                | 0.383   | 0.382       | 2.894                          | 9.5                           | 0.73                                     | 261.09      | 345.51                           |  |
|                   | <sup>e</sup> g of acetone required to dissolve 1 g of solute; <sup>f</sup> volume (cm <sup>3</sup> ) of acetone required to dissolve 1 g of solute. |             |                                |                               |  |             | one                              |  |
|                   |   |             | AUXIL                          | IARY INFORMA                  | TION                                     |             |                                  |  |
| METHOD/AP         | PARATUS/PR  | OCEDURE :   |                                | SOURCE                        | AND PURITY OF                            | MATERIALS   | :                                |  |
| A specia          | al all-glas   | ss app was  | constructed                    | ena- The s                    | ource of the m                           | naterials w | as not speci-                    |  |
| bling th          | ne prepn of   | satd solr   | ns, agitation                  | n by fied.                    |  |             |                                  |  |
| bubbling          | g a stream  | of acetone  | e-satd N, fi                   | ltra- absen                   |  |             |                                  |  |
| -                 |   |             | vent without                   |                               | - confirmed by procedures of the German  |             |                                  |  |
|                   |   |             | eable dissolu                  | 1                             | Pharmacopeia VI and Spanish Pharmacopeia |             |                                  |  |
|                   | vessels used depending on the soly of   |             |                                |                               | VIII. The purity of the solute was not   |             |                                  |  |
|                   |   |             | ed in a ther                   | -                             | tied.                                    |             |                                  |  |
| •                 |   |             | used were 15                   |                               |  |             |                                  |  |
|                   |   |             | ime was 2-2                    | E Salur                       | TED ERROR:<br>measurements               | s were repe | ated until 2                     |  |
|                   |   |             | l, weighed, t                  |                               | values not d                             | liffering i | n the second                     |  |
|                   |   |             | residues were<br>l examd for t | . 1                           | decimal were<br>±0.1 <sup>0</sup> C (aut |             | (autnor).                        |  |
|                   | e of solvat   | -           |                                | the Temp:<br>REFERE           |  | hor).       |                                  |  |
| 1 - 0001100       |   |             |                                |                               |  |             |                                  |  |
|                   |   |             |                                |                               |  |             |                                  |  |
|                   |   |             |                                |                               |  |             |                                  |  |
|                   |   |             |                                |                               |  |             |                                  |  |
|                   |   |             |                                |                               |  |             |                                  |  |
|                   |   |             |                                |                               |  |             |                                  |  |

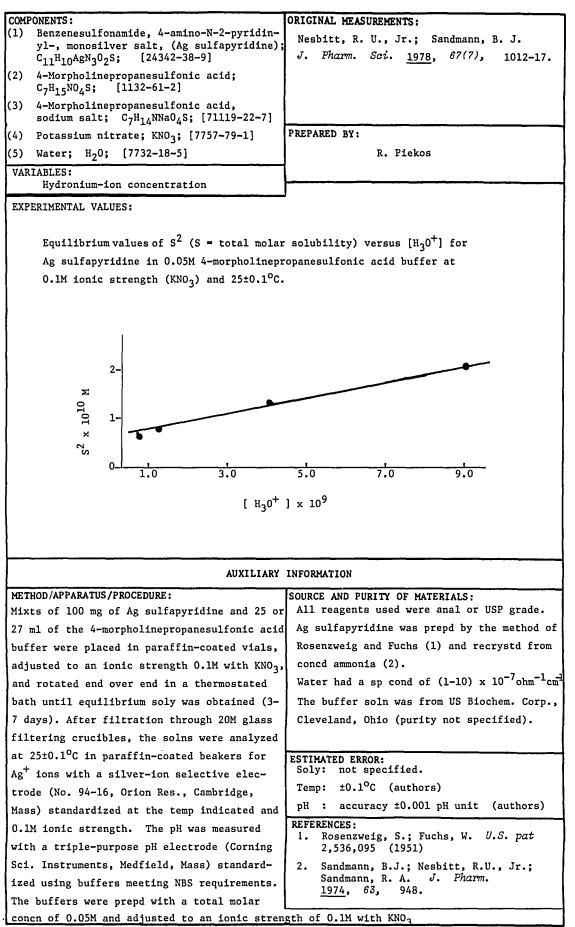
| COMPONENTS .   | 10    | DETCIMAL MEASUREN                          | ENTC .             |                                      |
|--|-------|--|--------------------|--------------------------------------|
| COMPONENTS:<br>(1) Hydroxycalcium, (4-amino-N-2-pyridinyl-   |       | ORIGINAL MEASUREMENTS:<br>Gutierrez, F. H. |                    |                                      |
| benzenesulfonamidato)-, dihydrate;   |       | -  |                    | 11 10/5                              |
| C <sub>11</sub> H <sub>11</sub> CaN <sub>3</sub> O <sub>3</sub> S·2H <sub>2</sub> O; [77400-71-6]  |       | Anales fis. q<br>537-60.                   | uım. (Madı         | rid) <u>1945</u> , 41,               |
|  |       | 557-60.                                    |                    |                                      |
| (2) 2-Propanone (acetone); C <sub>3</sub> H <sub>6</sub> O;<br>[67-64-1]   |       |  |                    |                                      |
|  |       |  |                    |                                      |
| VARIABLES:   | 1     | PREPARED BY:                               |                    |                                      |
| Temperature  |       | R.   | Piekos             |                                      |
|  |       |  |                    |                                      |
| EXPERIMENTAL VALUES:<br>t/°C G <sup>a</sup> E <sup>b</sup> X <sub>-</sub> /1 <sup>C</sup>  | mol/  | nd   | P                  | af                                   |
| t/°C G <sup>a</sup> E <sup>b</sup> X <sub>g</sub> /1 <sup>c</sup>  | aceto | •  | 1:X <sup>-</sup> g | $1 + x_{cc}^{f}$                     |
| 0 0.526 0.523 4.285  | 12.6  | 0.90                                       | 190.80             | 233.10                               |
| 5 0.531 0.528 4.295  | 12.7  |  | 188.32             | 232.49                               |
| 10 0.541 9.538 4.344   | 12.8  | 0.91                                       | 184.84             | 230.41                               |
| 15 0.648 0.644 5.165   | 15.2  |  | 154.32             | 193.61                               |
| 20 0.621 0.617 4.893   | 14.4  | 1.06                                       | 157.21             | 204.37                               |
| 25 0.588 0.585 4.617   | 13.6  |  | 170.07             | 216.57                               |
| 30 0.550 0.547 4.286   | 12.6  | 0.94                                       | 181.82             | 233.32                               |
| 35 0.520 0.517 4.021   | 11.8  | 0.89                                       | 192.31             | 248.69                               |
| 40 0.479 0.476 3.676   | 10.7  | 0.82                                       | 208.77             | 275.30                               |
| 45 0.469 0.466 3.571   | 10.5  | 0.80                                       | 213.21             | 280.03                               |
| 50 0.392 0.390 2.962   | 8.8   | 0.67                                       | 255.102            | 337.95                               |
| ${}^{b}E = \frac{G}{G+100}$ ; ${}^{c}g/l$ acetone; ${}^{d}$ should be mmol/l acetone ( compiler );<br>${}^{e}g$ of acetone required to dissolve 1 g of solute; ${}^{f}volume$ (cm <sup>3</sup> ) of acetone<br>required to dissolve 1 g of solute. |       |  |                    |                                      |
| AUXILIARY INFORMATION  |       |  |                    |                                      |
| METHOD/APPARATUS/PROCEDURE:  | f     | SOURCE AND PURITY                          | OF MATERI          | AI.S.                                |
| A special all-glass app was constructed  |       |  |                    | s was not speci-                     |
| bling the prepn of satd solns, agitation   | 1     |  |                    | was used. The                        |
| bubbling a stream of acetone-satd N, fi  | -     | absence of impu                            | rities and         | water in it was                      |
| tion, and distn off the solvent without  |       | confirmed by pr                            | ocedures of        | the German Phar-                     |
| tact with air. Two exchangeable dissol   | n     | macopeia VI and                            | Spanish Ph         | armacopeia VIII.                     |
| vessels of 15 and 8 cm <sup>3</sup> working capacit  | у     | The purity of t                            | he solute w        | as not specified.                    |
| were used depending on the soly of solu  | te.   |  |                    |                                      |
| The app was immersed in a thermostat.  | The   |  |                    |                                      |
| vols of acetone used were 15 or 5 ${ m cm}^3$ , a  | and   | ESTIMATED ERROR:                           |                    |                                      |
| the equilibration time was 2-2.5 h. The  | e     | •  |                    | epeated until 2<br>in the second de- |
| satd solns were filtered, weighed, the   | sol-  | cimal wer                                  | e obtained         |                                      |
| vent was distd off, the residues were d  | ried  |  | (author).          |                                      |
| at 105 <sup>0</sup> C, weighed, and examd for the pre  | e-    | REFERENCES :                               |                    |                                      |
| sence of solvated acetone.   |       |  |                    |                                      |
|  |       |  |                    |                                      |
|  |       |  |                    |                                      |
|  |       |  |                    |                                      |

| COMPONENTS   | •                          | / N 0  | ORIGINAL MEASUREMENTS:  |  |
|--|----------------------------|--|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyridinyl-, monosodium salt (sodium<br/>sulfapyridine); C<sub>11</sub>H<sub>10</sub>N<sub>3</sub>NaO<sub>2</sub>S;<br/>[127-57-1]</li> </ol> |                            |  | Clark, W. G.; Strakosch, E. A.;   |  |
|  |                            |  | Levitan, N.I. J. Lab. Clin. Med.  |  |
|  |                            | <sup>H</sup> 10 <sup>N</sup> 3 <sup>Na0</sup> 2 <sup>S</sup> ; | <u>1942</u> , 28, 188-9.  |  |
| -  | -                          | 10 51  |   |  |
| (2) water  | ; H <sub>2</sub> 0; [7732- |  |   |  |
| VARIABLES:   |                            |  | PREPARED BY:  |  |
|  | Temperature                |  | R. Piekos   |  |
|  |                            |  | L   |  |
| EXPERIMENT   | AL VALUES:                 |  |   |  |
|  |                            |  |   |  |
|  |                            |  |   |  |
|  |                            |  |   |  |
|  | t/ <sup>o</sup> C          |  | Solubility  |  |
| g/100 g water  |                            | g/100 g water  | mol kg <sup>-1</sup> water <sup>a</sup>   |  |
|  | 25                         | 52.0   | 1.92  |  |
|  | 37                         | 80.0   | 2.95  |  |
|  |                            |  |   |  |
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|  |                            | AUXILIARY  | INFORMATION   |  |
|  | PARATUS/PROCEDUR           |  | SOURCE AND PURITY OF MATERIALS:   |  |
|  |                            | ntainer contg excess   | Neither source nor purity of Na sulfa-  |  |
|  | • •                        | er was shaken in a   | pyridine was specified.   |  |
|  |                            | or 24 h. The satd  | CO <sub>2</sub> -free distd water was used.   |  |
|  |                            | by aspiration through  | l l l l l l l l l l l l l l l l l l l   |  |
|  |                            | stos filter stick  |   |  |
| into a w   | eighed weighing            | bottle. The entire   |   |  |
| app was 1  | kept at the tem            | p at which the compd   |   |  |
| was diss   | - 1 1 (01)                 |  |   |  |
| detd by  | olved. The amt             | dissolved was then   |   |  |
| (1), usi   |                            | dissolved was then<br>ratton and Marshall                      | ESTIMATED ERROR:  |  |
|  | the method of B            |  | ESTIMATED ERROR:<br>Soly: not specified.  |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:  |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1 <sup>0</sup> C (authors).  |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1 <sup>O</sup> C (authors).<br>REFERENCES:                               |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1 <sup>O</sup> C (authors).<br>REFERENCES:                               |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |  |
|  | the method of B            | ratton and Marshall  | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |  |

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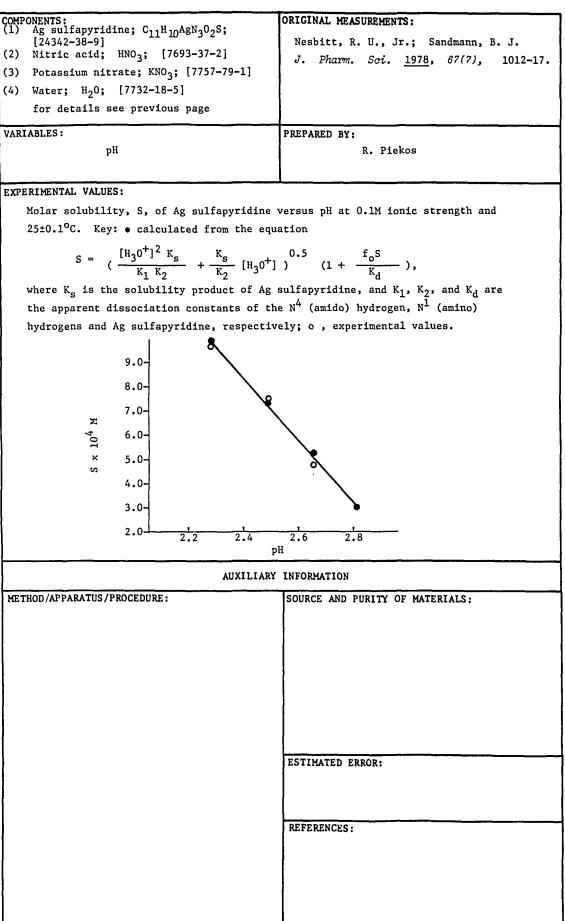
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                       |
|---|--|
| (1) Zinc, ( <u>T</u> -4)-bis(4-amino- <u>N</u> -2-pyridiny1-  |  |
| benzenesulfonamidato- <u>N<sup>N</sup>,0</u> )-   | Fox, Ch. L., Jr.; Modak, S.                                  |
| Zn(II) sulfapyridine); C <sub>22</sub> H <sub>18</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub> Zn; | Standford, J. W.; Fox, P. L.                                 |
| [71261-89-7]  | Scand. J. Plast. Reconstr. Surg.                             |
| (2) Water; $H_20$ ; [7732-18-5]   | <u>1979</u> , <i>13(1)</i> , 89-94.                          |
| (2) waser,  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperture: 28-30 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of Zn(II) sulfapyridine in w   | ater at room temperature (28-30 <sup>0</sup> C) <sup>a</sup> |
| is 44.6 mg% ( 7.94 x $10^{-4}$ mol dm <sup>-3</sup> solu  |  |
| 18 44.6 mg/ ( 7.94 x 10 · mol dm - sold   | ition, compiler ).   |
| <sup>a</sup> Value given by one of the authors (S.  | M.) in personal communication.                               |
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| AUXILIARY   | INFORMATION  |
|   |  |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                              |
| Satd soln of Zn(II) sulfapyridine was prepd   | The Zn(II) sulfapyridine was prepd by the                    |
| in water and after 24 h aliquots from the   | authors as follows: an inorg Zn salt was                     |
| clear supernatant were assayed for sulfa-   | reacted with Na salt of sulfapyridine and                    |
| pyridine content using the colorimeter me-  | the ppt was analyzed and characterized.                      |
| thod of Bratton and Marshall (1). The soly  | No details were given, however.                              |
| value was then calcd from the molecular for-  |  |
| mula.   |  |
|   |  |
|   | ESTIMATED ERROR:   |
|   |  |
|   | Nothing specified  |
|   |  |
|   | REFERENCES :   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                      |
|   | J. Biol. Chem. <u>1939</u> , 120, 537.                       |
|   | <u> </u>   |
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|   | 55   |
|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-pyridin-<br/>yl-, monosilver salt; (Ag sulfapyridine);</li> </ol>  |  |
| $C_{11}H_{10}AgN_{3}O_{2}S$ [24342-38-9]  | J. Pharm. Sci. <u>1978</u> , 67(7), 1012-17.   |
| (2) Nitric acid; HNO <sub>3</sub> ; [7697-37-2]   | <i>b. mann. bet.</i> <u>1970</u> , <i>br(7)</i> , 1012–17.   |
| (3) Potassium nitrate; KNO3; [7757-79-1]  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
|   |  |
| рН  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
| Comparison of Total Silver Sulfapyridin   | e Molar Solubility, S. Determined  |
| by the Method of Known Subtraction with   | -  |
| Silver Ion Determined by Direct Potentia  |  |
| 25±0.1°, 0.1M Ionic Strength, in Nitric   | • •  |
| 2510.1 , 0.1M IONIC Screngen, in Mitric   | were harlet  |
| рН 2.294  | рН 2.486   |
| $\frac{1}{10^{3}}$ [Ag <sup>+</sup> ] x 10 <sup>3</sup>   | $\frac{1}{5 \times 10^3}$ [Ag <sup>+</sup> ] x 10 <sup>3</sup>   |
|   |  |
| 8.973 8.143<br>8.889 8.018  | 5.472 7.425<br>5.514 7.514   |
| 9.030 8.143   | 5.579 7.632  |
| 9.030 8.143   | 5.304 7.484  |
| 8.889 8.018   | 5.514 7.514  |
| Mean 8.962 8.093  | 5.660 7.454<br>5.508 7.504   |
| pH 2.583  | рН 2.848   |
| $\frac{5 \times 10^3}{[\text{Ag}^+] \times 10^3}$   | $\frac{1}{5 \times 10^3}$ [Ag <sup>+</sup> ] × 10 <sup>3</sup>   |
| <u>5.366</u> | <u>3.031</u> 2.954   |
| 5.336 4.488   | 2.974 2.874  |
| 5.356 4.401   | 2.866 2.774  |
| 5.346 4.505   | 2.979 2.863  |
| 5.366 4.470   | 2.788 2.678  |
| 5.356 4.436<br>Mean 5.354 4.473   | 2.928 2.839 to be contd.   |
|   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| Mixts of 100 g of Ag sulfapyridine and 25 or  | All reagents were anal or USP grade. Ag  |
| 27 ml of the nitric acid buffer were placed<br>in paraffin-coated vials, adjusted to an   | sulfapyridine was prepd by the method of   |
| ionic strength 0.1M with KNO3, and rotated  | Rosenzweig and Fuchs (1) and recrystd from   |
| end over end in a thermostated bath until   | concd ammonia (2).   |
| equilibrium soly was obtained (3-7 days).<br>After filtration through 20M glass filtering   | Water had a sp cond of $(1-10) \times 10^{-7}$ ohm <sup>-1</sup>   |
| crucibles, the solns were analyzed at 25±0.1  | $cm^{-1}$ .  |
| <sup>o</sup> C in paraffin coated beakers for Ag <sup>+</sup> ions  | The source of the reagent was not specified.   |
| with a silver-ion selective electrode (No.<br>94-16, Orion Res. Cambridge, Mass) standard-  |  |
| ized at the temp indicated and 0.1M ionic   |  |
| strength. The pH was measured with a triple<br>purpose pH electrode (Corning Sci. Instru-   | ESTIMATED ERROR:<br>Soly: not specified.   |
| ments, Medfield, Mass) standardized using   | Temp: ±0.1 <sup>o</sup> C (authors)  |
| buffers meeting NBS requirements. The ni-<br>tric acid buffers were prepd by diln of  | pH : accuracy ±0.001 pH unit (authors).  |
| 0.1M HNO <sub>3</sub> and were adjusted to an ionic   | REFERENCES:  |
| strength of 0.1M with KNO <sub>3</sub> .  | 1. Rosenzweig, S.; Fuchs, W. U.S. pat.<br>2,536,095 (1951)   |
|   | <ol> <li>Sandmann, B.J.; Nesbitt, R. U., Jr.<br/>Sandmann, R. A.; J. Pharm. Sci.<br/>1974, 63, 948.</li> </ol> |
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|--------------|--------------------------------------|--|---|--|
| COMPONENTS   | :                                    |  | ORIGINAL MEASUREMEN                         | NTS:                                   |
|              |                                      |  | Nesbitt, R. U., J                           | r.; Sandmann, B. J.                    |
|              |                                      |  | J. Pharm. Sci.                              | <u>1978</u> , 67(7), 1012-17.          |
| Continue     | d from previous pa                   | age  |   |  |
|              |                                      |  |   |  |
|              |                                      |  |   |  |
| VARIABLES:   |                                      |  | PREPARED BY:                                | <sup></sup>                            |
| pH R. Piekos |                                      | Piekos                                     |   |  |
|              |                                      |  |   |  |
| EXPERIMENT   | AL VALUES:                           |  | ••••••••••••••••••••••••••••••••••••••      |  |
|              |                                      |  |   | a                                      |
|              |                                      |  | of Ag Sulfapyridine                         | r, K <sub>s</sub> , at                 |
|              | C and 0.1M Ionic :                   | [Ag <sup>+</sup> ]                         | c   | V                                      |
| PH           | fo                                   | -  | S   | $\frac{K_{s}}{1.02 \times 10^{-11}}$   |
|              | $1.418 \times 10^{-7}$               |  | $8.890 \times 10^{-3}$                      |  |
| 2.486        | $3.066 \times 10^{-7}$               | $5.508 \times 10^{-3}$                     | $7.504 \times 10^{-3}$                      | $1.27 \times 10^{-11}$                 |
| 2.583        | $4.480 \times 10^{-7}$               |  | $5.354 \times 10^{-3}$                      | $1.07 \times 10^{-11}$                 |
| 2.848        | 1.184 x 10 <sup>-6</sup>             | 2.828 x 10-3                               |   | $9.80 \times 10^{-12}$                 |
|              |                                      | <u></u>                                    | Mean  | (1.09 ± 0.13)10 <sup>-11</sup>         |
|              | afr                                  | om eq. K <sub>s</sub> = f <sub>o</sub> [Ag | +1S, where                                  |  |
|              |                                      |  |   |  |
|              | f                                    | $= (1 + \frac{[H_30^+]}{K_2} +$            | $\frac{[H_{3}0^{+}]^{2}}{-1}$               |  |
|              | 0                                    | $(1 + \frac{K_2}{K_2} + \frac{K_2}{K_2})$  | $\frac{K_1 K_2}{K_1 K_2}$                   |  |
|              | S is the tot                         | al molar solubilit                         | y, and K <sub>1</sub> and K <sub>2</sub> ar | e the                                  |
|              |                                      |  | s of the $N^4$ - (amin                      |  |
|              | and $N^1$ - (am                      | ido) hydrogens of                          | sulfapyridine, resp                         | ectively.                              |
|              | <sup>a</sup> K <sub>s</sub> reported | as mean ± SD.                              |   |  |
|              |                                      |  | to b  | e contd                                |
|              |                                      |  |   |  |
|              |                                      | AUXILIARI                                  | INFORMATION                                 |  |
| METHOD/APP   | PARATUS/PROCEDURE:                   |  | SOURCE AND PURITY                           | OF MATERIALS;                          |
|              |                                      |  |   |  |
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|              |                                      |  | ESTIMATED ERROR:                            | · · · · · · · · · · · · · · · · · · ·  |
| 1            |                                      |  |   |  |
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|              |                                      |  |   | ······                                 |
|              |                                      |  | REFERENCES:                                 |  |
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| <pre>COMPONENTS:<br/>(1) Acetamide, N-[4-[(2-pyridinylamino)-<br/>sulfonyl]phenyl]-<br/>(acetyl sulfapyridine) C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S;<br/>[19077-98-6]</pre> | EVALUATOR:<br>Anthony N. Paruta<br>Department of Pharmaceutics<br>University of Rhode Island<br>Kingston, Rhode Island, USA |
|--|---|
| (2) Water  | and<br>Ryszard Piekos<br>Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986                                   |
| CRITICAL EVALUATION:<br>Table I: Solubility of Acetyl sulfapyridin.  | th water 310V   |
|  |   |
|  | <sup>3</sup> mol dm <sup>-3</sup><br>310K   |
|  | 4   |
| 2 0  | 721   |
| 3 1  | .1  |
| 4 0  | .51   |
| r 0  | .82 - 1.1 (pH 6.6-7.2)  |

Solubility values are reported for acetyl sulfapyridine in water at 310K and are shown in Table I. These values (1-6) are quite divergent and should not be averaged, not even to an approximate degree. It would seem that a value of less that 2.0 x  $10^{-3}$  mol dm<sup>-3</sup> would be expected since the acetyl derivatives should possess a lower solubility that the unacetylated parent compound. An approximate value of 1 x  $10^{-3}$  mol dm<sup>-3</sup> can be suggested. This is about one-half the value for the parent compound.

In Table II, the solubility of acetyl sulfapyridine at 293K at various pH values are shown.

Table II: Solubility of Acetyl sulfapyridine at various pH levels, 293K

|           |     | $10^3 \text{ mol } \text{dm}^{-3}$ |
|-----------|-----|------------------------------------|
| Reference | рН  | 293K                               |
| 6         | 5.9 | 1.06                               |
| 7         | 6.0 | 0.75                               |
| 6         | 7.0 | 1.10                               |
| 7         | 7.0 | 1.0                                |
| 6         | 8.0 | 1.60                               |
| 7         | 8.0 | 1.3                                |
|           |     |                                    |

The values of Krllger-Thiemer (7) refer to two hour equilibrium which is considered inadequate. Pulver and Suter (8) do not specify the techniques used, their results, however are consistant. It appears that between a pH of 5 to 7, the solubility is about the same and an approximate value of 1 x  $10^{-3}$  mol dm<sup>-3</sup> in phosphate buffer 0.067 mol dm<sup>-3</sup> at 293K is suggested. At a pH of 8, there should be an increase in solubility due to the formation of a greater concentration of water soluble species according to the Henderson-Hasselbach expression. The approximate solubility in phosphate buffer (0.067 mol  $dm^{-3}$ ) at 293K is about 1.5 x  $10^{-3}$  mol dm<sup>-3</sup>.

**REFERENCES:** 

16, (1)

- Hug, E. Rev. soc. Argentina biol. <u>1940</u>, 16, 662-6. Lebel, H.; Schroeder, E.; Simesen, M. Acta Med. Scand. <u>1940</u>, (2)105(4), 395-410 Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P. J. Am. Chem. Soc. (3) 1940, 62, 2002-5.
- Durel, M.P.; Allinne, M. Bull. Soc. Med. Hop. Paris III <u>1941</u>, Sapozhnikova, N.V.; Postovskii, I.Ya. Zh. Prikl. Khim. <u>1944</u>, J. (4) 251-9.
- <u>1944,</u> 291–301. (5) 427-34.
- 19<u>48,</u> 205, (6) Langecker, H. Arch. Exptl. Path. Pharmakol.
- 183**,** 1942, 90-116. (7) Krüger-Thiemer, E. Arch. Dermatol. Syphilis

| COMPONENTS:<br>(1) Acetamide, N-[4-[(2-pyridinylamino)sul-<br>fonyl]phenyl]- (acetyl sulfapyridine);<br>C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6]<br>(2) Water; H <sub>2</sub> O; [7732-18-5]<br>VARIABLES:<br>One temperature: 37°C<br>EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup><br>solution, compiler ). |
|--|
| 10hy1jpichy1j       (acety1 sulfapyridine);         1140, 16, 662-6.         (2) Water; H <sub>2</sub> 0; [7732-18-5]         VARIABLES:         One temperature: 37°C         R. Piekos         EXPERIMENTAL VALUES:         Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES:<br>One temperature: 37°C<br>EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>   |
| VARIABLES:       PREPARED BY:         One temperature: 37°C       R. Piekos         EXPERIMENTAL VALUES:         Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>  |
| VARIABLES:       PREPARED BY:         One temperature: 37°C       R. Piekos         EXPERIMENTAL VALUES:         Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>  |
| One temperature: 37°C R. Piekos<br>EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>   |
| EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>  |
| EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfapyridine in water at 37°C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>  |
| Solubility of acetyl sulfapyridine in water at 37 <sup>0</sup> C is 60 mg% based on<br>sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x 10 <sup>-3</sup> mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
| sulfapyridine (62 mg% as acetyl sulfapyridine = 2.4 x $10^{-3}$ mol dm <sup>-3</sup>   |
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| solution, compiler ).  |
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| AUXILIARY INFORMATION  |
| METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS:  |
| A satd soln of acetyl sulfapyridine was Nothing specified.   |
| prepd by heating on a water bath. The soln   |
| was then cooled down to 37°C and maintained  |
| at this temp for 7 days.   |
| at this temp for / days.   |
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| ESTIMATED ERROR:   |
| ESTIMATED ERROR:<br>Nothing specified.   |
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| Nothing specified.   |
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| Nothing specified.   |
| Nothing specified.   |
| Nothing specified.   |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| <ol> <li>Acetamide, N-[4-[(2-pyridinylamino)sul-<br/>fonyl]phenyl]- (acetyl sulfapyridine);<br/>C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S; [19077-98-6]</li> </ol> | Lebel, H.; Schroeder, E.; Simesen, M.<br><i>Acta. Med. Scand.</i> <u>1940</u> , <i>105(4)</i> ,<br>395-410. |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 35 <sup>0</sup> C   | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
|  |   |
|  |   |
| Solubility of acetyl sulfapyridine in  | water at $35^{\circ}$ C is 1:1750 corresponding   |
| to 57 mg% (2.1 x $10^{-3}$ mol dm <sup>-3</sup> solut  |   |
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|  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>Nothing specified   | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified  |
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|  | ESTIMATED ERROR:  |
|  | Nothing specified   |
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|  | REFERENCES :  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                 |
|---|--|
| <ol> <li>Acetamide, N-[4-[(2-pyridinylamino)</li> </ol>   | Roblin, R. O., Jr.; Williams, J. H.;                   |
| sulfony1]pheny1]- (acetyl sulfapyridine);   | Winnek, P. S.; English, J. P.                          |
| C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6]   | J. Am. Chem. Soc. 1940, 62, 2002-5.                    |
|   |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
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| EXPERIMENTAL VALUES:  |  |
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| Solubility of acetyl sulfapyridine in   | water at $37^{\circ}$ C is 21.0 mg/100 cm <sup>3</sup> |
| solution $(7.21 \times 10^{-4} \text{ mol dm}^{-3},  compine the second second$ | ler )  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                        |
| Excess acetyl sulfapyridine in water was  | Acetyl sulfapyridine was prepd by con-                 |
|   |  |
| heated and stirred on a steam bath for 30   | densing recrystd acetylsulfanilyl chloride             |
| min. The suspension was then agitated for   | with 2-aminopyridine in a pyridine soln.               |
| 24 h in a thermostat at 37 <sup>0</sup> C. A sample of  | The crude product was recrystd from EtOH               |
| the satd soln was withdrawn through a glass   | or PrOH (2).   |
| filter, dild, and analyzed by the Marshall  | Purity of the water was not specified.                 |
|   |  |
| method (1) using a General Electric spec-   |  |
| trophotometer for comparing the colors de-  |  |
| veloped with those of the standards.  | ESTIMATED ERROR:                                       |
|   | Nothing specified                                      |
|   |  |
|   |  |
|   | REFERENCES:  |
|   | 1. Bratton, A.C.; Marshall, E. K., Jr.                 |
|   | J. Pharmacol <u>1939</u> , 66, 4.                      |
|   | 2. Winterbottom, R. J. Am. Chem. Soc.                  |
|   |  |
|   | <u>1940,</u> 62, 160.                                  |
|   |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |  |
|---|---|--|
|   |   |  |
| (1) Acetamide, N-[4[(2-pyridinylamino)sul-                                    | Durel, M. P.; Allinne, M.                 |  |
| <pre>fonyl]phenyl]- (acetyl sulfapyridine);</pre>                             | Bull. Soc. Med. Hop. Paris III            |  |
| C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6] | <u>1941,</u> 251-9.                       |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                      |   |  |
| VARIABLES:  | PREPARED BY:                              |  |
|   |   |  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                 |  |
| EXPERIMENTAL VALUES:  | I   |  |
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|   |   |  |
| Solubility of acetyl sulfapyridine in v                                       | vator at $37^{\circ}$ C is 0.32 g/liter   |  |
|   |   |  |
| $(1.1 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler }).$                |   |  |
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| AUXILIARY   | INFORMATION                               |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:           |  |
| A mixt of acetyl sulfapyridine and water                                      | Source and purity of acetyl sulfapyridine |  |
| was agitated for 24 hours at 37 <sup>0</sup> C.                               | was not specified.                        |  |
|   | Distilled water was used.                 |  |
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|   | ESTIMATED ERROR:                          |  |
|   | LOTIMIED ERION:                           |  |
|   | Nothing specified.                        |  |
| · · ·   |   |  |
|   | REFERENCES:                               |  |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Acetamide, N-[4-[(2-pyridinylamino)sul-<br/>fonyl]phenyl]- C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S;<br/>[19077-98-6]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Sapozhnikova, N. V.; Postovskii, I. Ya.<br><i>Zh. Prikl. Khim.</i> <u>1944</u> , <i>17</i> , 427-34. |
| VARIABLES:   | PREPARED BY:   |
| Temperature  | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |

#### Solubility t/<sup>o</sup>C 10<sup>3</sup> mol kg<sup>-1</sup> water<sup>a</sup> Weight% 0.0056 0.19 20 0.015 0.51 37 0.026<sup>b</sup> 0.89 50 0.067 75 2.30 99 0.20 6.88

<sup>a</sup>calculated by compiler

<sup>b</sup>calculated from the heat of dissolution

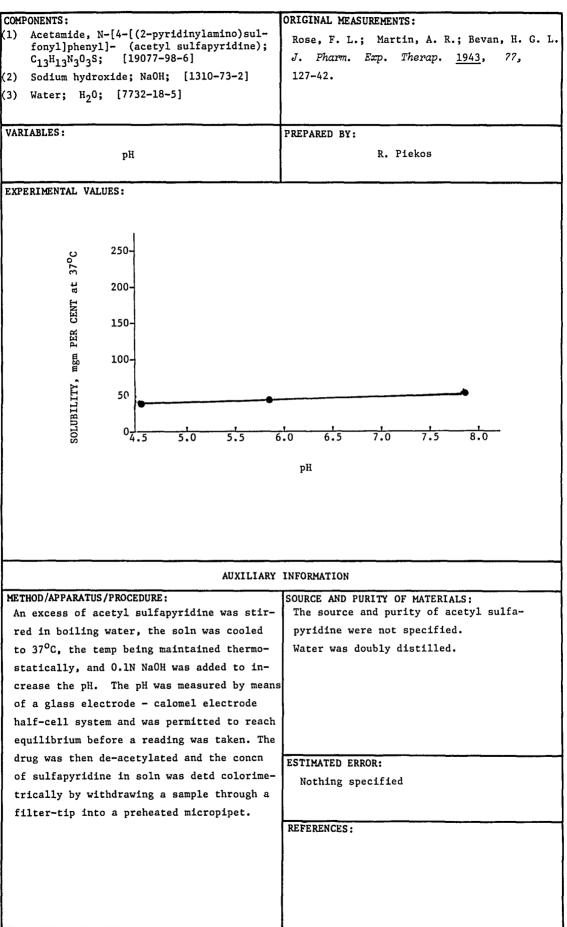
 $(10,480 \text{ cal mol}^{-1})$ 

# AUXILIARY INFORMATION

| METHOD / APPARATUS / PROCEDURE :                       | SOURCE AND PURITY OF MATERIALS:   |
|--|---|
| The sulfonamide was dissolved in water to              | Pure, recrystd sulfonamide was used.  |
| form a satd soln which was occasionally agi-           | Its mp conformed to that reported in the  |
| tated in a glass vessel immersed in a ther-            | literature.   |
| mostat. The equilibrium was usually attain-            | Purity of the water was not specified.  |
| ed after 1 h. Five -'to 100-cm <sup>3</sup> samples of |   |
| the satd soln were placed in Pt crucibles or           |   |
| dishes and evapd to dryness at temps lower             |   |
| than 110-115 <sup>0</sup> C. The residue was dried to  |   |
| const wt at 105-110 <sup>0</sup> C and weighed.        | ESTIMATED ERROR:<br>Soly: quite reliable results were obtained<br>over the temp range 20-75°C. At higher temps<br>the accuracy was poor due to evapn of water<br>during sampling (authors). Temp: ±0.05°C<br>(authors)<br>REFERENCES: |

| COMPONENTS:   |                     | ORIGINAL MEASUREMENTS:  |
|---|---------------------|---|
| (1) Acetamide, N-[4-[(2-pyr   |                     | Langecker, H.   |
| fonyl]phenyl]- (acety)  |                     | Arch. Exptl. Path. Pharmakol. <u>1948</u> ,   |
| C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-9 | 8-6]                | 205, 291-301.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-                                    | -5]                 |   |
| VARIABLES:  |                     | PREPARED BY:  |
| pH  |                     | R. Piekos   |
| EXPERIMENTAL VALUES:  |                     | L   |
|   |                     |   |
|   |                     |   |
|   |                     |   |
|   | Solubili            | ty at 37 <sup>0</sup> C   |
| рН  | mg% 10 <sup>3</sup> | mol dm <sup>-3</sup> a  |
| 7.2   | 31 3                | 1.1   |
| 6.6   | 24 (                | 0.82  |
|   | <u></u>             |   |
| a   | Calculated by comp  | ller .  |
|   |                     |   |
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|   | AUXILIARY           | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   |                     | SOURCE AND PURITY OF MATERIALS:   |
| An excess of acetyl sulfapy   | ridine in water     | Source and purity of the materials were   |
| was boiled for 1 h in a sea   |                     | not specified.  |
| by keeping the soln at 37°C   | . Before assay-     |   |
| ing, the solute was treated   |                     |   |
| soln (1) to cleave the acet   |                     |   |
| sulfapyridine was detd colo   |                     |   |
| the method of Bratton and M   |                     |   |
| a Havemann colorimeter (3),   |                     |   |
| microanal detn of the solid   | residue.            | ESTIMATED ERROR:  |
|   |                     | Nothing specified   |
|   | •                   |   |
|   |                     | REFERENCES :  |
|   |                     | <ol> <li>Scudi, J. V. J. Lab. Clin. Med. <u>1940</u>,<br/>25, 404.</li> </ol>             |
|   |                     | 2. Bratton, A. G.; Marshall, E. K., Jr.   |
|   |                     | J. Biol. Chem. <u>1939</u> , 128, 537.<br>3. Havemann, R. Klin. Wochenschr. <u>1940</u> , |
|   |                     | p. 503.   |





| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Acetamide, N-[4-[(2-pyridinylamino)sul-   | Krüger-Thiemer, E.   |
| fonyl]phenyl]- (acetyl sulfapyridine);<br>C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6] | Arch. Dermatol. Syphilis <u>1942</u> , 183,                        |
| 13 13 3 3   | 90-116.  |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> [7558-94-4]                                     |  |
| (3) Water; $H_20$ ; [7732-18-5]   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: ca 20°C; one pH: 8.74  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  | I  |
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| Solubility of acetyl sulfapyridine in   |  |
| pH 8.74 at room temperature ( about 20  | $0^{\circ}$ C ) is 0.042 g% ( 1.4 x $10^{-3}$ mol dm <sup>-3</sup> |
| solution, compiler ).   |  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                                    |
|   |  |
| Acetyl sulfapyridine (0.5 g) was dissolved  | Acetyl sulfapyridine (source not specified)                        |
| in 10 cm <sup>3</sup> of the 0.705M (10%) Na <sub>2</sub> HPO <sub>4</sub> soln   | gave no coloration upon diazotization of                           |
| of pH 8.74, shaken for 2 h at room temp (a-   | its satd soln, thus showing absence of sul-                        |
| bout 20°C), and filtered. The filtrate was  | fapyridine. The source and purity of the                           |
| treated with equal vol of 2N HCl and reflux-  | - remaining materials were not specified.                          |
| ed for 15 min. After proper diln, a 1-cm <sup>3</sup>   |  |
| aliquot was withdrawn, acidified, cooled,   |  |
| and the sulfonamide content was detd colori-  |  |
| metrically (as sulfapyridine) by the Mar-   | ESTIMATED ERROR:<br>Soly: precision ±5% (author).                  |
| shall method modified by Kimmig (1) using   | Temp: not specified.   |
| an Authenrieth colorimeter. The pH was detd   | nH + +0.05 nH unit (author)  |
| On an ultraionograph using a glass electrode  | REFERENCES :   |
|   |  |
|   | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> ,                        |
|   | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398                          |
|   |  |
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| 7 | 2 |
|---|---|
| 1 | 2 |

| 72  |   |
|---|---|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
| <ul> <li>Acetamide, N-[4-[(-pyridinylamir<br/>fonyl]phenyl]- (acetyl sulfapyr<br/>C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S; [19077-98-6]</li> </ul>  | ridine); Krüger-Thiemer, E.   |
| <ul> <li>(2) Phosphoric acid, monopotassium s<br/>KH<sub>2</sub>PO<sub>4</sub> [7778-77-0]</li> </ul>   | salt; Arch. Dermatol. Syphilis <u>1942</u> , 183,<br>90-116.  |
| (3) Water; $H_20$ ; [7732-18-5]   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: ca 20°C; one pH:   | 4.37 R. Piekos  |
| EXPERIMENTAL VALUES:  |   |
|   | idine in a 0.735M (10%) $KH_2PO_4$ solution of pH<br>out 20°C ) is 0.020 g% ( 6.9 x $10^{-4}$ mol dm <sup>-3</sup>  |
|   | WXILIARY INFORMATION  |
|   |   |
| METHOD/APPARATUS/PROCEDURE:<br>Acetyl sulfapyridine (0.5 g) was dia<br>in 10 cm <sup>3</sup> of the 0.735M (10%) KH <sub>2</sub> PO,<br>shaken for 2 h at room temp (about 2<br>and filtered. The filtrate was treat<br>equal vol of 2N HCl, and refluxed for<br>After proper diln, a 1-cm <sup>3</sup> aliquot y<br>drawn, acidified, cooled, and the su<br>amide content was detd colorimetrica | 4 soln, gave no coloration upon diazotization of its<br>20°C), satd soln, thus showing absence of sulfa-<br>ated with pyridine. The source and purity of the re-<br>or 15 min maining materials were not specified.<br>was with-<br>ulfon-<br>ally by |
| the Marshall method modified by Kim<br>using an Authenrieth colorimeter.<br>was detd on an ultraionograph using<br>electrode.   | The pH Soly: precision ±5% (author).  |
|   |   |

| COMPONENTS :  |  |   |                | ORIG   | INAL MEASUREME   | NTS :               |  |
|---|--|---|----------------|--------|--|---------------------|--|
| fonyl]pl<br>C <sub>13</sub> H <sub>13</sub> N<br>(2) Phosphor<br>Na <sub>2</sub> HPO <sub>4</sub> | de, N-[4-[(2-<br>heny1]- (ace<br>303S; [1907<br>ric acid, dis<br>; [7558-94- | tyl sulfapy<br>7-98-6]<br>odium salt;<br>4] | ridine)        | - Krł  | lger-Thiemer E<br>bh. Dermtol.<br>-116.                      | •                   | <u>1942</u> , <i>183</i> ,                                 |
|   | ric acid, mon<br>[7778-77-0]   |   | sait;          |        |  |                     |  |
|   | H <sub>2</sub> 0; [7732-   |   |                | PREP   | ARED BY:   |                     |  |
| VARIABLES:  | Temperature;   | рН  |                |        | R. P   | iekos               |  |
| • •   | on of 1/15M ;<br>fer solutions   | •••   | _ pH           | Room t | So<br>emp (ca 20 <sup>0</sup> C)                             | lubility            | 37°C   |
| Na2HPO4   | кн <sub>2</sub> ро <sub>4</sub>  | %Content                                    |                | g%     | 10 <sup>3</sup> mol dm <sup>-</sup><br>solution <sup>a</sup> | 3 g%                | 10 <sup>3</sup> mol dm <sup>-3</sup> solution <sup>a</sup> |
| 1   |  |   |                |        |  |                     |  |
| 1.0   | 99.0   | 0.91  | 4.944          | 0.030  | 1.03   | -                   | -  |
| 1.0<br>10.0   | 99.0<br>90.0   | 0.91<br>0.91                                | 4.944<br>5.906 |        | 1.03<br>1.06   | -<br>0.030          | -<br>1.03  |
|   |  |   |                | 0.031  |  | -<br>0.030<br>0.033 | -<br>1.03<br>1.13  |

<sup>a</sup>Calculated by compiler.

94.7

<sup>b</sup>Molar content; 10% buffer solution.

5.3 0.95 8.018 0.047 1.60

### AUXILIARY INFORMATION

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| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;              |
|--|--|
| Acetyl sulfapyridine (0.5 g) was dissolved                             | Acetyl sulfapyridine (source not specified)  |
| in 10 $cm^3$ of a buffer soln, shaken for 2 h                          | gave no coloration upon diazotization of its |
| at 20 <sup>o</sup> C (or left for 48 h at 37 <sup>o</sup> C), and fil- | satd soln, thus showing absence of sulfa-    |
| tered at respective temp. The filtrate was                             | pyridine. The source and purity of the re-   |
| treated with equal vol of 2N HCl and reflux-                           | maining materials were not specified.        |
| ed for 15 min. After proper diln, a 1-cm <sup>3</sup>                  |  |
| aliquot was withdrawn, acidified, cooled,                              |  |
| and the sulfonamide content was detd (as                               |  |
| sulfapyridine) colorimetrically by the Mar-                            | ESTIMATED ERROR:                             |
| shall method modified by Kimmig (1) using an                           |  |
| Authenrieth colorimeter. The pH was detd on                            | Temp: not specified.                         |
| an ultraionograph using a glass electrode.                             | pH : ±0.05 pH unit (author).                 |
|  | REFERENCES:                                  |
|  | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> ,  |
|  | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.   |
|  |  |
|  |  |
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| COMP<br>(1) | fonyl]phenyl]  | [4-[(2-pyridinylamino)su<br>- (acetyl sulfapyridine  | e); Pulver, R.; Suter, R.   |
|-------------|--|--|---|
| (2)         | C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6]<br>(2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] |  | Schweiz. Med. Wochenschr<br>73(13), 403-8.  |
| (3)         |  | id, monopotassium salt;                              |   |
| (4)         |  | [7732-18-5]  | PREPARED BY:  |
|             |  |  |   |
|             | IABLES:<br>ERIMENTAL VALUE   | рН<br>5:   | R. Piekos   |
|             |  | Solubility of acetyl                                 | R. Piekos<br>sulfapyridine in M/15<br>according to Sørensen ) at 20 <sup>0</sup> C                    |
|             | ERIMENTAL VALUE  | Solubility of acetyl                                 | sulfapyridine in M/15   |
|             | ERIMENTAL VALUE  | Solubility of acetyl<br>phosphate buffers ( a        | sulfapyridine in M/15<br>according to Sørensen ) at 20 <sup>0</sup> C                                 |
|             | PH   | Solubility of acetyl<br>phosphate buffers ( a<br>mg% | sulfapyridine in M/15<br>according to Sørensen ) at $20^{\circ}$ C<br>$10^{3}$ mol dm <sup>-3</sup> a |

<u>1943</u>,

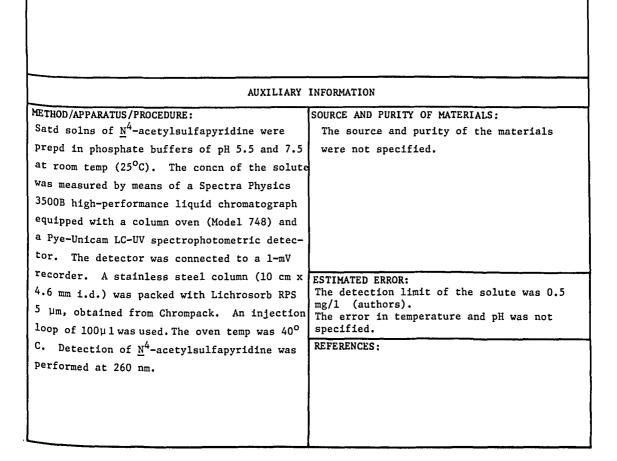
| A                                | UXILIARY INFORMATION            |
|----------------------------------|---------------------------------|
| METHOD / APPARATUS / PROCEDURE : | SOURCE AND PURITY OF MATERIALS: |
| Nothing specified                | Nothing specified               |
|                                  |                                 |
|                                  |                                 |
|                                  |                                 |
|                                  |                                 |
|                                  |                                 |
|                                  | ESTIMATED ERROR:                |
|                                  | Nothing specified               |
|                                  |                                 |
|                                  | REFERENCES:                     |
|                                  |                                 |
|                                  |                                 |
|                                  |                                 |
|                                  |                                 |

| COMPO | ONENTS:  | ORIGINAL MEASUREMENTS:                                       |
|-------|--|--|
| (1)   | Acetamide, N-[4-[(2-pyridinylamino)-<br>sulfonyl]phenyl]- ( <u>N</u> <sup>4</sup> -acetyl sulfa-<br>pyridine); C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6] | Hekster, Y. A.; Vree, T. B.<br>Damsma, J. E.; Friesen, W. T. |
| (2)   | Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | J. Antimicrob. Chemother. <u>1981</u> , 8, 133-44.           |
| (3)   | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |  |
| (4)   | Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:   |
| VARI  | ABLE: pH   | R. Piekos  |

EXPERIMENTAL VALUES:

|     | Sol                         | ubility at 25°C |
|-----|-----------------------------|-----------------|
| рН  | $mg/1$ $10^3 mol dm^{-3} a$ |                 |
| 5.5 | 313                         | 1.07            |
| 7.5 | 440                         | 1.51            |

<sup>a</sup>Calculated by compiler



| COMPONENTS :  | ORIGINAL MEASUREMENTS:                                |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(5-bromo-</li> </ol>                       |   |
| 2-pyridinyl)-; C <sub>11</sub> H <sub>10</sub> BrN <sub>3</sub> 0 <sub>2</sub> S; | Roblin, R. O., Jr.; Winnek, P. S.                     |
| [16805-99-5]  | J. Am. Chem. Soc. <u>1940</u> , 62,                   |
| [10805-99-5]  | 1999-2002.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37°C   | R. Piekos   |
|   |   |
|   | L   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of 4-amino-N-(5-bromo-2-py   | ridinvl)benzenesulfonamide in water                   |
|   |   |
| at $37^{\circ}$ C is 3.8 mg/100 cm <sup>3</sup> solution (                        | 1.2 x $10^{-4}$ mol dm <sup>-3</sup> , compiler ).    |
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|   | INFORMATION   |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                       |
| Excess sulfonamide in water was heated and  | The sulfonamide, mp 199-200 <sup>0</sup> C (cor), was |
| stirred on a steam bath for 30 min. The   | prepd by the authors. Anal: %C 40.2 (calcd            |
| suspension was then agitated for 24 h in a  | 40.2); %H 3.0 (3.0).                                  |
| thermostat at 37°C. A sample of the satd  | Purity of the water was not specified.                |
| -   | raries of the water was not specified.                |
| soln was withdrawn through a glass filter,  |   |
| dild, and analyzed by the modified Marshall                                       |   |
| method (1) using a General Electric record-                                       |   |
| ing spectrophotometer for comparing the co-                                       |   |
| lors with those of the standards.   | ESTIMATED ERROR:                                      |
|   |   |
|   | Nothing specified                                     |
|   |   |
|   | REFERENCES:   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.               |
|   |   |
|   | J. Pharmacol. <u>1939</u> , 66, 4.                    |
|   | 1   |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(5-iodo-                                     | Roblin, R. O., Jr.; Winnek P. S.<br>J. Am. Chem. Soc. 1940, 62,                 |
| 2-pyridinyl); C <sub>11</sub> H <sub>10</sub> N <sub>3</sub> 0 <sub>2</sub> S; | J. Am. Chem. Soc. <u>1940</u> , 62,<br>1990-2002.                               |
| [71119-21-6]   | 1330-2002.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                       |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
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|  |   |
|  |   |
| Solubility of 4-amino-N(5-iodo-2-pyric   |   |
| at $37^{\circ}$ C is 1.3 mg/100 cm <sup>3</sup> solution ( 2                   | $3.5 \times 10^{-5} \text{ mol dm}^{-3}$ , compiler ).                          |
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|  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and      | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 220-1°C (cor), was prepd |
| stirred on a steam bath for 30 min. The  | by the authors. Anal: %C 35.2 (calcd  |
| suspension was then agitated for 24 h in a                                     | 35.2); %H 2.5 (2.7). Purity of the water  |
| thermostat at 37°C. A sample of the satd                                       | was not specified.  |
| soln was withdrawn through a glass filter,                                     |   |
| dild, and analyzed by the modified Marshall                                    |   |
| method (1) using a General Electric record-                                    |   |
| ing spectrophotometer for comparing the  |   |
| colors with those of the standards.  | ESTIMATED ERROR:  |
|  | Nothing specified   |
|  | worling spectree  |
|  |   |
|  | REFERENCES :  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|  | J. Pharmacol. <u>1939</u> , 66, 4.  |
|  |   |
|  |   |

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|----|

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(5-nitro-                      | ORIGINAL MEASUREMENTS:                         |
|---|--|
|   | Roblin, R. O., Jr.; Winnek, P. S.              |
| 2-pyridinyl)-; C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>4</sub> S; | J. Am. Chem. Soc. <u>1940</u> , 62, 1999-2002. |
| [39588-36-8]<br>(2) Water; H <sub>2</sub> O; [7732-18-5]                        |  |
| (2) water; $n_20; [7732-16-5]$  |  |
|   |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                      |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(5-nitro-2-py   | ridinyl)benzenesulfonamide in                  |
| water at 37°C is 3.7 mg/100 cm <sup>3</sup> solut                               | ion (1.3 x $10^{-4}$ mol dm <sup>-3</sup> .    |
| compiler ).   |  |
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| AUXILIARY   | INFORMATION                                    |
| METHOD/APPARATUS/PROCEDURE:   |  |
|   | SOURCE AND PURITY OF MATERIALS:                |
| Excess sulfonamide in water was heated and                                      | The sulfonamide, mp 220-1°C (cor) was prepd    |
| stirred on a steam bath for 30 min. The   | by the authors. Anal: %C 45.0 (calcd           |
| suspension was then agitated for 24 h in a                                      | 44.9); %H 3.2 (3.4).                           |
| thermostat at 37°C. A sample of the satd  | Purity of the water was not specified.         |
| soln was withdrawn through a glass filter,                                      |  |
| dild, and analyzed by the modified Marshall                                     |  |
| method (1) using a General Electric record-                                     |  |
| ing spectrophotometer for comparing the   |  |
| colors with those of the standards.   | ESTIMATED ERROR:                               |
|   | Nothing specified                              |
|   |  |
|   | REFERENCES :                                   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.        |
| 1   | J. Pharmacol. <u>1939</u> , 66, 4.             |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                 |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(5-amino-   | Roblin, R. O., Jr.; Winnek, P. S.                      |
| 2-pyridiny1)-; C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>2</sub> S;                     | J. Am. Chem. Soc. <u>1940,</u> 62, 1999-2002.          |
| [16840-28-1]  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(5-amino-2-pyrid  | dinyl)benzenesulfonamide in water                      |
| at $37^{\circ}$ C is 418 mg/100 cm <sup>3</sup> solution ( 1.                                       | $58 \times 10^{-2}$ mol dm <sup>-3</sup> , compiler ). |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                        |
| Excess sulfonamide in water was heated and  | The sulfonamide, mp 157-8°C (cor), was                 |
| stirred on a steam bath for 30 min. The sus-  |  |
| pension was then agitated for 24 h in a there<br>months at $27^{\circ}$ A same to of the satisfiest | 1  |
| mostat at 37°C. A sample of the satd soln   | Purity of the water was not specified.                 |
| was withdrawn through a glass filter, dild,   |  |
| and analyzed by the modified Marshall method  |  |
| (1) using a General Electric recording spec-<br>trophotometer for comparing the colors with         |  |
| those of the standards.   |  |
|   | ESTIMATED ERROR:                                       |
|   | Nothing specified                                      |
|   |  |
|   | REFERENCES :   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                |
|   | J. Pharmacol. <u>1939</u> , 66, 4.                     |
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|  | ORIGINAL MEASUREMENTS:  |
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| <ol> <li>Benzenesulfonamide, 4-amino-N-(3-ethoxy-<br/>2-pyridiny1)-; C<sub>13</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>S;</li> </ol> | Roblin, R. O., Jr.; Winnek, P. S.   |
| [71119-19-2]   | J. Am. Chem. Soc. <u>1940</u> , 62, 1999–2002.                              |
| (2) Water; H <sub>2</sub> O; [7732-18-5]   |   |
|  |   |
| VARIABLES:   |   |
|  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-(3-ethoxy-2-py   |   |
| water at $37^{\circ}$ C is 23.5 mg/100 cm <sup>3</sup> ( 8.47  | $7 \times 10^{-4} \text{ mol dm}^{-3}$ , compiler ).                        |
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|  | INFORMATION   |
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| METHOD/APPARATUS/PROCEDURE:<br>Excesss sulfonamide in water was heated and   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 198-200°C (cor), was |
|  |   |
| stirred on a steam bath for 30 min. The sus-   | prepd by the authors. Anal: %C 53.0   |
| pension was then agitated for 24 h in a ther-  | (calcd 53.2); %H 5.0 (5.1).   |
| mostat at 37 <sup>0</sup> C. A sample of the satd soln   | Purity of the water was not specified.                                      |
| was withdrawn through a glass filter, dild,  |   |
| and analyzed by the modified Marshall method   |   |
| (1) using a General Electric recording spec-   | ESTIMATED ERROR:  |
| trophotometer for comparing the colors with  | Nothing specified   |
| those of the standards.  |   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                                     |
|  |   |
|  | J. Pharmacol. <u>1939</u> , 66, 4.  |
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|   | ORIGINAL MEASUREMENTS:                     |  |
|---|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-[1(2-                        |  |  |
| hydroxyethyl)-1,2-dihydro-2-pyridinyl]-;                                      | Shepherd, R. G.; Bratton, A. C.;           |  |
|   | Blanchard, K. C. J. Am. Chem. Soc.         |  |
| C <sub>13</sub> H <sub>17</sub> N <sub>3</sub> O <sub>3</sub> S; [71119-27-2] | <u>1942,</u> 64, 2532-7.                   |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                      |  |  |
|   |  |  |
| VARIABLES:  | PREPARED BY:                               |  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                  |  |
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| EXPERIMENTAL VALUES:  |  |  |
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| Solubility of 4-amino-N-[1-(2-hydroxyet                                       | hv1)=1 2-dihvdro-2-nvridinv1]-             |  |
| benzenesulfonamide at 37°C is 440 mg% (                                       |  |  |
| -   | 1.5 x 10 - mol dm - solution,              |  |
| compiler ).   |  |  |
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|   | INFORMATION                                |  |
| AUXILIARY INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:            |  |
| The sulfonamide was assayed colorimetri-                                      | The sulfonamide, m.p. 184-5°C, was synthe- |  |
| cally (1). No details were reported.  | sized by the authors. Analysis: %C 53.41   |  |
| carry (1). No decarrs were reported.  | · · · · ·                                  |  |
|   | (calcd 53.23); %H 5.18 (5.15), %N 14.35    |  |
|   | (14.33). Colorimetric factor 0.630         |  |
|   | (calcd 0.587).                             |  |
|   | Purity of the water was not specified.     |  |
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| [   | ESTIMATED ERROR:                           |  |
| [   | BUILTED ERROR:                             |  |
|   | Nothing specified.                         |  |
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|   | REFERENCES:                                |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |  |
| 1   | J. Biol. Chem. <u>1939</u> , 128, 537.     |  |
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| COMPO | NENTS:  | ORIGINAL MEASUREMENTS:   |
|-------|---|--|
| (1)   | Benzenesulfonamide, 4-amino-N-(1-   | Shepherd, R. G.; Bratton, A. C.;   |
|       | carboxymethy1-1,2-dihydro-2-pyridiny1)-;                                      | Blanchard, K. C., J. Am. Chem. Soc.  |
|       | C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>4</sub> S; [71119-28-3] | <u>1942</u> , <i>64</i> , 2532-7.  |
| (2)   | Water; H <sub>2</sub> 0; [7732-18-5]  |  |
|       |   |  |
| VARI  | ABLES:  | PREPARED BY:   |
|       | One temperature: 37 <sup>0</sup> C  | R. Piekos  |
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| EXPE  | RIMENTAL VALUES:  |  |
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| 1     | Solubility of 4-amino-N-(1-carboxymethyl                                      | -1,2-dihydro-2-pyridinyl)benzene-  |
|       | sulfonamide in water at 37 <sup>0</sup> C is 754 mg%                          | $(2.45 \times 10^{-2} \text{ mol dm}^{-3} \text{ solution}.$   |
|       |   |  |
|       | compiler ).   |  |
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|       | AUXILIARY   | INFORMATION  |
| METT  | IOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| 1     | sulfonamide was assayed colorimetrically                                      |  |
|       | . No details were reported.   | thesized by the authors. Analysis: %C  |
|       |   | 50.75 (calcd 50.81), %H 4.37 (4.26), %N  |
|       |   | 13.59 (13.67). Colorimetric factor 0.570   |
| }     |   | (calcd 0.560). Purity of the water was not   |
|       |   | specified.   |
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| 1     |   | ESTIMATED ERROR:   |
|       |   | Nothing specified  |
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| 1     |   | REFERENCES:  |
| 1     |   | 1. Bratton, A. C.; Marshall, E. K., Jr.  |
|       |   | J. Biol. Chem. <u>1939</u> , 128, 537.   |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(2-chloro-                  | Roblin, R. O., Jr.; Winnek, P. S.         |
| 5-pyridiny1)-; $C_{11}H_{10}CIN_{3}O_{2}S;$                   | J. Am. Chem. Soc. <u>1940</u> , 62, 1999- |
| [34392-82-0]  | 2002.                                     |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                      |   |
|   |   |
| VARIABLES:  | PREPARED BY:                              |
| One temperature: 37 <sup>0</sup> C                            | R. Piekos                                 |
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| EXPERIMENTAL VALUES:  |   |
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| Solubility of 4-amino-N-(2-chloro-5-pyr                       | idinyl)benzenesulfonamide in              |
| water at $37^{\circ}$ C is 18.0 mg/100 cm <sup>3</sup> ( 6.34 |   |
| water at 57 6 15 15.0 mg/100 cm (0.34                         | A 10 moi um , compilei ).                 |
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| AUXILIARY   | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:                                   | SOURCE AND PURITY OF MATERIALS:           |
| An excess of the sulfonamide was heated and                   | The sulfonamide: m.p. (cor.) 186-7°C.     |
| stirred on a steam bath for 30 min. The sus                   | 1   |
| pension was then agitated for 24 h at $37^{\circ}C$ .         |   |
| A sample of the satd. soln. was withdrawn                     |   |
| through a sintered glass filter into a bot-                   |   |
| tle held at the same temp. An aliquot of the                  |   |
| satd. soln. was dild. and analyzed by the                     |   |
| Marshall method (1). A General Electric                       |   |
| recording spectrophotometer was used in                       | ESTIMATED ERROR:                          |
| comparing the colors developed with those                     | None specified                            |
| of the standards.   |   |
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|   | REFERENCES:                               |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|   | J. Pharmacol. <u>1939</u> , 66, 4.        |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                                |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(2-bromo-                  | Roblin, R. O., Jr.; Winnek, P. S.                     |
| 5-pyridiny1)-; $C_{11}H_{10}BrN_{3}O_{2}S;$                  | J. Am. Chem. Soc. <u>1940</u> , 62, 1999-             |
| [17103-43-4]   | 2002.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                     |   |
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| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C                           | R. Piekos   |
| one temperature. 57 0  |   |
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| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-(2-bromo-5-pyr                       |   |
| water at $37^{\circ}$ C is 12.2 mg/100 cm <sup>3</sup> ( 3.7 | $2 \times 10^{-4}$ mol dm <sup>-3</sup> - compiler ). |
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|  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:                                  | SOURCE AND PURITY OF MATERIALS:                       |
| An excess of the sulfonamide was heated and                  | The sulfonamide: m.p. (cor.) 196-7°C.                 |
| stirred on a steam bath for 30 min. The                      | Purity of the water was not specified.                |
| suspension was then agitated for 24 h at                     |   |
| 37 <sup>0</sup> C. A sample of the satd. soln. was with-     | 1   |
| drawn through a sintered glass filter into                   |   |
| a bottle held at the same temp. An aliquot                   |   |
| of the satd soln was dild and analyzed by                    |   |
| the Marshall method (1). A General Electri                   | c   |
| recording spectrophotometer was used in com-                 |   |
| paring the colors developed with those of                    |   |
| the standards.   | None specified  |
|  |   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.               |
|  | J. Pharmacol. 1939, 66, 4.                            |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2-   | Roblin, R. O., Jr.; Winnek, P. S.                        |
| hydroxy-5-pyridiny1)-;  | J. Am. Chem. Soc. <u>1940</u> , 62, 1999-                |
| C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub> S; [71119-20-5] | 2002.  |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                      |  |
| (2) water, 120, [//32-10-3]   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
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| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(2-hydroxy-5-p  | yridinyl)benzenesulfonamide in                           |
| water at 37 <sup>°</sup> C is 258 mg/100 cm <sup>3</sup> soluti               | on ( $9.72 \times 10^{-3} \text{ mol } \text{dm}^{-3}$ , |
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| compiler ).   |  |
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|   | INFORMATION  |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                          |
| Excess sulfonamide in water was heated and                                    | The sulfonamide, mp 243-4°C (dec, cor) was               |
| stirred on a steam bath for 30 min. The                                       | prepd by the authors. Anal: %C 49.8 (calcd               |
| suspension was then agitated for 24 h in a                                    | 49.8); ZH 4.2 (4.2).                                     |
| thermostat at 37 <sup>0</sup> C. A sample of the satd                         | Purity of the water was not specified.                   |
| soln was withdrawn through a glass filter,                                    |  |
| dild, and analyzed by the modified Marshall                                   | . }  |
| method (1) using a General Electric record-                                   |  |
| ing spectrophotometer for comparing colors                                    |  |
| with those of the standards.  | ESTIMATED ERROR:   |
|   | Nothing specified  |
|   | Nothing specified  |
|   |  |
|   | REFERENCES :   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                  |
|   | J. Pharmacol. <u>1939</u> , 66, 4.                       |
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                           |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2-amino-                                     | Roblin, R. O., Jr.; Winnek, P. S.                |
| 5-pyridiny1)-; C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; | J. Am. Chem. Soc. <u>1940</u> , 62, 1999-2002.   |
| [17103-45-6]  |  |
|   |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                     |
| One temperature: 37°C   | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Colubility of A andre N (2 andre 5 and  |  |
| Solubility of 4-amino-N-(2-amino-5-pyr  |  |
| water at 37 <sup>0</sup> C is 129 mg/100 cm <sup>3</sup> soluti                 | on ( $4.88 \times 10^{-3} \text{ mol dm}^{-3}$ , |
| compiler).  |  |
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| AUXILIARY   | INFORMATION                                      |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                  |
| Excess sulfonamide in water was heated and                                      | The sulfonamide, mp 207-8°C (cor), was           |
| stirred on a steam bath for 30 min. The   | probably that synthesized by Winterbottom        |
| suspension was then agitated for 24 h in a                                      | (2). Purity of the water was not specified.      |
| thermostat at 37 <sup>0</sup> C. A sample of the satd                           |  |
| soln was withdrawn through glass filter,  |  |
| dild, and analyzed by the modified Marshall                                     |  |
| method (1) using a General Electric record-                                     |  |
| ing spectrophotometer for comparing the   |  |
| colors with those of the standards.   | ESTIMATED ERROR:                                 |
|   |  |
|   | Nothing specified                                |
|   |  |
|   | REFERENCES :                                     |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.          |
|   | J. Pharmacol. 1939, 66, 4.                       |
|   | 2. Winterbottom, R. J. Am. Chem. Soc.            |
|   | <u>1940</u> , <i>62</i> , 160.                   |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                                |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(2-  | Roblin, R. O., Jr.; Winnek, P. S.                     |
| ethoxy-5-pyridinyl)-; C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub> S; | J. Am. Chem. Soc. <u>1940</u> , 62, 1999–2002.        |
| [71720-65-5]   |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| -  |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-(2-ethoxy-5-pyr  | ridinyl)benzenesulfonamide in water                   |
| at $37^{\circ}$ C is 3.6 mg/100 cm <sup>3</sup> solution ( 1.                          | $3 \times 10^{-4}$ mol dm <sup>-3</sup> , compiler ). |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                       |
| Excess sulfonamide in water was heated and   | The sulfonamide, mp 207-8°C (cor), was                |
| stirred on a steam bath for 30 min. The  | prepd by the authors. Anal: %C 53.2                   |
| suspension was then agitated for 24 h in a   | (calcd 53.2); %H 5.1 (5.1).                           |
| thermostat at 37°C. A sample of the satd   | Purity of the water was not specified.                |
| soln was withdrawn through a glass filter,   |   |
| dild, and analyzed by the modified Marshall  |   |
| method (1) using a General Electric record-  |   |
| ing spectrophotometer for comparing colors   |   |
| with those of the standards.   | ESTIMATED ERROR:                                      |
|  | Nothing specified                                     |
|  |   |
|  |   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.               |
|  | J. Pharmacol. <u>1939</u> , 66, 4.                    |
|  |   |
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| COMP | DNENTS:                                    | EVALUATOR:                                |
|------|--|---|
| (1)  | Benzenesulfonamide, 4-amino-N-methyl-      | Anthony N. Paruta                         |
|      | $N-2-pyridiny1-; C_{12}H_{13}N_{3}O_{2}S;$ | Department of Pharmaceutics               |
|      | [51543-29-4]                               | University of Rhode Island                |
|      |  | Kingston, Rhode Island, USA               |
| (2)  | Water                                      | and                                       |
|      |  | Ryszard Piekos                            |
|      |  | Faculty of Pharmacy, University of Gdansk |
|      |  | Gdansk, Poland 1986                       |

#### CRITICAL EVALUATION:

The solubility of the compound was reported by Kitao et al. (2) in 1973, and 31 years earlier by Shepherd et al. (1). It is conceivable that this low-melting solid be rather in -soluble in water and the average of the two reported values should be considered as the recommended value at 310K in water,  $4.96 \times 10^{-3}$  mol dm<sup>-3</sup>.

#### **REFERENCES:**

- (1) Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C. J. Am. Chem. Soc. <u>1942</u>, 64, 2532-7.
- (2) Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. Chem. Pharm. Bull. 1973, 21, 2417-26.

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-methyl-<br>N-2-pyridinyl-; C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; | Shepherd, R. G.; Bratton, A. C.;<br>Blanchard, K. C.; J. Am. Chem. Soc.                            |
| [51543-29-4]  | <u>1942</u> , 64, 2532-7.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37°C   | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
| Solubilty of 4-amino-N-methyl-N-2-pyrid<br>37 <sup>0</sup> C is 136 mg% ( 5.17 x 10 <sup>-3</sup> mol dm <sup>3</sup>         | -  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| The sulfonamide was assayed colorimetrically  | The sulfonamide, mp 86.5-7.0 <sup>0</sup> C, was syn-  |
| (1). No details were given.   | thesized by the authors. Anal: %C 54.76  |
|   | (54.74); %H 4.82 (4.98); %N 15.94 (15.96).   |
|   | Colorimetric factor: 0.658 (calcd 0.654).  |
|   | Purity of the water was not specified.   |
|   |  |
|   |  |
|   | ESTIMATED ERROR:   |
|   | Nothing specified  |
|   | REFERENCES :   |
|   | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.<br/>J. Biol. Chem. <u>1939</u>, 128, 537.</li> </ol> |
|   |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                        |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-methyl-  | Kitao, K.; Kubo, K.; Morishita, T.;           |
| N-2-pyridiny1-; C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; | Yata, N.; Kamada, A.                          |
| [51543-29-4]   | Chem. Pharm. Bull. <u>1973</u> , 21, 2417-26. |
|  |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:                                  |
| One temperature: 37 <sup>o</sup> C   | R. Piekos                                     |
|  |   |
| EXPERIMENTAL VALUES:   |   |
| EARENIAL VALUES.   |   |
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| Solubility of 4-amino-N-methyl-N-2-pyri  | dinylbenzenesulfonamide in water              |
| at $37^{\circ}$ C is 4.74 mmol dm <sup>-3</sup> solution.                        |   |
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|  | INFORMATION                                   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:               |
| The sulfonamide was assayed by diazotizati-                                      | The sulfonamide was synthesized by the        |
| on. No details were given.   | authors. Its purity was not specified.        |
|  | Deionized water was used.                     |
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|  | ESTIMATED ERROR:                              |
|  | Soly: not specified.                          |
|  | Temp: ±1 <sup>0</sup> C (authors).            |
|  |   |
|  | REFERENCES:                                   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                              |  |
| (1) Benzenesulfonamide, 4-amino-N-methyl-  | Kitao, K.; Kubo, K.; Morishita, T.;                 |  |
| N-2-pyridinyl-; C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; | Yata, N.; Kamada, A.                                |  |
| [51543-29-4]   | Chem. Pharm. Bull. <u>1973</u> , 21, 2417-26.       |  |
| (2) Methane, trichloro-; CHCl <sub>3</sub> ;                                     |   |  |
| [67-66-3]  |   |  |
| VARIABLES:   | PREPARED BY:  |  |
| One temperature: 37°C  | R. Piekos   |  |
|  |   |  |
| EXPERIMENTAL VALUES:   |   |  |
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| Solubility of 4-amino-N-methyl-N-2-pyr   | 5   |  |
| at $37^{\circ}$ C is more than 2630 mmol dm <sup>-3</sup> so                     | lution.   |  |
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| AUXILIARY INFORMATION  |   |  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                     |  |
| One ml of the sulfonamide soln in CHCl <sub>3</sub>                              | The sulfonamide was prepd by the authors.           |  |
| at equilibrium was taken into a test tube.                                       | Its purity was not specified. Neither               |  |
| After evapn of the solvent, the residue  | source nor purity of the CHCl <sub>3</sub> was spe- |  |
| was dissolved in 1N HC1, the soln was pro-                                       | cified.   |  |
| perly dild with deionized water, and the   |   |  |
| concn of the sulfonamide was detd by diazo-                                      |   |  |
| tization.  |   |  |
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| }  | ESTIMATED ERROR:                                    |  |
|  |   |  |
|  | Soly: not specified.                                |  |
|  | Temp: ±1 <sup>0</sup> C (authors).                  |  |
|  | REFERENCES :  |  |
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| COME<br>(1) | ONENTS:<br>Benzenesulfonamide, 4-amino-N-(1-methy1-                           | EVALUATOR:<br>Anthony N. Paruta           |
|-------------|---|---|
|             | 1,2-dihydro-2-pyridinyl)-;  | Department of Pharmaceutics               |
|             | C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; [51543-30-7] | University of Rhode Island                |
|             | 12 13 3 2 4   | Kingston, Rhode Island, USA               |
| (2)         | Water   | and                                       |
| <b>(</b> )  |   | Ryszard Piekos                            |
| 1           |   | Faculty of Pharmacy, University of Gdansk |
|             |   | Gdansk, Poland 1986                       |

## CRITICAL EVALUATION:

There were two reports on the solubility of this compound in water at 310K (1,2). Shepherd et al. (1) gave a solubility value of  $4.25 \times 10^{-3} \text{ mol dm}^{-3}$  in 1942. Kitao et al. (2) gave a value of  $3.69 \times 10^{-3} \text{ mol dm}^{-3}$ . These values are about 15% in difference, and can be used to indicate a tentative value of  $3.97 \times 10^{-3} \text{ mol dm}^{-3}$  in water at 310K.

#### **REFERENCES:**

- (1) Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C. J. Am. Chem. Soc. <u>1942</u>, 64, 2532-7.
- (2) Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. Chem. Pharm. Bull. 1973, 21, 2417-26.

| COMPONENTE  | ODICINAL WEACHDENENDER                     |  |
|---|--|--|
|   | ORIGINAL MEASUREMENTS:                     |  |
| (1) Benzenesulfonamide, 4-amino-N-(1-   | Shepherd, R. G.; Bratton, A. C.;           |  |
| <pre>methy1-1,2-dihydro-2-pyridiny1)-;</pre>                                  | Blanchard, K.C. J. Am. Chem. Soc.          |  |
| C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; [51543-30-7] | <u>1942</u> , 64, 2532-7.                  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                      |  |  |
| (1) water, 120, [7752 10 5]   |  |  |
| VARIABLES:  | PREPARED BY:                               |  |
| One temperature: 37 C   | R. Piekos                                  |  |
| one temperature: 57 C   | R. FIEROS                                  |  |
|   |  |  |
| EXPERIMENTAL VALUES:  |  |  |
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| Solubility of 4-amino-N-(1-methyl-1,2-d)                                      | ihydro-2-pyridinyl)benzenesulfonamide      |  |
| in water at $37^{\circ}$ C is 112 mg% ( 4.25 x 10                             | $0^{-3}$ mol dm <sup>-3</sup> , compiler ) |  |
|   | o mor um , comprier ).                     |  |
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| AUXILIARY   | INFORMATION                                |  |
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| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:            |  |
| The sulfonamide was assayed colorimetrically                                  |  |  |
| (1). No details were given.   | sized by the authors. Analysis: %C 54.68   |  |
|   | (calcd 54.74); %H 4.85 (4.98); %N 15.90    |  |
|   | (15.96). Colorimetric factor: 0.670        |  |
|   | (calcd 0.654).                             |  |
|   | Purity of the water was not specified.     |  |
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|   | ESTIMATED ERROR:                           |  |
|   | Nothing specified                          |  |
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|   | REFERENCES:                                |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |  |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.     |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(1-   | Kitao, K.; Kubo, K.; Morishita, T.;          |
| <pre>methyl-1,2-dihydro-2-pyridinyl)-;</pre>                                  | Yata, N.; Kamada, A.                         |
| C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; [51543-30-7] | Chem. Pharm. Bull. <u>1973,</u> 21, 2417-26. |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                      |  |
|   |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 37°C   | R. Piekos                                    |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(1-methyl-1,2-  |  |
| sulfonamide in water at 37 <sup>0</sup> C is 3.69 m                           | mol dm <sup>-3</sup> solution.               |
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| AUXILIARY   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| The sulfonamide was assayed by diazotiza-                                     | The sulfonamide was synthesized by the       |
| tion. No details were given.  | authors. Its purity was not specified.       |
| tion. No details were given.  | Deionized water was used.                    |
|   | belonized water was used.                    |
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|   | ESTIMATED ERROR:                             |
|   | Soly: not specified.                         |
|   | Temp: $\pm 1^{\circ}C$ (authors).            |
|   | Temp: II C (authors).                        |
|   | REFERENCES :                                 |
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| Components :  | ORIGINAL MEASUREMENTS:                             |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(1-methy1-                                  | Kitao, K.; Kubo, K.; Morishita, T.;                |
| 1,2-dihydro-2-pyridinyl)-;  | Yata, N.; Kamada, A.                               |
| C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S; [51543-30-7] | Chem. Pharm. Bull. <u>1973</u> , 21, 2417–26.      |
| (2) Methane, trichloro-; CHC1 <sub>3</sub> ;                                  |  |
| [67-66-3]   |  |
| VARIABLES:  | PREPARED BY:                                       |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(2-methyl-1,2-a                                       |  |
| sulfonamide in CHCl <sub>3</sub> at 37 <sup>o</sup> C is 5.53 m               | nol dm <sup>-3</sup> solution.                     |
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| AUXILIARY   | INFORMATION  |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                    |
| One ml of the sulfonamide soln in CHCl <sub>3</sub>                           | The sulfonamide was prepd by the authors.          |
| at equilibrium was taken into a test tube.                                    | Its purity was not specified.                      |
| After evapn of the solvent the residue was                                    | Neither source nor purity of the CHCl <sub>3</sub> |
| dissolved in 1N HCl, the soln was properly                                    | 5  |
| dild with deionized water, and the concn                                      | "do opcorried"                                     |
|   |  |
| of the sulfonamide was detd by diazotiza-                                     |  |
| tion.   |  |
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|   | ESTIMATED ERROR:                                   |
|   | Soly: not specified.                               |
|   | Temp: ±1 <sup>0</sup> C (authors).                 |
|   | DEDEDRIVANA  |
|   | REFERENCES:  |
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:   |
|---|--|
| <ol> <li>Pyridine, 2,5-bis[[(4-aminopheny1)-<br/>sulfony1]amino]-; C<sub>17</sub>H<sub>17</sub>N<sub>5</sub>O<sub>4</sub>S<sub>2</sub>;<br/>[71119-18-1]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Roblin, R. O., Jr.; Winnek, P. S.<br><i>J. Am. Chem. Soc.</i> <u>1940</u> , <i>62</i> , 1999-<br>2002. |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>°</sup> C  | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
| Solubility of 2,5-bis[[(4-aminophenyl)<br>at 37 <sup>0</sup> C is 49.5 mg/100 cm <sup>3</sup> solution (1   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| Excess sulfonamide in water was heated and  | The sulfonamide, mp 215-6°C (cor), was   |
| stirred on a steam bath for 30 min. The   | prepd by the authors. Anal: %C 48.8  |
| suspension was then agitated for 24 h in a  | (calcd 48.7); %H 4.1 (4.1).  |
| thermostat at $37^{\circ}$ C. A sample of the satd  | Purity of the water was not specified.   |
| soln was withdrawn through a glass filter,  |  |
| dild, and analyzed by the modified Marshall   |  |
| method (1) using a General Electric record-   |  |
| ing spectrophotometer for comparing colors  |  |
| with those of the standards.  | ESTIMATED ERROR:   |
|   | Nothing specified  |
|   | REFERENCES :   |
|   | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.</li> <li>J. Pharmacol. <u>1939</u>, 66, 4.</li> </ol>    |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-3-  | Anderson, G. W.; Faith, H. E.; Marson, H.W. |
| pyridazinyl-; C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S;                                | Winnek, P. S.; Roblin, R. O., Jr.           |
| [515-62-8]  | J. Am. Chem. Soc. <u>1942</u> , 64, 2902–5. |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:                                |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                   |
| EXPERIMENTAL VALUES:  | L <u> </u>                                  |
| Solubility of 4-amino-N-3-pyridazinylber<br>37 <sup>0</sup> C is 221 mg/100 cm <sup>3</sup> solution ( 8.83 : |   |
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|   | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and                                     | SOURCE AND PURITY OF MATERIALS:             |
| stirred on a steam bath for 30 min. The   | The sulfonamide, mp 189-90°C, was prepd     |
| suspension was then agitated for 24 h in a  | by the authors. Anal: %C 47.7 (calcd        |
| thermostat. A sample of the satd soln was   | 48.0); ZH 4.0 (4.0); ZN 22.8 (22.4).        |
| withdrawn through a glass filter, dild, and   | Purity of the water was not specified.      |
| analyzed by the Marshall method (1) using   |   |
| a General Electric recording spectrophoto-  |   |
| meter for comparing the colors developed with   | 1   |
| those of the standards.   | ESTIMATED ERROR:                            |
|   | Nothing specified                           |
| · ·   |   |
|   | REFERENCES :                                |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.     |
|   | J. Pharmacol. <u>1939</u> , 66, 4.          |
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|    | PONENTS:<br>Benzenesulfonamide, 4-amino-N-(6-chloro- |

3-pyridazinyl)- (sulfachlorpyridazine); C10H9ClN402S; [80-32-0] (2) Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]

(4) Water; H<sub>2</sub>0; [7732-18-5] VARIABLES: One temperature: 20°C; one pH: 7.4 Riess, W. Intern. Congr. Chemotheraphy, Proc. 3rd, Stuttgart <u>1963</u>, 1, 627-32.

ORIGINAL MEASUREMENTS:

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfachlorpyridazine in a M/15 Strensen buffer solution ( pH 7.4 ) at  $20^{\circ}$ C is 1200 mg% ( 4.215 x  $10^{-2}$  mol dm<sup>-3</sup> solution, compiler ).

## AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: Sörensen buffer solns of pH varying between Nothing specified 7 and 8 were prepd, satd with sulfachlorpyridazine at 20°C, their pH was measured at equilibrium, and the sulfachlorpyridazine was assayed colorimetrically. The measured pH values were then plotted against concn, and the soly at pH 7.4 was detd by interpolation (personal comunication). ESTIMATED ERROR: Nothing specified **REFERENCES:** 

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                  |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(6-chloro-</li> </ol>   |   |
| 3-pyridazinyl)- (sulfachlorpyridazine);  | Intern. Congr. Chemotherapy, Proc.      |
| $C_{10}H_9Cln_4O_2S;$ [80-32-0]  | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| (2) Methane, trichloro- (chloroform);  | , e, e, e, e,                           |
| CHCl <sub>3</sub> ; [67-66-3]  |   |
| VARIABLES:   | PREPARED BY:                            |
| One temperature: 20°C  | R. Piekos                               |
|  |   |
| EXPERIMENTAL VALUES:   |   |
| Solubility of sulfachlorpyridazine in (<br>( 2.1 x 10 <sup>-3</sup> mol dm <sup>-3</sup> solution, compi |   |
|  |   |
|  |   |
| AUXILIARY  | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |
| Nothing specified  | Nothing specified                       |
|  |   |
|  | ESTIMATED ERROR:                        |
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|  | Nothing specified                       |
|  | REFERENCES:                             |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
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| (1) Benzenesulfonamide, 4-amino-N-(6-methyl-   | Riess, W.  |
| 3-pyridazinyl)-(sulfamethylpyridazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>2</sub> S; [5433-63-6]  | Intern. Congr. Chemotherapy, Proc.   |
| (2) Phosphoric acid, disodium salt;  | 3rd, Stuttgart <u>1963</u> , 1, 627-32.  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-77-0]<br>(3) Phosphoric acid, monopotassium salt;   |  |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:   |
| VARIABLES:<br>One temperature: 20 <sup>0</sup> C; one pH: 7.4  | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
|  |  |
| Solubility of sulfamethylpyridazine in   |  |
| ( pH 7.4 ) at $20^{\circ}$ C is 140 mg% ( 5.30 x   | $10^{-3} \text{ dm}^{-3}$ solution, compiler ).  |
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| AUXILIARY  | INFORMATION  |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:   |
|  | SOURCE AND PURITY OF MATERIALS:  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| METHOD/APPARATUS/PROCEDURE:<br>SUrensen buffer solns of pH varying between   | SOURCE AND PURITY OF MATERIALS:  |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-   | SOURCE AND PURITY OF MATERIALS;<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured  | SOURCE AND PURITY OF MATERIALS;<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured   | SOURCE AND PURITY OF MATERIALS;<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn  | SOURCE AND PURITY OF MATERIALS;<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured   | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpolar | SOURCE AND PURITY OF MATERIALS;<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpola  | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpola- | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified   |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpola  | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified<br>e<br>ESTIMATED ERROR:<br>Nothing specified |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpola  | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified<br>e<br>ESTIMATED ERROR:<br>Nothing specified |
| METHOD/APPARATUS/PROCEDURE:<br>Sörensen buffer solns of pH varying between<br>7 and 8 were prepd, satd with sulfamethyl-<br>pyridazine at 20°C, their pH was measured<br>at equilibrium, and the sulfamethylpyridazine<br>was assayed colorimetrically. The measured<br>pH values were then plotted against concn<br>and the soly at pH 7.4 was detd by interpola  | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified<br>e<br>ESTIMATED ERROR:<br>Nothing specified |

| COMPONENTS :   | ORIGINAL MEASUREMENTS:                                    |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(6-methyl-</li> </ol>                         | Reiss, W.   |
| 3-pyridazinyl)- (sulfamethylpyridazine);   | Reiss, w.<br>Intern. Congr. Chemotherapy, Proc.           |
| $C_{11}H_{12}N_4O_2S;$ [5433-63-6]   | 3rd, Stuttgart <u>1963</u> , 1, 627-32.                   |
| (2) Methane, trichloro- (chloroform);  | <u></u> , , ,   |
| CHC1 <sub>3</sub> ; [67-66-3]  |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 20 <sup>0</sup> C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfamethylpyridazine in   | $a$ chloroform at $20^{\circ}$ C is $144$ mc <sup>9</sup> |
|  |   |
| ( 5.45 x $10^{-3}$ mol dm <sup>-3</sup> solution, comp                               | iler).  |
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| AUXILIARY  | INFORMATION   |
| AUXILIARY INFORMATION<br>METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: |   |
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| Nothing specified  | Nothing specified   |
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|  | ESTIMATED ERROR:  |
|  | Nothing specified   |
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|  | REFERENCES :  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                           |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(6-meth-  | Yamazaki, M.; Aoki, M.; Kamada, A.;              |
| oxy-3-pyridazinyl)- (sulfamethoxypyri-  | Yata, N. <i>Yakuzaigaku</i> <u>1967</u> , 27(1), |
| dazine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [80-35-3] | 37-40.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
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| VARIABLES:  | PREPARED BY:                                     |
| One temperature: 30 <sup>0</sup> C  | R. Piekos  |
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| EVDEDINGNITAL VALUES.   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamethoxypyridazine  | in water at 30°C is 3.36 mmol/L                  |
|   |  |
| $(0.942 \text{ g dm}^{-3}, \text{ compiler}).$                                      |  |
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| AUXILIARY   | INFORMATION                                      |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                  |
| Sulfamethoxypyridazine (0.5 g) was placed   | Nothing specified                                |
| in an L-shaped tube together with 20 ml of  |  |
| water. The mixt was shaken in a thermostat  |  |
| until equilibrium was attained. The sulfa-  |  |
| methoxypyridazine was assayed in the super-   | 1  |
| natant spectrophotometrically at .545 nm on   |  |
|   |  |
| a Beckmann DU spectrophotometer. The re-  |  |
| sults were taken from a calibration graph.  |  |
|   | ESTIMATED ERROR:                                 |
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|   | Soly: not specified                              |
|   | Temp: ±1 <sup>0</sup> C (authors)                |
|   | REFERENCES :                                     |
|   | In DIENCES;                                      |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(6-meth-                           | ORIGINAL MEASUREMENTS:                        |
|---|---|
| oxy-3-pyridaziny1)- (sulfamethoxypyri-  | Ogata, H.; Shibazaki, T.; Inoue, T.;          |
| dazine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [80-35-3] | Ejima, A. Chem. Pharm. Bull. <u>1979,</u>     |
| (2) Hydrochloric acid; HCl; [7647-01-0]   | 27(6), 1281-6.                                |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
|   |   |
| VARIABLES:  | PREPARED BY:                                  |
| One temperature: 37°C   | R. Piekos                                     |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamethoxypyridazine ir   | 0 1N HCl at 37 <sup>0</sup> C is 17 243 mg/ml |
|   |   |
| ( 6.1516 x $10^{-2}$ mol dm <sup>-3</sup> , compiler ).                             |   |
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| AIIXILIARY  | INFORMATION                                   |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:               |
| A centrifuge tube contg 30 ml of 0.1N HCl   | Comm available 250-mg uncoated tablets of     |
| and 0.5-3.0 g of the sulfamethoxypyridazine   | sulfamethoxypyridazine were used.             |
| powder was tightly sealed and shaken at $37^{\circ}$                                | C Hydrochloric acid was of reagent grade.     |
| The concn of the dissolved drug was detd  |   |
| spectrophotometrically following filtration   |   |
| through a Millipore filter (type EH, pore   |   |
| size 0.5 $\mu$ m), and the procedure was repeat-                                    |   |
| ed every 24 h until a const concn was ob-   | ······································        |
| tained.   | ESTIMATED ERROR:                              |
|   | Nothing specified                             |
|   |   |
|   | REFERENCES:                                   |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(6-<br>methoxy-3-pyridazinyl)- (sulfamethoxy-<br>pyridazine); $C_{11}H_{12}N_4O_3S$ ; [80-35-3]<br>(2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]<br>(3) 1,2,3-Propanetricarboxylic acid, 2-<br>hydroxy- (citric acid); $C_6H_8O_7$ ;<br>[77-92-9]<br>(4) Water; $H_2O$ ; [7732-18-5]<br>VARIABLES:<br>pH  | ORIGINAL MEASUREMENTS:<br>Bertazzoli, C.; Buogo, A.; Ciceri, C.;<br>Ghione, M.; Turolla, E.; Zavaglio, V.<br>Minerva Med. <u>1961</u> , 52(40), 1789-96.<br>PREPARED BY:<br>R. Piekos |
|--|---|
| EXPERIMENTAL VALUES:<br>5000-<br>4500-<br>4000-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500-<br>500 | •   |
|  | 7 8<br>SH<br>INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfamethoxypyridazine in McIl-<br>vaine's Na <sub>2</sub> HPO <sub>4</sub> - citric acid buffer solns<br>was detd under agitation at 37°C. No details<br>were given.   |   |
|  | ESTIMATED ERROR:<br>Nothing specified<br>REFERENCES:  |

| COMP | ONENTS:  | ORIGINAL MEASUREMENTS: |
|------|--|------------------------|
| (1)  | Benzenesulfonamide, 4-amino-N-(6-methoxy-<br>3-pyridazinyl)- (sulfamethoxypyridazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>3</sub> S; [80-35-3] |                        |
| (2)  | Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | 48, 177-81.            |
| (3)  | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |                        |
| (4)  | Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:           |
| VAR  | IABLES: pH   | R. Piekos              |

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in buffers of varying mixtures of  $Na_2HPO_4 \cdot ^{7H}2^0$ (71.6 g/l distilled water; 0.27 mol dm<sup>-3</sup>, compiler) and  $KH_2PO_4$  (36.3 g/l distilled water; 0.27 mol dm<sup>-3</sup>, compiler) at  $37^{\circ}C$ .

| Initial pH        | Solubility        |                               |
|-------------------|-------------------|-------------------------------|
|                   | mg/100 m1         | $10^2 \text{ mol } dm^{-3} a$ |
| 4.5               | 720               | 2.57                          |
| 5.0               | 740               | 2.64                          |
| 5.5               | 770               | 2.75                          |
| 6.0               | 800               | 2.85                          |
| 6.5               | 920               | 3.28                          |
| 7.0               | 1380              | 4.923                         |
| 5.5<br>6.0<br>6.5 | 770<br>800<br>920 | 2.75<br>2.85<br>3.28          |

<sup>a</sup>calculated by compiler

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                            | SOURCE AND PURITY OF MATERIALS:           |
|--|---|
| Solns were prepd by adding an excess of sul-           | Neither source nor purity of the reagents |
| famethoxypyridazine to 10 ml of buffer soln            | were specified. Distilled water was used. |
| at each pH level in 18 x 150-mm test tubes,            |   |
| stoppering the tubes and placing them in a             |   |
| water bath at $37^{\circ}$ C with gentle agitation for |   |
| 24 h. The mixt was then filtered and a 1-ml            |   |
| aliquot was accurately pipetted into a volu-           |   |
| metric flask for diln and analysis. The ba-            |   |
| lance was retained for pH detn to ascertain            | ESTIMATED ERROR:                          |
| any change in pH value. The sulfonamide was            | Soly: av values of duplicate runs are re- |
| assayed colorimetrically by the method of              | ported (authors).                         |
| Bratton and Marshall as described in detail            | Temp and pH: not specified.               |
| by Biamonte and Schneller (1). A standard              | REFERENCES :                              |
| curve was prepd using accurately prepd stand-          | 1. Biamonte, A. R.; Schneller, G. E.      |
| ard solutions.   | J. Am. Pharm. Assoc., Sci. Ed.,           |
|  | <u>1952</u> , <i>41</i> , 341.            |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-                              | ORIGINAL MEASUREMENTS:                  |
|---|---|
| 3-pyridazinyl)- (sulfamethoxypyridazine);   | Kless, w.                               |
| $C_{11}H_{12}N_4O_3S;$ [80-35-3]  | Intern, Congr. Chemotherapy, Proc.      |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]     | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0] |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:                            |
| VARIABLES:<br>One temperature: 20 <sup>0</sup> C; one pH: 7.4                             | R. Piekos                               |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamethoxypyridazine in   | a M/15 Sörensen buffer solution         |
| ( pH 7.4 ) at 20 <sup>°</sup> C is 200 mg% ( 7.13 x 1                                     |   |
| ( pH /.4 ) at 20°C is 200 mg% ( /.13 x .  | to mol dm - solution, compiler ).       |
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| AUXILIARY   | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:         |
| Sörensen buffer solutions of pH varying be-   | Nothing specified                       |
| tween 7 and 8 were prepd, satd with sulfa-  |   |
| methoxypyridazine at 20°C, their pH was mea-  |   |
| sured at equilibrium, and the sulfamethoxy-   |   |
| pyridazine was assayed colorimetrically.  |   |
| The measured pH values were plotted against   |   |
| concn, and the soly at pH 7.4 was detd by   |   |
| interpolation (personal communication).   |   |
|   | ESTIMATED ERROR:                        |
|   | Nothing specified                       |
|   |   |
|   | REFERENCES :                            |
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|   | ORIGINAL MEASUREMENTS:                      |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-methoxy-   | Verenelid M. Kelid M. Keredo A.             |
| 3-pyridazinyl)- (sulfamethoxypyridazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [80-35-3] | Yamazaki, M.; Aoki, M.; Kamada, A.;         |
|   | Yata, N. Yakuzaigaku <u>1967,</u> 27(1),    |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                                   | 37-40                                       |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                               |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:<br>R. Piekos                   |
| VARIABLES:  | R. Flekos                                   |
| One temperature: 30 <sup>0</sup> C; one pH: 7.4   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamethoxypyridazine in   | a phosphate buffer solution of              |
|   |   |
| pH 7.4 ( $\mu$ = 0.17 ) at 30 <sup>o</sup> C is 6.12 mmoJ   | ./L ( 1.71 g dm <sup>-3</sup> , compiler ). |
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|   | INFORMATION                                 |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| Sulfamethoxypyridazine (0.5 g) was placed in  | Nothing specified.                          |
| an L-shaped tube together with 20 ml of the   |   |
| buffer soln. The mixt was shaken in a ther-   |   |
| mostat until equilibrium was attained. The  |   |
| 1   |   |
| sulfamethoxypyridazine was assayed in the   |   |
| supernatant spectrophotometrically at 545 nm  |   |
| on a Beckmann DU spectrophotometer. The   |   |
| results were taken from a calibration curve.  |   |
|   |   |
|   | ESTIMATED ERROR:                            |
|   | Soly and pH: not specified.                 |
|   | Temp: ±1 <sup>0</sup> C (authors)           |
|   |   |
|   | REFERENCES:                                 |
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COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(6-methoxy-

ORIGINAL MEASUREMENTS: Bandelin, F. J.; Malesh, W. 3-pyridaziny1)- (sulfamethoxypyridazine);  $C_{11}H_{12}N_4O_3S;$  [80-35-3] J. Am. Pharm. Assoc., Sci. Ed. (2) Calcium chloride; CaCl<sub>2</sub>; [10043-52-4] <u>1959</u>, 48, 177-81. (3) Magnesium chloride; MgCl<sub>2</sub>; [7786-30-3] (4) Phosphoric acid, monoammonium salt; NH4H2PO4; [7722-76-1] PREPARED BY: (5) Potassium chloride; KC1; [7447-40-7] (6) Sodium chloride; NaCl; [7647-14-5] R. Piekos (7) Urea; CH<sub>4</sub>N<sub>2</sub>O; [57-13-6] (8) Water; H<sub>2</sub>0; [7732-18-5] VARIABLES: pH at 37°C

**EXPERIMENTAL VALUES:** 

Solubility of sulfamethoxypyridazine in a solution containing  $CaCl_2$  0.1143,  $MgC1_2$  0.121,  $NH_4H_2PO_4$  0.300, KC1 1.660, NaCl 2.950 and urea 20 g/dm<sup>3</sup> (synthetic urine, Mosher Vehicle ) at 37° Solubility

|                | Solubility |                                   |
|----------------|------------|-----------------------------------|
| Equilibrium pH | mg/100 ml  | $10^2 \text{ mol/dm}^3 \text{ a}$ |
| 4.5            | 460        | 1.64                              |
| 5.0            | 466        | 1.66                              |
| 5.5            | 475        | 1.69                              |
| 6.0            | 488        | 1.74                              |
| 6.5            | 552        | 1.97                              |
| 7.0            | 862        | 3.07                              |
|                |            |                                   |

<sup>a</sup>calculated by compiler

| AUXILIARY   | INFORMATION  |
|---|--|
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfamethoxypyridazine was added to<br>aliquots of synthetic urine solns and 1%<br>H <sub>3</sub> PO <sub>4</sub> or 1% NaOH solns were used to adjust<br>the pH to the required value. The solns were<br>agitated for 24 h with addn of acid or base<br>to keep them at the desired pH level until<br>equilibrium was attained. Then the solns<br>were filtered and in aliquots the sulfon-<br>amide was assayed spectrophotometrically by<br>the method described by Biamonte and | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified<br>ESTIMATED ERROR:<br>Soly: average values of 2 detns were given   |
| Schneller (1).  | <pre>Temp: not specified.<br/>pH ; not specified<br/>REFERENCES:<br/>1. Biamonte, A. R.; Schneller, G. E.<br/>J. Am. Pharm. Assoc., Sci. Ed.<br/><u>1952</u>, 41, 341.</pre> |

| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-<br/>3-pyridazinyl)- (sulfamethoxypyridazine);<br/>C11<sup>H</sup>12<sup>N</sup>4<sup>0</sup>3<sup>S</sup>; [80-35-3]<br/>(2) Ethanol, 2,2'-iminodi-(diethanolamine);<br/>C4<sup>H</sup>11<sup>N0</sup>2; [111-42-2]<br/>(3) 1,3 -Propanediol; C3<sup>H</sup>8<sup>0</sup>2; [504-63-2]<br/>(4) Water; H<sub>2</sub>0; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Lombard1, R. B.<br><i>Rev. Farm. (Buenos Aires)</i> <u>1968,</u><br><i>110(7-8)</i> , 154-9. |
|--|--|
|  | PREPARED BY:   |
| VARIABLES:   |  |
| One temperature: 20 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| Maximum concentration of sulfamethoxypy<br>amine 1 ml, 1,3-propanediol 60 ml, and<br>( 0.50 mol kg <sup>-1</sup> solvent, compiler ).  |  |
|  | INFORMATION  |
|  | •  |
| METHOD/APPARATUS/PROCEDURE:<br>To the diethanolamine solution in water   | SOURCE AND PURITY OF MATERIALS:<br>The source and purity of the materials,   |
| warmed up to $40^{\circ}$ C, sulfamethoxypyridazine  | with the exception of water, was not spe-  |
| 1  | cified.  |
| was added followed by 1,3-propanediol pre-<br>viously warmed to 50°C, and the mixt was   | Distd water was used.  |
| agitated. The pH of the mixt was 7.9 at 20°C.  | Distu water was used.  |
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|  | ESTIMATED ERROR:   |
|  | Nothing specified.   |
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|  | REFERENCES:  |
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|-------------|--|
| COMP<br>(1) | DNENTS:<br>Benzenesulfonamide, 4-amino<br>3-pyridazinyl)- (sulfameth<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [80-35-3] |

(2) Ethanol; C<sub>2</sub>H<sub>6</sub>0; [64-17-5]

R. Piekos

|     | 2-furar                           | v1)met                           | hv1]ω-hva              | lroxy-(glycofuro  | 1): |          |     |
|-----|-----------------------------------|----------------------------------|------------------------|-------------------|-----|----------|-----|
|     | (C <sub>2</sub> H <sub>4</sub> 0) | n <sup>C</sup> 5 <sup>H</sup> 10 | 0 <sub>2</sub> ; [3169 | 2-85-0]           |     | PREPARED | BY: |
| (5) | Water;                            | <sup>H</sup> 2 <sup>0</sup> ;    | [7732-18-              | 5]                |     |          |     |
| ARI | ABLES: C                          | )ne tem                          | perature:              | 20 <sup>0</sup> C |     |          |     |

EXPERIMENTAL VALUES:

Maximum concentration of sulfamethoxypyridazine in a mixture of ethanol  $96^{\circ}GL$  10 ml, piperazine 3.750 g, glycofurol 70 ml, and water 20 ml, at  $20^{\circ}$ C, is 18-19% ( 0.64 - 0.68 mol kg<sup>-1</sup> solvent, compiler ).

## AUXILLARY INFORMATION

| AUXILIANI   | INFORMATION                                 |
|---|---|
| METHOD/APPARATUS/PROCEDURE:                               | SOURCE AND PURITY OF MATERIALS:             |
| To glycofurol, warmed to 60 <sup>0</sup> C, through which | The source and purity of the materials were |
| a stream of nitrogen was bubbled, sulfameth-              | not specified, with the exception of water. |
| oxypyridazine was added, followed by an aq                | Water for injection was used.               |
| piperazine soln and EtOH. The stream of ni-               |   |
| trogen was bubbled throughout. The pH of the              |   |
| soln was 7.9 at 20 <sup>0</sup> C.                        |   |
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|   | ESTIMATED ERROR:                            |
|   | Nothing specified.                          |
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|   | REFERENCES :                                |
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| COMPONENTS:<br>(1) Benzenesulfonamide,4-amino-N-(6-methoxy-  | ORIGINAL MEASUREMENTS:                    |
|--|---|
| 3-pyridazinyl)- (sulfamethoxypyridazine);  | Lombardi, R. B.                           |
| $C_{11}H_{12}N_4O_3S;$ [80-35-3]   | REv. Farm. (Buenos Aires) 1968,           |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> 0; [64-17-5]  |   |
| (3) Piperazine; C <sub>4</sub> H <sub>10</sub> N <sub>2</sub> ; [110-85-0]                               | 110(7-8), 154-9.                          |
| (4) Poly(oxy-1,2-ethanediy1), $\alpha$ -hydro - $\omega$ -   |   |
| hydroxy- (PEG 300); (C <sub>2</sub> H <sub>4</sub> O) <sub>n</sub> H <sub>2</sub> O;<br>[25322-68-3] 300 |   |
| (5) Water; H <sub>2</sub> O; [7732-18-5]   | PREPARED BY:                              |
| VARIABLES:   | R. Piekos                                 |
| One temperature: 20 <sup>0</sup> C   |   |
| EXPERIMENTAL VALUES:   |   |
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| Maximum concentration of sulfamethoxyp   | vridazine in a mixture of ethanol         |
|  | -1 and writer (0 =1 at 2000               |
| 96 <sup>0</sup> GL 10 ml, piperazine 2 g, PEG 300 50   | J m1, and water 40 m1, at 20°C ,          |
| is 18% ( 0.64 mol kg <sup>-1</sup> solvent, compi  | ler ).                                    |
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| AUXILIARY  | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:           |
| To a soln of piperazine in water, EtOH was   | The source and purity of the materials,   |
| added, followed by sulfamethoxypyridazine,   | with the exception of water, were not     |
| and PEG 300 previously warmed to 50-55°C.  | specified. Water for injections was used. |
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| Nitrogen was bubbled through the mixt to   |   |
| ensure agitation. The pH of the mixt was   |   |
| 7.8 at 20 <sup>0</sup> C.  |   |
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| 1  | PETTMATED EDDOD.                          |
|  | ESTIMATED ERROR:                          |
|  | Nothing specified                         |
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|  | DEPENDING.                                |
|  | REFERENCES:                               |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-   | ORIGINAL MEASUREMENTS:                    |
|--|---|
| <ol> <li>(1) Benzenesulionamide, 4-aminova-(0-methoxy-<br/>3-pyridazinyl)-(sulfamethoxypyridazine);<br/>C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>0<sub>3</sub>S; [80-35-3]</li> <li>(2) Piperazine; C<sub>4</sub>H<sub>10</sub>N<sub>2</sub>; [110-85-0]</li> <li>(3) Poly(oxy-1,2-ethanediyl), α-hydro- ω -<br/>hydroxy- (PEG 300); (C<sub>2</sub>H<sub>4</sub>0)<sub>n</sub>H<sub>2</sub>0;</li> </ol> |   |
| [25322-68-3] 300   |   |
| (4) 1,3-Propanedio1; C <sub>3</sub> H <sub>8</sub> 0; [504-63-2]<br>(5) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                              |
| VARTABLES:   | R. Piekos                                 |
| One temperature: 20°C  |   |
| EXPERIMENTAL VALUES:   |   |
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| Maximum concentration of sulfamethoxypyri  | ldazine in a mixture of piperazine        |
| 3.5 g, PEG 300 40 ml, 1,3-propanedio1 40   | ml, and water 27.5 ml, at $20^{\circ}$ C, |
| is 15% ( $0.54$ mol kg <sup>-1</sup> solvent, compiler   |   |
| 15 15% ( 0.54 mor kg Sorvene, comprise   | · <b>)</b> •                              |
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| AUXILIARY  | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;           |
| To a soln of piperazine in water, a mixt of  | The source and purity of the materials,   |
| PEG 300 and 1,3-propanediol, previously heat-  | with the exception of water, were not     |
| ed to 50°C, was added, followed by sulfameth-  | specified.                                |
| oxypyridazine. Nitrogen was bubbled through  | Water for injections was used.            |
| the mixt to ensure agitation. The pH of the  |   |
|  |   |
| mixt was 7.8 at 20 <sup>0</sup> C.   |   |
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|  | ESTIMATED ERROR:                          |
|  | 1   |
|  | Nothing specified                         |
|  | Nothing specified.                        |
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|  | Nothing specified. REFERENCES:            |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                       |  |  |
|--|--|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(6-methoxy-  | Piere U                                      |  |  |
| 3-pyridazinyl)-(sulfamethoxypyridazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>3</sub> S; [80-35-3] |  |  |  |
|  | Intern. Congr. Chemotherapy, Proc.           |  |  |
| (2) Methane, trichloro- (chloroform);  | 3rd, Stuttgart <u>1963</u> , 1, 627-32.      |  |  |
| CHCl <sub>3</sub> ; [67-66-3]  |  |  |  |
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| VARIABLES:   | PREPARED BY:                                 |  |  |
| One temperature: 20°C  | R. Piekos                                    |  |  |
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| EXPERIMENTAL VALUES:   |  |  |  |
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| Solubility of sulfamethoxypyridazine in  | n chloroform at 20 <sup>0</sup> C is 390 me% |  |  |
|  |  |  |  |
| ( 1.39 x $10^{-2}$ mol dm <sup>-3</sup> solution, compine  | ler ).                                       |  |  |
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| AUXILIARY  | INFORMATION                                  |  |  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:              |  |  |
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| Nothing specified  | Nothing specified                            |  |  |
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|  | ESTIMATED ERROR:                             |  |  |
|  | Nothing specified                            |  |  |
|  | Nothing sheetited                            |  |  |
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|  | REFERENCES:                                  |  |  |
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| COMPONENTS:                               |   | ORIGINAL MEASUREMENTS:                    |  |  |
|---|---|---|--|--|
| (1)                                       | Benzenesulfonamide, 4-amino-N-(6-   | Yamazaki, M.; Aoki, M.; Kamada, A.;       |  |  |
| (/  | methoxy-3-pyridazinyl)- (sulfamethoxy-  |   |  |  |
|   | pyridazine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>3</sub> S; [80-35-5] | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |  |  |
| (2)                                       | Vethers trichland (chlanaform);   | 37-40.                                    |  |  |
| (2)                                       | Methane, trichloro- (chloroform);   |   |  |  |
|   | CHC1 <sub>3</sub> ; [67-66-3]   |   |  |  |
| VAR                                       | IABLES:   | PREPARED BY:                              |  |  |
|   | One temperature: 30 <sup>0</sup> C  | R. Piekos                                 |  |  |
|   | one cemperacute. 50 0   | Nº TICKUB                                 |  |  |
| EXPI                                      | ERIMENTAL VALUES:   |   |  |  |
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|   | Solubility of sulfamethoxypyridazine ir   | $a$ chloreform at $20^{\circ}$ C do 14.02 |  |  |
|   |   | r chioroform at 50 C is 14.05             |  |  |
| ł   | mmol/L ( $3.933 \text{ g dm}^{-3}$ , compiler ).  |   |  |  |
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|   |   | INFORMATION                               |  |  |
|   | HOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;           |  |  |
|   | famethoxypyridazine (0.5 g) was placed in   | Nothing specified                         |  |  |
| an  | L-shaped tube together with 20 ml of  |   |  |  |
| ch1                                       | oroform. The mixt was shaken in a ther-   |   |  |  |
| <br>                                      | tat until equilibrium was attained. The   |   |  |  |
|   |   |   |  |  |
| sulfamethoxypyridazine was assayed in the |   |   |  |  |
|   | ernatant spectrophotometrically at 545 nm   |   |  |  |
| on  | a Beckmann DU spectrophotometer. The  |   |  |  |
| res                                       | ults were taken from a calibration graph.   |   |  |  |
|   |   | ESTIMATED ERROR:                          |  |  |
|   |   | Soly: not specified                       |  |  |
|   |   | Temp: ±1 <sup>o</sup> C (authors)         |  |  |
|   |   | remp. 11 (authors)                        |  |  |
|   |   | REFERENCES:                               |  |  |
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| COMPONENTS:<br>(1) Cobalt, bis [4-an                     | ino-N-(6-met  | hory-3-             | ORIGINA            | L MEASUREMENTS:                                  |                                    |
|--|---------------|---------------------|--------------------|--|------------------------------------|
| pyridazinyl)benzenesulfonamidato-]diaqua-                |               | Gogori              | Lshvili, P. V.; Ts | kitishvili, M. G.;                               |                                    |
| $(CoR_2 \cdot 2H_20); C_{22}H_2CoN_80_6S_2 \cdot 2H_20;$ |               | Chrela              | ashvili, M. V.     |  |                                    |
| [72384-11-3]   |               |                     | Izv.               | Akad. Nauk Gruz.                                 | SSR, Ser. Khim                     |
| (2) Hydrochloric acid                                    |               | 7-01-0]             | 1979,              | 5(3), 199-204.                                   |                                    |
| (3) Water; H <sub>2</sub> 0; [77                         | 32-18-5]      |                     |                    |  |                                    |
| VARIABLES:   | <u> </u>      |                     | PREPARI            | ED BY:   |                                    |
| Concentration of H                                       | IC1 (pH)      |                     |                    | R. Piekos  |                                    |
|  |               |                     |                    |  |                                    |
| EXPERIMENTAL VALUES:                                     |               |                     |                    | <u>_</u>   |                                    |
| Concentration of HO                                      | :1 pH         | Solubility          | (mol/:             | l) at 25 <sup>0</sup> C based                    | 10 <sup>11</sup> x K <sub>so</sub> |
|  |               |                     | on                 |  |                                    |
|  |               | [Co <sup>2+</sup> ] |                    | [RH <sup>+</sup> ]                               |                                    |
|  |               | 1.3 x               |                    |  | <u></u>                            |
| $2.5 \times 10^{-2}$                                     | 6.15          |                     | _                  | $8.09 \times 10^{-3}$<br>5.15 x 10 <sup>-3</sup> | -                                  |
| $1.0 \times 10^{-2}$                                     | 6.25          | 6.6 x<br>3.6 x      |                    |  | 1.51                               |
| $5.0 \times 10^{-3}$                                     | 6.62          |                     |                    | $4.36 \times 10^{-3}$                            | 1.56                               |
| $2.5 \times 10^{-3}$                                     | 6.92          | 2.0 x               |                    | $2.80 \times 10^{-3}$                            | 1.50                               |
| $1.0 \times 10^{-3}$                                     | 7.31          | 1.28 x              |                    | $8.45 \times 10^{-4}$                            | 1.53                               |
| $5.0 \times 10^{-4}$                                     | 7.54          | 1.05 x              |                    | $8.32 \times 10^{-4}$                            | 1.51                               |
| $2.5 \times 10^{-4}$                                     | 7.78          | 5.84 x              |                    | $8.23 \times 10^{-4}$                            | 1.55                               |
| $1.0 \times 10^{-4}$                                     | 7.92          | 5.67 x              | -                  | $7.90 \times 10^{-4}$                            | 1.50                               |
| $5.0 \times 10^{-5}$                                     | 8.12          | 5.51 x              |                    | $7.87 \times 10^{-4}$                            | 1.50                               |
| $2.5 \times 10^{-5}$                                     | 8.23          | 5.48 x              | 10-4               | 7.15 x $10^{-4}$                                 | 1.52                               |
|  |               |                     |                    | Mear   | 1.52                               |
|  |               |                     |                    |  |                                    |
|  |               | AUXILIARY           | INFORMA            | TION   | ,                                  |
| METHOD/APPARATUS/PROCI                                   | DURE :        |                     | SOURCE             | AND PURITY OF MATE                               | RIALS:                             |
| CoR <sub>2</sub> •2H <sub>2</sub> O was placed           | in a close    |                     |                    | ing specified                                    |                                    |
| 100 ml of aq HCl was                                     |               |                     | Notin              | the apecifica                                    |                                    |
| was shaken for 6 h                                       |               |                     |                    |  |                                    |
|  |               |                     |                    |  |                                    |
| After attaining equi<br>of Co <sup>2+</sup> and S were o |               |                     |                    |  |                                    |
|  | ieta, and the | рп шеа-             |                    |  |                                    |
| sured.   |               |                     |                    |  |                                    |
|  |               |                     |                    |  |                                    |
|  |               |                     | ESTIMA             | TED ERROR:                                       |                                    |
|  |               |                     | Soly:              | not specified                                    | 10                                 |
| 1  |               |                     | ĸ <sub>so</sub> :  | standard deviatic (compiler).                    | on 5.64 x $10^{-13}$               |
|  |               |                     | Temp:              | not_specified.                                   |                                    |
|  |               |                     | REFERE             | NCES:  |                                    |
|  |               |                     |                    |  |                                    |
|  |               |                     |                    |  |                                    |
|  |               |                     |                    |  |                                    |
| 1  |               |                     |                    |  |                                    |
|  |               |                     |                    |  |                                    |

| COMPONENTS:   | ORIGINA             | L MEASUREMENTS:               |                                       |                   |
|---|---------------------|-------------------------------|---------------------------------------|-------------------|
| (1) Cobalt, bis[4-amino-N-(6-methoxy-3-   | Gogori              | shvili, P. V.; T              | skitishvi                             | 11. M. G.:        |
| pyridazinyl)benzenesulfonamidato]diaqua-<br>(CoR <sub>2</sub> •2H <sub>2</sub> 0); C <sub>22</sub> H <sub>22</sub> CoN <sub>8</sub> O <sub>6</sub> S <sub>2</sub> •2H <sub>2</sub> 0; |                     | shvili, M. V.                 | 01120201112                           |                   |
| [72384-11-3]  |                     | Akad. Nauk Gruz               | . SSR.                                | Ser. Khim.        |
| (2) Acetic acid, cobalt(2+) salt;<br>C <sub>4</sub> H <sub>6</sub> CoO <sub>4</sub> ; [71-48-7]   | 1979,               | - ( - )                       | · · · · · · · · · · · · · · · · · · · |                   |
| (3) Benzenesulfonamide, 4-amino-N-(6-methoxy  | ,- <u> </u>         | 1))*204.                      |                                       |                   |
| 3-pyridazinyl)-, monosodium salt, (NaR)   |                     |                               |                                       |                   |
| $\begin{array}{c} C_{11}H_{11}NaN_4O_3S;  [2577-32-4] \\ (4)  Water;  H_2O;  [7732-18-5] \end{array}$   | PREPARE             |                               |                                       |                   |
|   | ┩                   | R. Piekos                     |                                       |                   |
| Co <sup>2+</sup> /R <sup>-</sup> ratio; pH<br>EXPERIMENTAL VALUES:  |                     |                               |                                       |                   |
| 2+.   | ess of              | [R <sup>-</sup> ]             | 81 10                                 | based on          |
| of 0.1M solns pH mol/1 NaR  | or Co <sup>2+</sup> | mo1/1                         |                                       |                   |
| of Co <sup>2+</sup> acetate ace   | ate                 |                               | [Co <sup>2+</sup> ]                   | [R <sup>-</sup> ] |
|   |                     |                               |                                       |                   |
|   | x 10 <sup>-3</sup>  | $7.02 \times 10^{-3}$         | 5.16                                  | 5.45              |
|   | x 10 <sup>-3</sup>  | $4.04 \times 10^{-3}$         | 4.69                                  | 4.71              |
| 251/5 01/5  | x 10 <sup>-3</sup>  | $2.58 \times 10^{-3}$         | 4.44                                  | 4.43              |
|   | x 10 <sup>-3</sup>  | $1.43 \times 10^{-3}$         | 3.80                                  | 3.79              |
| $1:20$ 7.95 7.52 x $10^{-4}$  | -                   | $1.49 \times 10^{-3}$         | 3.32                                  | 3.30              |
| $35:65$ 7.85 $4.76 \times 10^{-4}$ 2.5  | x 10 <sup>-4</sup>  | $4.83 \times 10^{-4}$         | 3.91                                  | 3.82              |
| 40:60 7.75 $1.37 \times 10^{-3}$ 1.0  | x 10 <sup>-3</sup>  | $7.59 \times 10^{-4}$         | 3.65                                  | 3.64              |
| 50:50 7.62 $4.04 \times 10^{-3}$ 2.5  | x 10 <sup>-3</sup>  | $1.47 \times 10^{-3}$         | 3.10                                  | 3.09              |
| $60:40 	7.49 	7.67 	10^{-3} 	4.0$   | x 10 <sup>-3</sup>  | $7.48 \times 10^{-3}$         | 2.78                                  | 2.44              |
| 70:30 7.46 $1.14 \times 10^{-2}$ 5.5  | x 10 <sup>-3</sup>  | $1.19 \times 10^{-2}$         | 2.59                                  | 2.59              |
| 80:20 7.40 $1.51 \times 10^{-2}$ 7.0  | x 10 <sup>-3</sup>  | $1.50 \times 10^{-2}$         | 2.48                                  | 2.46              |
| 90:10 7.33 $1.88 \times 10^{-2}$ 8.5  | x 10 <sup>-3</sup>  | $2.02 \times 10^{-2}$         | 2.41                                  | 2.41              |
| <sup>a</sup> pLi = -log (solubility), solubi<br>measured at 25 <sup>0</sup> C.  | lity being          | g expressed in mo             | 1/1 and                               |                   |
| AUXILIAR  | INFORMA             | TION                          |                                       |                   |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE              | AND PURITY OF MAT             | ERIALS:                               |                   |
| The effect of the concns of $Co^{2+}$ and $R^-$ on  |                     | H <sub>2</sub> O was obtained |                                       | together          |
| the soly of $CoR_2 \cdot H_20$ was detd by the method   | 1 0.1M              | solns of Co <sup>2+</sup> ace | tate and                              | NaR.              |
| of isomolar series of solns. The ppt of   | Neith               | er source nor pur             | ity of th                             | e reagents        |
| CoR <sub>2</sub> was obtained by mixing together 0.1M   | was s               | pecified.                     |                                       |                   |
| solns of Co <sup>2+</sup> acetate and NaR taken in pro-   | .                   |                               |                                       |                   |
| portions specified in the Table (cf. Exper:   | -                   |                               |                                       |                   |
| mental Values box). The total vol after   |                     |                               |                                       |                   |
| mixing was always 100 ml. After attaining   |                     |                               |                                       |                   |
| equilibrium by shaking for 6 h, the pH, and   | ESTIMAT             | TED ERROR:                    |                                       |                   |
| the $Co^{2+}$ and S content were detd in soln.  |                     |                               |                                       |                   |
|   |                     | ning specified                |                                       |                   |
|   |                     |                               |                                       |                   |
|   | REFEREN             | NCES:                         |                                       |                   |
|   |                     |                               |                                       |                   |
|   |                     |                               |                                       |                   |
|   |                     |                               |                                       |                   |
|   |                     |                               |                                       |                   |
|   |                     |                               |                                       |                   |

| CONTINUE AND READURENCES         CONTINUE READURENCES         AUXILIARY INFORMATION         EXPERIMENTAL VALUES:         AUXILIARY INFORMATION         CONTINUE READURENCES         AUXILIARY INFORMATION         MAIL LARY INFORMATION <td al="" all<="" and="" as="" colspance="" form="" mg(oac)2,="" monosodius="" pure="" th="" to=""><th>COMPONENTS .</th><th>ORIGINAL MEASUREMENTS:</th></td>   | <th>COMPONENTS .</th> <th>ORIGINAL MEASUREMENTS:</th>                   | COMPONENTS .  | ORIGINAL MEASUREMENTS: |
|---|---|---|------------------------|
| Tektifshvili, M. G.; SNvelashvili, A. E.;         maidato.lydrate; C22H20K9K9695."H20;         (Addata: L. I.; Korzholani, N. B.;         Correction acid; HC1; [7647-01-0]         (3) Water; H20; [7732-18-5]         PH         R. Piekos         PH         R. Piekos         Auxiliary INFORMATION         Super State | COMPONENTS:<br>(1) Magnesium, ( <u>T</u> -4)-bis[4-amino- <u>N</u> -(6- |   |                        |
| (194012-83-9)<br>(2) Hydrochloric acid; HCI; [7647-01-0]<br>(3) Water; H_20; [7732-18-5]<br>PH CARTABLES:<br>pH R. Piekos EXPERIMENTAL VALUES: R. Piekos EXPERIMENTAL VALUES: R. Piekos EXPERIMENTAL VALUES: Kgo over the HCI concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , at 25°C, is 2.00 x 10 <sup>-3</sup> . SOURCE AND FURITY OF MATERIALS: Distribution of the solution of the solution of the materials was not specified. EXTENDIAPPARATUS/PROCEDURE: The earlier described apparatus and method was used (1): in a glass vessel , a mixt of 100 nl of HCI of appropriate conce and the solute were placed and shaken for 6 h in a water themostat at 25°C. After attaining equilibrium, the pH of the solu was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured on a pH 673 pH meter. ESTIMATED ERROR: Nothing specified REFERENCES: I. Taktrishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Bauk Gruz. 558   |   |   |                        |
| (2) Hydrochloric acid; HC1; [7647-01-0]         (3) Water; H <sub>2</sub> 0; [7732-18-5]         PH         R. Piekos         PH         R. Piekos         EXPERIMENTAL VALUES:         Kgo over the HC1 concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , at 25°C, is 2.00 x 10 <sup>-3</sup> .         AUXILIARY INFORMATION         METHOD/AFPARATUS/PROCEDURE:         The earlier described apparatus and method was used (1): in a glass vessel, a mixe of 100 ml of HCl of appropriate concn and the solute were placed and baken for 6 h in a water thermostat at 25°C. After attaining equilibrium, the pH of the solu was measured and the Mg <sup>24</sup> and S content was measured and the Mg <sup>24</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured on a pH 673 pH meter.         EXTERENCES:         1. Textitishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Nauk Grus. SSR  | [84812-83-9]  |   |                        |
| (3) Water; H <sub>2</sub> O; [7732-18-5]       Graz. SER, Ser. Któr. 1991, 77(4), 300-4.         (3) Water; H <sub>2</sub> O; [7732-18-5]       PREPARED BY:         pH       R. Piekos         EXPERIMENTAL VALUES:       R. Piekos         EXPERIMENTAL VALUES:       R. Piekos         EXPERIMENTAL VALUES:       R. Piekos         Kgo over the HCl concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , at 25°C, is 2.00 x 10 <sup>-3</sup> .         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         The earlier described apparatus and method was used (1): in a glass vessel , a mixt of 100 ml of HCl of appropriate concn and the solute were placed and shaken for 6 h in a water themostat at 25°C. After attaining equilibrium, the pH of the solu was measured and the Mg <sup>24</sup> and S content was determined to calculate K <sub>80</sub> The pH was measured on a pH 673 pH meter.         EXTIMATED ERROR:         KEFERENCES:         I. Takitishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Bauk Grus. SSR  |   |   |                        |
| JOU-4.         VARIABLES:         pH         R. Piekos         EXPERIMENTAL VALUES:         Kgo over the HCl concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , at 25°C, is 2.00 x 10 <sup>-3</sup> .         AUXILLARY INFORMATION         METHOD/APPARATUS/FROCEDURE:         The earlier described apparatus and method was used (1): in a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute were laced and shaken for 6 h in a water thermostat at 25°C. After attaining equilibrium, the pH of the solu was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>80</sub> . The pH was measured on a pH 673 pH meter.         FEFERENCES:       I. Tektrishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Nauk Grus. SSR  |   |   |                        |
| pH       R. Piekos         EXFERIMENTAL VALUES:         EXFERIMENTAL VALUES:         K <sub>30</sub> over the HCl concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , at 25°C, is 2.00 x 10 <sup>-3</sup> .         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         The carlier described apparatus and method vas used (1): in a glass vessel, a mixt of solid of the solute were placed and shaken for 6 b in a water thermostat at 25°C. After attaining equilibrium, the pH of the solute was measured on a pH 673 pH meter.         STINATED ERROR:         Nothing specified         REFERENCES;         1. Takitishvili, M. C.; Mikadze, I. I. Soobshoh. Akad. Nauk Grus. SSR  |   | 300-4.  |                        |
| EXPERIMENTAL VALUES:<br>K <sub>50</sub> over the HCl concentration range 5.0 x 10 <sup>-3</sup> to 1.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> ,<br>at 25°C, is 2.00 x 10 <sup>-3</sup> .<br>MINIMARY INFORMATION<br>METHOD/APPARATUS/PROCEDURE:<br>The earlier described apparatus and method<br>was used (1): in a glass vessel, a mixt of<br>100 ml of k01 of appropriate conen and the<br>solute were placed and shaken for 6 h in<br>a water thermostat at 25°C. After attaining<br>equilibrium, the pH of the soln was measured<br>and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>50</sub> . The pH was measured on a pH<br>673 pH meter.   | VARIABLES:  | PREPARED BY:  |                        |
| $\begin{tabular}{lllllllllllllllllllllllllllllllllll$   | рН  | R. Piekos   |                        |
| $\begin{tabular}{lllllllllllllllllllllllllllllllllll$   |   |   |                        |
| AUXILIARY INFORMATION METHOD/APPARATUS/PROCEDURE: The earlier described apparatus and method was used (1): in a glass vessel , a mixt of 100 ml of HCl of appropriate concn and the solute were placed and shaken for 6 h in a water thermostat at 25°C. After attaining equilibrium, the pH of the soln was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>go</sub> The pH was measured on a pH 673 pH meter. ESTIMATED ERROR: Nothing specified REFERENCES: 1. Tskitishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Nauk Grus. SSR   | EXPERIMENTAL VALUES:  |   |                        |
| AUXILIARY INFORMATION METHOD/APPARATUS/PROCEDURE: The earlier described apparatus and method was used (1): in a glass vessel , a mixt of 100 ml of HCl of appropriate concn and the solute were placed and shaken for 6 h in a water thermostat at 25°C. After attaining equilibrium, the pH of the soln was measured and the Mg <sup>2+</sup> and S content was determined to calculate K <sub>go</sub> The pH was measured on a pH 673 pH meter. ESTIMATED ERROR: Nothing specified REFERENCES: 1. Tskitishvili, M. G.; Mikadze, I. I. Soobshoh. Akad. Nauk Grus. SSR   |   |   |                        |
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| AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       soluce AND PURITY OF MATERIALS:         0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu       salt of sulfapyridazine, and HCl as well         100 ml of HCl of appropriate concn and the       solute were placed and shaken for 6 h in         a water thermostat at 25°C. After attaining       equilibrium, the pH of the soln was measured         equilate K <sub>so</sub> The pH was measured on a pH-         673 pH meter.       ESTIMATED ERROR:         Nothing specified       REFERENCES:         1. Tskitishvili, M. G.; Mikadze, I. I.       Soubshch. Akad. Nauk Gruz. SSR  | K <sub>so</sub> over the HCl concentration range                        | 5.0 x $10^{-3}$ to 1.5 x $10^{-5}$ mol dm <sup>-3</sup> , |                        |
| AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       soluce AND PURITY OF MATERIALS:         0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu       salt of sulfapyridazine, and HCl as well         100 ml of HCl of appropriate concn and the       solute were placed and shaken for 6 h in         a water thermostat at 25°C. After attaining       equilibrium, the pH of the soln was measured         equilate K <sub>so</sub> The pH was measured on a pH-         673 pH meter.       ESTIMATED ERROR:         Nothing specified       REFERENCES:         1. Tskitishvili, M. G.; Mikadze, I. I.       Soubshch. Akad. Nauk Gruz. SSR  | -   |   |                        |
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| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         The earlier described apparatus and method       0.1M solns of chem pure Mg(OAc) <sub>2</sub> , monosodiu         was used (1): in a glass vessel , a mixt of       100 ml of HCl of appropriate concn and the         solute were placed and shaken for 6 h in       a doubly distd water were used. The source         a water thermostat at 25°C. After attaining       of the materials was not specified.         equilibrium, the pH of the soln was measured       of the materials was not specified.         and the Mg <sup>2+</sup> and S content was determined to       ESTIMATED ERROR:         673 pH meter.       Nothing specified         REFERENCES:       1. Tskitishvili, M. G.; Mikadze, I. I.         Soubshch. Akad. Nauk Gruz. SSR       SSR   |   |   |                        |
| The earlier described apparatus and method<br>was used (1): in a glass vessel , a mixt of<br>100 ml of HCl of appropriate conen and the<br>solute were placed and shaken for 6 h in<br>a water thermostat at 25°C. After attaining<br>equilibrium, the pH of the soln was measured<br>and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>so</sub> The pH was measured on a pH-<br>673 pH meter.   | AUXILIARY   | INFORMATION   |                        |
| <pre>was used (1): in a glass vessel , a mixt of<br/>100 ml of HCl of appropriate concn and the<br/>solute were placed and shaken for 6 h in<br/>a water thermostat at 25°C. After attaining<br/>equilibrium, the pH of the soln was measured<br/>and the Mg<sup>2+</sup> and S content was determined to<br/>calculate K<sub>so</sub> The pH was measured on a pH-<br/>673 pH meter.</pre> ESTIMATED ERROR:<br>Nothing specified<br>REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  | METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                           |                        |
| <pre>was used (1): in a glass vessel , a mixt of<br/>100 ml of HCl of appropriate concn and the<br/>solute were placed and shaken for 6 h in<br/>a water thermostat at 25°C. After attaining<br/>equilibrium, the pH of the soln was measured<br/>and the Mg<sup>2+</sup> and S content was determined to<br/>calculate K<sub>so</sub> The pH was measured on a pH-<br/>673 pH meter.</pre> ESTIMATED ERROR:<br>Nothing specified<br>REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  | The earlier described apparatus and method                              | 0.1M solns of chem pure Mg(OAc), monosodium               |                        |
| <pre>100 ml of HCl of appropriate concn and the<br/>solute were placed and shaken for 6 h in<br/>a water thermostat at 25°C. After attaining<br/>equilibrium, the pH of the soln was measured<br/>and the Mg<sup>2+</sup> and S content was determined to<br/>calculate K<sub>so</sub> The pH was measured on a pH-<br/>673 pH meter.</pre> ESTIMATED ERROR:<br>Nothing specified REFERENCES: 1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  |   | -   |                        |
| solute were placed and shaken for 6 h in<br>a water thermostat at 25°C. After attaining<br>equilibrium, the pH of the soln was measured<br>and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>so</sub> The pH was measured on a pH-<br>673 pH meter.  |   |   |                        |
| a water thermostat at 25°C. After attaining<br>equilibrium, the pH of the soln was measured<br>and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>so</sub> The pH was measured on a pH-<br>673 pH meter.<br>ESTIMATED ERROR:<br>Nothing specified<br>REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  |   |   |                        |
| equilibrium, the pH of the soln was measured<br>and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>so</sub> The pH was measured on a pH-<br>673 pH meter.   |   | -   |                        |
| and the Mg <sup>2+</sup> and S content was determined to<br>calculate K <sub>SO</sub> The pH was measured on a pH-<br>673 pH meter.   |   |   |                        |
| calculate K <sub>so</sub> The pH was measured on a pH-<br>673 pH meter.   |   |   |                        |
| 673 pH meter.<br>ESTIMATED ERROR:<br>Nothing specified<br>REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR   |   |   |                        |
| Nothing specified<br>REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  |   |   |                        |
| REFERENCES:<br>1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR   | ovs primeter.   |   |                        |
| 1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  |   | Nothing specified   |                        |
| 1. Tskitishvili, M. G.; Mikadze, I. I.<br>Soobshch. Akad. Nauk Gruz. SSR  | · ·   |   |                        |
| Soobshch. Akad. Nauk Gruz. SSR  |   | REFERENCES:   |                        |
|   |   | 1. Tskitishvili, M. G.; Mikadze, I. I.                    |                        |
| <u>1978,</u> 89(3), 589.  |   | Soobshch. Akad. Nauk Gruz. SSR                            |                        |
|   |   | <u>1978,</u> 89(3), 589.                                  |                        |
|   |   |   |                        |
|   |   |   |                        |

| (1)<br>(2)   | pyridazinyl)t<br>hydrate; C <sub>22</sub> H<br>[84812-82-8] | s[4-amino- <u>N</u> -(6-methoxy-3-<br>enzenesulfonamidato)-<br>1 <sub>20</sub> MnN <sub>8</sub> 0 <sub>6</sub> S <sub>2</sub> •nH <sub>2</sub> 0;<br>acid; HC1; [7647-01-0]<br>[7732-18-5] | Tski<br>Mikao<br>Chrei   | NAL MEASUREMENTS:<br>tishvili, M. G.; Shvelashvili, A. E.;<br>dze, I. I.; Zhorzholiani, N. B.;<br>lashvili, M. V. Izv. Akad. Nauk<br>. SSR, Ser. Khim <u>1981</u> , 7(4),<br>4. |  |
|--|---|--|--|---|--|
| VARIA  | BLES:   |  | PREPA  | PREPARED BY:<br>R. Peikos   |  |
| EXPER  | RIMENTAL VALUE  | :S:  |  |   |  |
|  |   | Concentration of HC1<br>(mol/l)  | рН   | 10 <sup>6</sup> K <sub>so</sub> at 25 <sup>0</sup> C  |  |
|  |   | $1.0 \times 10^{-2}$   | 7.65   | 1.99  |  |
|  |   | $5.0 \times 10^{-3}$   | 7.71   | 1.97  |  |
|  |   | $2.5 \times 10^{-3}$   | 7.73   | 1.94  |  |
|  |   | $1.0 \times 10^{-3}$   | 7.75   | 1.99  |  |
|  |   | $5.0 \times 10^{-4}$   | 7.76   | 2.00  |  |
|  |   | $2.5 \times 10^{-4}$   | 7.78   | 1.97  |  |
|  |   | $1.0 \times 10^{-4}$   | 7.80   | 2.02  |  |
|  |   | $5.0 \times 10^{-5}$   | 7.82   | 2.04  |  |
|  |   | $1.5 \times 10^{-5}$   | 7.83   | 1.99  |  |
|  |   |  | Me   | an 1.99   |  |
|  |   |  |  |   |  |
|  |   | AUXILIA  | Y INFORM   | MATION  |  |
|  | OD/APPARATUS/   |  |  | E AND PURITY OF MATERIALS:  |  |
| The earlier described apparatus and method was used (1): in a glass vessel, a mixt of  |   |  |  | solns of chem pure Mn(OAc) <sub>2</sub> , monosodium<br>of sulfapyridazine, and HCl as well   |  |
| was used (1): In a glass vessel, a mixt of<br>100 ml of HCl of appropriate concn and the<br>solute were placed and shaken for 6 h in a<br>water thermostat at 25°C. After attaining<br>equilibrium, the pH of the soln was meas-<br>ured and the Mn <sup>2+</sup> and S content was deter- |   |  |  | as doubly distd water were used. The source   |  |
|  |   |  | of t   | he materials was not specified.   |  |
|  |   |  |  |   |  |
|  |   |  |  |   |  |
|  |   |  | ed   |   |  |
| mined to calculate K <sub>so</sub> . The pH was measured<br>on a pH-673 pH meter.  |   | ESTIN<br>K <sub>so</sub>   | MATED ERROR:<br>: std deviation 3 x 10 <sup>-8</sup> (compiler).<br>and pH: not specified. |   |  |

**REFERENCES:** 

1. Tskitishvili, M. G.; Mikadze, I. I. Soobshch. Akad. Nauk Gruz. SSR <u>1978</u>, *89(3)*, 589.

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| <pre>COMPONENTS:<br/>(1) Nickel, bis[4-amino-<u>N</u>-6-methoxy-3-<br/>pyridazinyl)benzenesulfonamidato]-<br/>hydrate; C<sub>22</sub>H<sub>20</sub>N<sub>8</sub>Ni0<sub>6</sub>S<sub>2</sub>•nH<sub>2</sub>0;<br/>[84825-01-4]<br/>(2) Hydrochloric acid; HC1; [7647-01-0]<br/>(3) Water; H<sub>2</sub>0; [7732-18-5]<br/>VARIABLES:</pre> | ORIGINAL MEASUREMENTS:<br>Tskitishvili, M. G.; Shvelashvili, A. E.;<br>Mikadze, I. I.; Zhorzholiani, N. B.;<br>Chrelashvili, M. V.;<br>Izv. Akad. Nauk Gruz. SSR, Ser. Khim.<br><u>1981</u> , 7(4), 300-4.<br>PREPARED BY: |
|--|--|
| рН   | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| Concentration of HCl pH<br>(mol/l)   | 10 <sup>7</sup> K <sub>so</sub> at 25 <sup>o</sup> C   |
| $1.0 \times 10^{-2}$ 7.1.  | 5 1.88   |
| $5.0 \times 10^{-3}$ 7.3   | 3 1.87   |
| $2.5 \times 10^{-3}$ 7.6   | 5 1.86   |
| $1.0 \times 10^{-3}$ 7.9   | 0 1.87   |
| $5.0 \times 10^{-4}$ 8.0   | 1 1.84   |
| $2.5 \times 10^{-4}$ 8.0   | 4 1.83   |
| $1.0 \times 10^{-4}$ 8.0   | 7 1.79   |
| $5.0 \times 10^{-5}$ 8.0   | 7 1.80   |
| $2.5 \times 10^{-5}$ 8.0   | 7 <u>1.80</u>  |
|  | Mean 1.84  |
|  |  |
|  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>The earlier described apparatus and method  | SOURCE AND PURITY OF MATERIALS:<br>0.1M solns of chem pure Ni(OAc) <sub>2</sub> , monosodium   |
| was used (1): in a glass vessel, a mixt of   | salt of sulfapyridazine, and HCl as well   |
| 100 ml of HCl of appropriate concn and the   | as doubly distd water were used. The source  |
| solute were placed and shaken for 6 h in a   | of the materials was not specified.  |
| water thermostat at 25°C. After attaining  |  |
| equilibrium, the pH of the soln was measured<br>and the Ni <sup>2+</sup> and S content was determined  |  |
| to calculate K <sub>so</sub> The pH was measured on a  |  |
| pH-673 pH meter.   | ESTIMATED ERROR:   |
|  | $K_{so}$ : std deviation 3.5 x 10 <sup>-9</sup> (compiler).  |
|  | Temp and pH: not specified.  |
|  | REFERENCES:  |
|  | <ol> <li>Tskitishvili, M. G.; Mikadze, I. I.<br/>Soobshch. Akad. Nauk Gruz. SSR<br/><u>1978</u>, 89(3), 589.</li> </ol>  |
| L  |  |

| COMP | ONENTS:   | ORIGINAL MEASUREMENTS:  |
|------|---|---|
| (1)  | Acetamide, N-[4-[[(6-methoxy-2-py-<br>ridazinyl)amino]sulfonyl]phenyl]-<br>(acetyl sulfamethoxypyridazine);<br>C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [127-75-3]<br>Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] | Bandelin, F. J.; Malesh, W.<br><i>J. Am. Pharm. Assoc., Sci. Ed.</i> <u>1959</u> ,<br>48, 177-81. |
| (3)  | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7889-77-0]   | PREPARED BY:  |
| (4)  | Water; H <sub>2</sub> 0; [7732-18-5]  | R. Piekos   |
| VARI | ABLES: pH   |   |

## EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethoxypyridazine in buffers of varying mixtures of  $Na_2HPO_4 \cdot 7H_2O$  (71.6 g/l distilled water; 0.27 mol dm<sup>-3</sup>, compiler ) and  $KH_2PO_4$  (36.3 g/l distilled water; 0.27 mol dm<sup>-3</sup>, compiler) at  $37^{\circ}C$ 

| Frudlichadum all | Solubility (based on | sulfamethoxypyridazine)                      |
|------------------|----------------------|--|
| Equilibrium pH   | mg/100 ml            | $10^3 \text{ mol } \text{dm}^{-3} \text{ a}$ |
| 4.5              | 22                   | 0.78   |
| 4.8              | 24                   | 0.86   |
| 5.4              | 26                   | 0.93   |
| 5.9              | 28                   | 1.0  |
| 6.2              | 30                   | 1.1  |
| 7.0              | 41                   | 1.5  |
|                  |                      |  |

### AUXILIARY INFORMATION

| METHOD / APPARATUS / PROCEDURE :               | COURCE AND DUDITY OF WATERLAND.                           |
|--|---|
| METHOD/AFFARATOS/FROCEDORE:                    | SOURCE AND PURITY OF MATERIALS:                           |
| Solns were prepd by adding an excess of ace-   | Neither source nor purity of the reagents                 |
| tyl sulfamethoxypyridazine to 10 ml of buffer  | were specified. Distilled water was used.                 |
| soln at each pH level in 18 x 150 mm test      |   |
| tubes, stoppering the tubes, and placing them  |   |
| in water bath at 37°C with gentle agitation    |   |
| for 24 h. The solute was then hydrolyzed       |   |
| with 5% $H_2SO_4$ for 1 h to liberate the free |   |
| sulfonamide. One-ml aliquot of the hydroly-    |   |
| zate was accurately pipetted into a volume-    | ESTIMATED ERROR:  |
| tric flask for diln and analysis. The sul-     | Soly: av values of duplicate runs are reported (authors). |
| fonamide was assayed colorimetrically by the   | Temp and pH: not specified.                               |
| method of Bratton and Marshall as described    |   |
| in detail by Biamonte and Schneller (1). A     | REFERENCES:   |
| standard curve was prepd using accurately      | 1. Biamonte, A. R.; Schneller, G. E.                      |
| prepd standard solutions.                      | J. Am. Pharm. Assoc., Sci. Ed.                            |
|  | <u>1952</u> , <i>41</i> , 341.                            |
|  |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:    |
|---|---------------------------|
| <ol> <li>Acetamide, N-[4[[(6-methoxy-2-pyridazin-<br/>yl)amino]sulfonyl]phenyl]-(acetyl sulfa-<br/>methoxypyridazine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S;<br/>[127-75-3]</li> <li>Calcium chloride; CaCl<sub>2</sub>; [10043-52-4]</li> <li>Magnesium chloride; MgCl<sub>2</sub>; [7786-30-3]</li> <li>Phosphoric acid, monoammonium salt;</li> </ol> |                           |
| NH <sub>4</sub> H <sub>2</sub> PO <sub>4</sub> ; [7722-76-1]<br>(5) Potassium chloride; KCl; [7447-40-7]<br>(6) Sodium chloride; NaCl; [7647-14-5]<br>(7) Urea; CH <sub>4</sub> N <sub>2</sub> O; [57-13-6]   | PREPARED BY:<br>R. Piekos |
| (8) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES: pH at 37 <sup>o</sup> C  |                           |

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethoxypyridazine in a solution containing  $CaCl_2$  0.143,  $MgCl_2$  0.121,  $NH_4H_2PO_4$  0.300, KCl 1.660, NaCl 2.950 and urea 20 g/dm<sup>3</sup> (synthetic urine, Mosher vehicle) at  $37^{\circ}C$ 

|                | Solubility                 |   |  |
|----------------|----------------------------|---|--|
| Equilibrium pH | mg/100 ml<br>as sulfametho | 10 <sup>2</sup> mol/dm <sup>3</sup> a<br>xypyridazine |  |
| 4.5            | 165                        | 0.51  |  |
| 5.0            | 168                        | 0.52  |  |
| 5.5            | 174                        | 0.54  |  |
| 6.0            | 182                        | 0.56  |  |
| 6.5            | 212                        | 0.66  |  |
| 7.0            | 290                        | 0.90  |  |

<sup>a</sup>calculated by compiler

| AUXILIARY   | INFORMATION |
|---|-------------|
| METHOD/APPARATUS/PROCEDURE:<br>Excess acetyl sulfamethoxypyridazine was add-<br>ed to aliquots of synthetic urine solns and<br>1% H <sub>3</sub> PO <sub>4</sub> or 1% NaOH solns were used to adjust<br>the pH to the required value. The solns were<br>agitated for 24 h with addn of acid or base<br>to keep them at the desired pH level until<br>equilibrium was attatined. Then the solns<br>were filtered and in aliquots the acetylsul- |             |
| fonamide was assayed spectrophotometrically<br>by the method described by Biamonte and<br>Schneller (1). Before detn the soln was re-<br>fluxed with $5\%$ H <sub>2</sub> SO <sub>4</sub> for 1 h to liberate the<br>free amino compound.   |             |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                  |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-[6-(methyl-<br/>thio)-3-pyridazinyl]- (sulfamethylmercap-</li> </ol> | Riess, W.                               |
| topyridazine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub> ; [7758-81-8]   |   |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                       | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                   |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:                            |
| VARIABLES:<br>One temperature: 20 <sup>o</sup> C; one pH: 7.4   | R. Piekos                               |
| one temperature: 20 C; one ph: 7.4  |   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| Solubility of sulfamethylmercaptopyrid  | azine in a M/15 Sörensen buffer         |
| solution ( pH 7.4 ) at 20 <sup>0</sup> C is 29 mg%  |   |
| solution ( pH 7.4 ) at 20°C is 29 mg%   | (9.8 X 10 mol dm solution,              |
| compiler ).   |   |
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| AUXILIARY   | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:         |
| Sörensen buffer solns of pH varying between   | Nothing specified                       |
| 7 and 8 were prepd, satd with sulfamethyl-  |   |
| mercaptopyridazine at 20 <sup>0</sup> C, their pH was   |   |
| measured at equilibrium, and the sulfamethy   |   |
| mercaptopyridazine was assayed colorimetri-   |   |
| cally. The measured pH values were plotted  |   |
| against concn, and the soly at pH 7.4 was   |   |
| detd by interpolation (personal communica-  |   |
| tion).  | ESTIMATED ERROR:                        |
|   | Nothing specified                       |
|   |   |
|   | DEPENSION -                             |
|   | REFERENCES:                             |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-<br>methylthio)-3-pyridazinyl]- (sulfame- | Reiss, W.                               |
| thylmercaptopyridazine);   |   |
| $C_{11}H_{12}N_4O_2S_2$ ; [7758-81-8]  | Intern, Congr. Chemotherapy, Proc.      |
| <pre>(2) Methane, trichloro- (chloroform);</pre>                               | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
|  |   |
| CHCl <sub>3</sub> ; [67-66-3]  |   |
| VARIABLES:   | PREPARED BY:                            |
| One temperature: 20 <sup>0</sup> C   | R. Piekos                               |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfamethylmercaptopyrid   | azine in chloroform at 20°C is          |
| 150 mg% ( $5.06 \times 10^{-3}$ mol dm <sup>-3</sup> solution                  | n, compiler ).                          |
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| AUXILIARY  | INFORMATION                             |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:         |
|  |   |
| Nothing specified  | Nothing specified                       |
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|  | ESTIMATED ERROR:                        |
|  | Nothing specified                       |
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|  | REFERENCES:                             |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfapyrimidine); | EVALUATOR:<br>Anthony N. Paruta<br>Department of Pharmaceutics   |
|--|--|
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]             | University of Rhode Island                                       |
| (2) Water  | Kingston, Rhode Island, USA<br>and                               |
|  | Ryszard Piekos   |
|  | Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986 |

CRITICAL EVALUATION:

There were twelve reports (1-12) giving values for the aqueous solubility of this compound at four temperatures as shown in Table I.

Table I: Solubility of Sulfapyrimidine in water at various temperatures

|           |       | $10^4 \text{ mol } dm^{-3}$ (* | *indicates mol | kg <sup>-1</sup> ) |
|-----------|-------|--------------------------------|----------------|--------------------|
| Reference | 293K  | 298K                           | 303K           | 310K               |
| 1         | -     | -                              | -              | 4.91               |
| 2         | -     | 3.08*                          | -              | 5.07               |
| 3         | -     | -                              | -              | 21.4               |
| 4         | -     | -                              | -              | 4.8                |
| 5         | -     | -                              | 6.0            | -                  |
| 6         | -     | -                              | 3.46           | -                  |
| 7         | -     | -                              | 5.4            | -                  |
| 8         | 1.81* | -                              | 3.04*          | 5.15               |
| 9         | 2.36  | -                              | -              | -                  |
| 10        | -     | -                              | -              | 5.07               |
| 11        | -     | -                              | -              | 5.11               |
| 12        | -     | -                              | -              | 5.11               |

The solubility at 298 was reported (2) only once and seems to be correct. At 293K, Elworthy and Worthington (8) and Corby and Elworthy (9), in two studies three years apart, used the same technique of percolation over a period of 5-14 days. The values differ by some 30% possibly due to the reported technique. While no recommended value can be given, an approximate solubility value of  $2 \times 10^{-4}$  mol dm<sup>-3</sup> for sulfapyrimidine can be suggested. At 303K, there were four values (5-8) reported. The only reasonable values appear to be those of Elworthy and Worthington (8), and Higuchi and Lach (6). Those given by Bhattacharyya (5) and Yamazaki et al. (7) are much larger and not considered further. The other values (6,8) do not agree well; the lower value being 84% of the higher value (6) given by Higuchi. Therefore, a recommended value cannot be given but a tentative solubility value of about 3.3  $\times 10^{-4}$  mol dm<sup>-3</sup> can be suggested at 303K and seems to be in accord with other temperature data. At 310K, there were eight values available (1-4,8,10-12). That given by Kikuth (3) was obviously out of line at about four times greater than the rest. The remaining values (1,2,4,8,10-12) were quite close, and the equilibrium time was at least 24 hours (1,2,4), up to 3 to 5 days (10-12), or 7-14 days (8). The average of these values, 5.03  $\times 10^{-4}$  mol dm<sup>-3</sup> is the recommended solubility of sulfapyrimidine in water at 310K.

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#### **REFERENCES:**

Roblin, R.O., Jr.; Williams, J. H.; Winnek, P. S.; English, J.P. J. Am. Chem. Soc. (1) <u>1940,</u> 62, 2002-5. Clark, W. G.; Strakosch, E. A.; Levitan, N. I.; J. Lab. Clin. Med. <u>1942</u>, (2) 28, 188-9. Kikuth, W. Med. Welt. 1943, 17(26/27), 483-6. (3)Langecker, H. ARch. Exptl. Path. Pharmakol Bhattacharyya, R. Basu, U. P. Indian Pharmacist <u>1948</u>, (4) 205. 291-301. 1950, (5) 6(3), 77-8,86. Higuchi, T. Lach, J. L. J. Amer. Pharm. Assoc., Sci. Ed. 1954, (6) *43*, 349-54. 27(1), (7) Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. Yakuzaigaku 1967, 37-40. Elworthy, P. H.; Worthington, H. E. C. J. Pharm. Pharmac. <u>1968</u>, Corby, T. C.; Elworthy, P. H. J. Pharm. Pharmac. <u>1971</u>, <u>23</u>, 20, (8) 830-5. (9) Suppl. 39S-48S. 24(11), Watari, N.; Kaneniwa, N. Chem. Pharm. Bull. 1976, (10)2577-84. (11) Kaneniwa, N.; Watari, N. Chem. Pharm. Bull. 1978,
(12) Watari, N.; Kaneniwa, N.; Hanano, M. Int. J. Pharm. 26(3) 813-26. 1980, 6(2), 155-66.

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                       |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       | Roblin, R. O., Jr.; Williams, J. H.;                         |
| <pre>pyrimidinyl- (sulfapyrimidine);</pre>                                 | Winnek, P. S.; English, J. P.                                |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9] | J. Am. Chem. Soc. <u>1940</u> , 62, 2002-5.                  |
|  | <u> </u>   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                   |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
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| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfapyrimidine in water                                     | at 37 <sup>0</sup> C is 12.3 mg/100 cm <sup>3</sup> solution |
|  |  |
| $(4.91 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler }).$            |  |
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| ALLETT TADY.   | INFORMATION  |
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| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                              |
| Excess sulfonamide in water was heated and                                 | Sulfapyrimidine, mp 255-6 <sup>°</sup> C (dec, cor),         |
| stirred on a steam bath for 30 min. The                                    | was prepd by the authors. Anal: %C 48.1                      |
| suspension was then agitated for 24 h in a                                 | (calcd 48.0); %H 4.0 (4.0); %N 21.7                          |
| thermostat at 37°C. A sample of the satd                                   | (22.4).  |
| soln was withdrawn through a glass filter,                                 | Purity of the water was not specified.                       |
|  | I unity of the water was not specified.                      |
| dild, and analyzed by the Marshall method                                  |  |
| (1) using a General Electric recording spec-                               |  |
| trophotometer for comparing the colors deve-                               |  |
| loped with those of the standards.   | ESTIMATED ERROR:   |
|  |  |
|  | Nothing specified  |
|  |  |
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|  | REFERENCES:  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                      |
|  | J. Pharmacol. 1939, 66, 4.                                   |
|  |  |
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| COMPONENTS:  |                   |                     | ORIGINAL MEASUREMENTS:                                 |
|--|-------------------|---------------------|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       |                   |                     | Clark, W. G.; Strakosch, E. A.;                        |
| pyrimidinyl- (sulfadiazine);   |                   |                     | Levitan, N. I. J. Lab. Clin. Med.                      |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |                   |                     | <u>1942</u> , 28, 188-9.                               |
| (2) Water; H <sub>2</sub> O;   | [7732-1           | 8-5]                |  |
|  |                   |                     |  |
| VARIABLES:   | rature            |                     | PREPARED BY:<br>R. Piekos                              |
| rempe.   | lacure            |                     | A. ILENUD  |
| EXPERIMENTAL VALUE   | s:                |                     | l  |
|  | •                 |                     |  |
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|  |                   |                     |  |
|  | t/ <sup>o</sup> C | Solu                | bility   |
|  |                   | g/100 g water 1     | 0 <sup>4</sup> mol kg <sup>-1</sup> water <sup>a</sup> |
|  | 25                | 0.0077              | 3.08   |
|  | 37                | 0.0127              | 5.07   |
|  |                   |                     |  |
|  |                   |                     |  |
|  | <sup>a</sup> Ca.  | lculated by compile | r  |
|  |                   |                     |  |
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|  |                   |                     | INFORMATION  |
| METHOD/APPARATUS/I   |                   |                     | SOURCE AND PURITY OF MATERIALS:                        |
|  |                   | ainer contg excess  | Neither source nor purity of sulfadiazine              |
|  |                   | shaken in a water   | was specified.   |
| bath thermostat for 24 h. The satd soln was                                |                   |                     | <i>4</i>   |
|  | •                 | on through a washed | i (  |
|  |                   | stick into a weigh  |  |
| ed weighing bottle. The entire app was kept                                |                   |                     |  |
|  |                   | compd was dissolved | •  |
| The amt dissolved was then detd by the me-                                 |                   |                     | ESTIMATED ERROR:                                       |
| thod of Bratton and Marshall (1) using a                                   |                   |                     | Soly: not specified.                                   |
| photoelectric colorimeter.   |                   | •                   | Temp: ±0.1°C (authors).                                |
|  |                   |                     |  |
|  |                   |                     | REFERENCES:  |
|  |                   |                     | 1. Bratton, a. C.; Marshall, E. K., Jr.                |
|  |                   |                     | J. Biol. Chem. <u>1939</u> , 128, 537.                 |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                               |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       | Kikuth, W.   |
| <pre>pyrimidinyl- (sulfapyrimidine);</pre>                                 | Med. Welt <u>1943</u> , 17(26/27), 483-6.            |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |  |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                   |  |
| (2) water, 120, [7752 10 5]  |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37°C  | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfapyrimidine in wate                                      | $x = 27^{\circ} c = 4a = 52 = 5 = ma / 100 = cm^{3}$ |
|  |  |
| solution ( 2.14 x $10^{-3}$ mol dm <sup>-3</sup> , comp                    | iler ).  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                      |
|  |  |
| Nothing specified  | Sulfapyrimidine was a product of Bayer.              |
|  | The pH of the water was 7.0.                         |
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|  | ESTIMATED ERROR:                                     |
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|  | Nothing specified.                                   |
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|  | REFERENCES :   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                 |
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| (1) Benzenesulfonamide, 4-amino-N-2-                                       | Langecker, H.  |
| pyrimidinyl- (sulfadiazine);   | Arch. Exptl. Fath. Pharmakol. <u>1948</u> ,            |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | 205, 291-301.  |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                   |  |
| 2  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
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| EXPERIMENTAL VALUES:   | · · · · · · · · · · · · · · · · · · ·                  |
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| Solubility of sulfadiazine in water a                                      | $137^{\circ}$ C is 12 mg% ( 4.8 x 10 <sup>-4</sup>     |
| mol dm <sup>-3</sup> , compiler ).   |  |
| mor um , compret ,.  |  |
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|  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                        |
| An excess of sulfadiazine was boiled with                                  | Source and purity of the materials were                |
| water and left for 24 h in a vessel protect-                               | not specified.   |
| ed from access of CO2. The concn of sulfa-                                 |  |
| diazine was detd colorimetrically by the                                   |  |
| method of Bratton and Marshall (1) using a                                 |  |
| Havemann colorimeter (2), as well as by                                    |  |
| microanal detn of the solid residue.                                       |  |
|  |  |
|  | ESTIMATED ERROR:                                       |
|  | Nothing specified                                      |
|  | ······ • ·····························                 |
|  | PEEDENCES.   |
|  | REFERENCES:<br>1. Bratton, A. G.; Marshall, E. K., Jr. |
|  | J. Biol. Chem. 1939, 128, 537.                         |
|  | 2. Havemann, R. Klin. Wochenschr.                      |
|  | <u>1940</u> , p. 503.                                  |
|  | <u></u> , p. 100                                       |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                          |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-</li> </ol>                       | Bhattacharyya, R.; Basu, U. P.                  |
| pyrimidinyl- (sulfadiazine);   | Indian Pharmacist <u>1950</u> , 6(3), 77-8, 86. |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |   |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                   |   |
| (2) water; n <sub>2</sub> 0; [7732-18-5]                                   |   |
| VARIABLES:   | PREPARED BY:                                    |
| One temperature: 30 <sup>0</sup> C   | R. Piekos                                       |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfadiazine in water a                                      | t 30 <sup>0</sup> C is 15 mg per 100 ml         |
| $(6.0 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler }).$             |   |
| ( 6.0 x 10 <sup>-</sup> mol dm <sup>-</sup> , compiler ).                  |   |
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| AUXILIARY  | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                 |
| A weighed sample of sulfadiazine was placed                                | Neither source nor purity of the sulfa-         |
| in a clean reagent bottle and a known vol of                               | diazine was specified.                          |
| water was added. The mixt was shaken in a                                  | Doubly distd water was used.                    |
| mech shaker at 80-100 strokes/min. After                                   |   |
| at least 24 h the mixt was filtered through                                |   |
| a clean, dried and weighed sintered-glass                                  |   |
| crucible. At the end of the filtration                                     |   |
| the crucible was washed with about 1 ml of                                 | ESTIMATED EDDODA                                |
| water, dried at $105^{\circ}$ C for 2-3 h, cooled, and                     | Soly: not specified.                            |
| weighed to const wt.   | Temp: $\pm 0.2^{\circ}C$ (authors).             |
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|  | REFERENCES:                                     |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                                     |
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| (1) Benzenesulfonamide, 4-amino-N-2-   | Higuchi, T.; Lach, J. L.                                   |
| pyrimidinyl- (sulfadiazine);   | J. Amer. Pharm. Assoc., Sci. Ed.                           |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]             | <u>1954</u> , <i>43</i> , 349-54.                          |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   | <u>1997</u> , 10, 949 940                                  |
| (2) "deer, "jo," [7752 10 5]   |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 30 <sup>0</sup> C   | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfadiazine in water a  | at $30^{\circ}$ C is 3.46 x $10^{-4}$ mol dm <sup>-3</sup> |
| solution (9.11 x $10^{-2}$ g dm <sup>-3</sup> , compi                                  |  |
| solution ( 9.11 x 10 " g dm ", compl.  | ler ).   |
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| AUXILIARY  | INFORMATION  |
| ME THOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                            |
| Excess sulfadiazine (25 mg) was placed in a  | Recrystd sulfadiazine (U.S.P.), mp 255-6°C,                |
| 125-ml glass-stoppered bottle together with  | and distilled water were used.                             |
| 50 ml of water. The bottle was placed in a   | and distilled water were used.                             |
| 1  |  |
| mech shaker in a const temp bath and equili-<br>brated for 8 h at 30°C. Aliquot of the |  |
|  |  |
| supernatant liquid was analyzed for sulfa-   |  |
| diazine by the method of Bratton and Mar-<br>shall (1).                                |  |
| shall (1).   | ESTIMATED ERROR:   |
|  |  |
|  | Nothing specified.   |
|  |  |
|  | REFERENCES:  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                    |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.                     |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                   |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-</li> </ol>                       | Yamazaki, M.; Aoki, M.; Kamada, A.;                      |
| pyrimidinyl- (sulfadiazine);   | Yata, N. Yakuzaigaku, <u>1967</u> , 27(1),               |
|  | 37-40.   |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | 57-40.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                   |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 30°C  | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfadiazine in water at                                     | $30^{\circ}C$ is 0.54 mmol/L ( 0.14 g dm <sup>-3</sup> , |
| compiler ).  |  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                          |
| Sulfadiazine (0.5 g) was placed in an L-                                   | Nothing specified.                                       |
| shaped tube together with 20 ml of water.                                  |  |
| The mixt was shaken in a thermostat until                                  |  |
| equilibrium was attained. The sulfadiazine                                 |  |
| content was assayed in the supernatant                                     |  |
| spectrophotometrically at 545 nm on a Beck-                                |  |
| mann DU spectrophotometer. The results were                                |  |
| taken from a calibration graph.  |  |
|  | ESTIMATED ERROR:   |
|  | Soly: not specified.                                     |
|  | Temp: ±1 <sup>0</sup> C (authors).                       |
|  |  |
|  | REFERENCES:  |
|  |  |
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| OMPONENTS                                      | •                   |                                | ORIGINAL MEASUREMENTS:   |
|--|---------------------|--------------------------------|--|
|  |                     | lde, 4-amino-N-2-              | Elworthy, P. H.; Worthington, H. E. C.   |
|  |                     | sulfadiazine);                 | J. Pharm. Pharmac. 1968, 20, 830-5.  |
|  | LON4025; [6         |                                |  |
|  | ; H <sub>2</sub> 0; |                                |  |
| (2) Wales                                      | ., 120,             | [7752-10-5]                    |  |
| ARIABLES:                                      |                     |                                | PREPARED BY:   |
|  | Temper              | rature                         | R. Piekos  |
|  |                     |                                |  |
| XPERIMENT                                      | AL VALUES:          |                                |  |
|  |                     |                                |  |
|  |                     |                                |  |
|  |                     | <b>.</b>                       |  |
|  | t/ <sup>o</sup> C   |                                | ubility  |
|  |                     | Weight % 10 <sup>6</sup> m     | ole fraction 10 <sup>4</sup> mol kg <sup>-1</sup> water <sup>a</sup>             |
|  | 20                  | 0.00454                        | 3.27 1.81  |
|  | 30                  | 0.00760                        | 5.47 3.04  |
|  |                     |                                |  |
|  | 40                  | 0.01290                        | 9.29 5.15  |
|  |                     |                                |  |
|  |                     | <sup>a</sup> Calculated by com | niler  |
|  |                     |                                | r  |
|  |                     |                                |  |
|  |                     | AUXILIA                        | RY INFORMATION   |
| ÆTHOD/APF                                      | ARATUS/PROC         | CEDURE:                        | SOURCE AND PURITY OF MATERIALS:  |
| Solns wer                                      | e presatd b         | by shaking with powd su        | 1- Sulfadiazine (B. P. quality) was twice re-                                    |
| fadiazine                                      | e for 24 h a        | and transferred to a so        |  |
| app which                                      | n was of the        | e percolation type and         |  |
|  |                     | used by Davies and             | Assay by the Pharmacopeial method gave   |
|  |                     | soln was recycled in t         |  |
| app through a sintered-glass filter until      |                     |                                | material dried at 105°C.   |
|  | -                   | Samples were dild wit          |  |
|  | • •                 | ectrophotometrically a         |  |
| 270 nm. Suitable calibration lines were prepd. |                     | libration lines were           | ESTIMATED ERROR:<br>Soly: mean values of duplicate runs are<br>given ( authors). |
|  |                     |                                | Temp: ±0.05°C (authors).   |
|  |                     |                                | REFERENCES:  |
|  |                     |                                | 1. Davies, M; Griffiths, D. M. L.  |
|  |                     |                                | Trans. Faraday Soc. <u>1953</u> , 49,  |
|  |                     |                                | 1405.  |
|  |                     |                                |  |
|  |                     |                                |  |
|  |                     |                                |  |

| 133  |
|--|
| ORIGINAL MEASUREMENTS:<br>Corby, T. C.; Elworthy, P. H.<br>J. Pharm. Pharmac. <u>1971</u> , 23, Suppl.<br>39S-48S.<br>PREPARED BY:   |
| R. Piekos  |
| turated aqueous solution at 20 <sup>0</sup> C<br>wt, compiler ).   |
| ( INFORMATION  |
| <ul> <li>SOURCE AND PURITY OF MATERIALS:</li> <li>Sulfadiazine (Macarthy's Ltd, Romford) was<br/>a British Pharmacopeia product. It was<br/>recrystd twice from a DMF-EtOH mixt (1:3)</li> <li>and dried at 40°C over P205. Its mp was<br/>254° (decompn).</li> <li>Tap water once distd from glass was used.</li> </ul> |
|  |

REFERENCES:

 Elworthy, P. H.; Lipscomb, F. J. J. Pharm. Pharmac. <u>1968</u>, 20, 790.

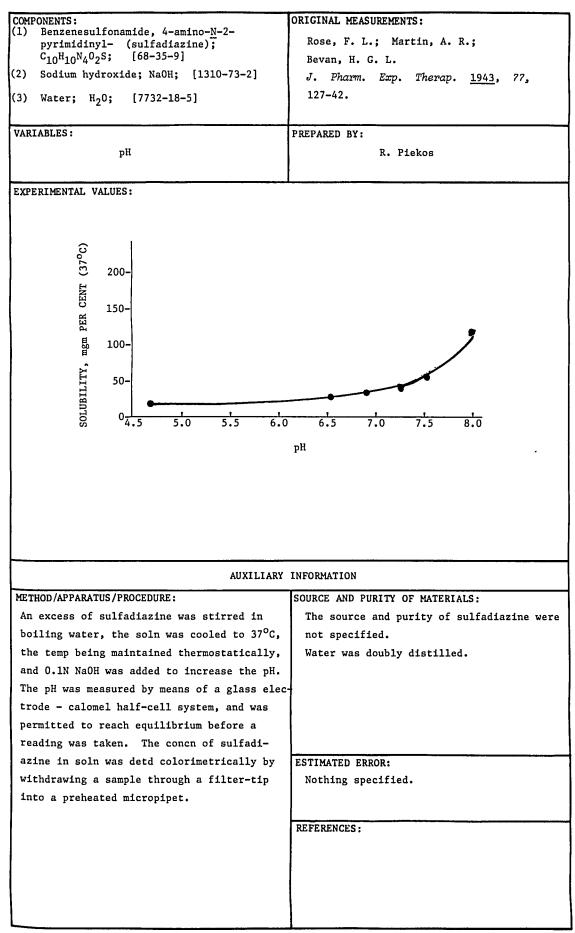
| 134  |  |
|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-            | ORIGINAL MEASUREMENTS:<br>Watari, N.; Kaneniwa, N. |
| pyrimidinyl- (sulfadiazine);                                   | Chem. Pharm. Bull. <u>1976</u> , 24(11),           |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]                               | 2577-84.   |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                       |  |
| $(2)$ water; $n_20$ ; $[7732-10-5]$                            |  |
| VARIABLES:   | PREPARED BY:                                       |
| One temperature: 37 <sup>0</sup> C                             | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  | $27^{\circ}$ $(127 - 2)^{\circ}$                   |
| Total solubility of sulfadiazine in wa                         | Let at 5/ G is 0.12/ mg/ml solution                |
| $(5.07 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler.})$ |  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:                                    | SOURCE AND PURITY OF MATERIALS:                    |
| An excess of sulfadiazine, required to sa-                     | Commercial sulfadiazine of the Japanese            |
| turate water, was placed in a flask contg                      | Pharmacopeia grade and distd water were            |
| 25 ml of water. The flask was shaken (2                        | used.  |
| strokes/s) at the amplitude of 3 cm in a                       | Į  |
| thermostatically controlled water bath at                      |  |
| 37 <sup>o</sup> C. One-ml sample was removed every 6 h         |  |
| (total equilibration period 3-5 days) using                    |  |
| a warmed Millipore filter syringe with a                       |  |
| filter pore size of 0.45 $\mu$ (Millipore HAWP                 | ESTIMATED ERROR:                                   |
| 01300) and the filtrate was dild with water                    | Temp: ±0.05 <sup>0</sup> C (authors).              |
| and assayed spectrophotometrically (1).                        | Soly: not specified.                               |
|  | PERPENDING   |
|  | REFERENCES :                                       |
|  | 1. Kaneniwa, N.; Watari, N.                        |
|  | Chem. Pharm. Bull. <u>1974</u> , 22, 1699.         |
|  |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Kaneniwa, N.; Watari, N.   |
| pyrimidinyl- (sulfadiazine);   | Chem. Pharm. Bull. <u>1978</u> , 26(3),  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]   | 813-26.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:<br>Solubility of sulfadiazine in water at 3<br>( 5.11 x 10 <sup>-4</sup> mol dm <sup>-3</sup> , compiler ). | 37°C is 0.128 mg/ml solution   |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| An excess of sulfadiazine was placed in a  | Commercial sulfadiazine of the Japanese  |
| flask contg 25 ml of water. The flask was  | Pharmacopeia grade and distd water were  |
| shaken (2 strokes/s at the amplitude of 3  | used.  |
| cm ) in a thermostatically controlled water  |  |
| bath at 37 <sup>0</sup> C. One-ml sample was withdrawn   |  |
| every 6 h ( total equilibration period was   |  |
| 3-5 days ) using a warmed Millipore filter   |  |
| syringe with a filter pore size of 0.45 $\mu$  |  |
| (Millipore HAWP 01300) and the filtrate was  | ESTIMATED ERROR:   |
| dild with water and assayed spectrophoto-  | Soly: not specified.   |
| metrically (1).  | Temp: ±0.05°C (authors).   |
|  |  |
|  | REFERENCES :   |
|  | l. Kaneniwa, N.; Watari, N.<br><i>Chem. Pharm. Bull.</i> <u>1974</u> , 22, 1699. |
|  |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Watari, N.; Kaneniwa, N.; Hanano, M.  |
| <pre>pyrimidinyl- (sulfadiazine);</pre>   | Int. J. Pharm. <u>1980</u> , 6(2), 155-66.                                    |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]                            |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| 2   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
| EXPERIMENTAL VALUES:  |   |
| EXILATED TAL VALUES.  |   |
| Solubility of sulfadiazine in water a<br>( 5.11 x 10 <sup>-4</sup> mol dm <sup>-3</sup> , compiler ). | t 37 <sup>0</sup> C is 12.8 mg/100 ml   |
|   |   |
|   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>The earlier developed method was employed                              | SOURCE AND PURITY OF MATERIALS:<br>Sulfadiazine was of the Japanese Pharmaco- |
| (1), whereby an excess of sulfadiazine, re-   | peia grade.   |
| quired to saturate medium, was placed in a  | Distilled water was used.   |
| flask contg 25 ml of water. The flask was   |   |
| stroked (2 strokes/s) at an amplitude of 3  |   |
| cm, in a thermostatically controlled bath.  |   |
| One-ml sample was removed every 6 h ( total   |   |
| equilibration time was 3-5 days) using a  |   |
| warmed Millipore filter syringe with a fil-   |   |
| ter pore size of 0.45 μ (Millipore HAWP   | ESTIMATED ERROR:<br>Soly: not specified.                                      |
| 01300) and the filtrate was dild with water   | Temp: ±0.05 <sup>°</sup> C (authors).   |
| and assayed spectrophotometrically).  |   |
|   | REFERENCES:   |
|   | 1. Kaneniwa, N.; Watari, N.   |
|   | Chem. Pharm. Bull. <u>1974</u> , 22, 1699.                                    |
|   |   |
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|  | 107   |
|--|---|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-              | ORIGINAL MEASUREMENTS:                          |
| pyrimidinyl- (sulfadiazine);<br>$C_{10}H_{10}N_4O_2S;$ [68-35-9] | Nogami, H.; Nagai, T.; Suzuki, A.               |
|  | Chem. Pharm. Bull. <u>1966</u> , 14(4), 339–50. |
| (2) Hydrochloric acid; HC1; [7647-01-0]                          |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]                         |   |
| VARIABLES:   | PREPARED BY:                                    |
| Concentration of HC1   | R. Piekos                                       |
|  |   |
| EXPERIMENTAL VALUES:   |   |
|  |   |
|  |   |
|  |   |
|  | ility of sulfadiazine at 37 <sup>0</sup> C      |
| mol dm <sup>-3</sup> mg/1  | $10^{4} \text{ mol dm}^{-3} \text{ a}$          |
| 10 <sup>-1</sup> 92  | .0 36.8   |
| 10 <sup>-2</sup> 18  | .0 7.19   |
| 10 <sup>-3</sup> 11  | .1 4.43   |
|  |   |
| <sup>a</sup> Calculated by compi                                 | ler   |
|  |   |
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| AUXILIARY  | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:                                      | SOURCE AND PURITY OF MATERIALS:                 |
| Soly of sulfadiazine was detd from dissoln                       | Commercial sulfadiazine J. P. was used.         |
| rate data obtained by the rotating disk                          | Purity of the remaining materials was not       |
| method.  | specified.                                      |
|  |   |
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|  |   |
|  |   |
|  | ESTIMATED ERROR:<br>Nothing specified.          |
|  | Nothing specified.                              |
| · ·  |   |
|  | REFERENCES:                                     |
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| COMPONENTS:  | - 11 0        | ORIGINAL MEASUREMENTS:                    |
|--|---------------|---|
| <ol> <li>Benzenesulfonamide, 4-amin<br/>pyrimidinyl- (sulfadiazi)</li> </ol> |               |   |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]   | ne);          | Krebs, H. A. ; Speakman, J. C.            |
| (2) Hydrochloric acid; HC1;  | [7647-01-0]   | J. Chem. Soc. <u>1945</u> , 593–5.        |
| (3) Sodium chloride; NaCl; [   |               |   |
| (4) Water; H <sub>2</sub> O; [7732-18-5                                      |               |   |
|  |               |   |
| VARIABLES:   |               | PREPARED BY:                              |
| pH   |               | R. Piekos                                 |
| £  |               |   |
|  |               |   |
| EXPERIMENTAL VALUES:   |               |   |
|  |               |   |
|  |               |   |
| рН   | Solubility    | of sulfadiazine at 25.0 <sup>0</sup> C    |
| at saturation  | -             | n of ionic strength 0.1M                  |
|  | maintained    |   |
|  | maintained    |   |
|  | mg/100 ml     | $10^3 \text{ mol } dm^{-3} a$             |
| ······································                                       |               |   |
| 1.00 <sup>b</sup>  | 68            | 2.7                                       |
| 1.26   | 66            | 2.6                                       |
| 1.55   | 25.2          | 1.01                                      |
|  |               | 1.01                                      |
| 1.89   | 16.5          | 0.659                                     |
|  |               |   |
| <sup>a</sup> Calculated by   | y compiler    |   |
| <sup>b</sup> in 0.15N HC1  |               |   |
|  |               |   |
|  |               |   |
|  |               |   |
|  | AUXILIARY     | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:  |               | SOURCE AND PURITY OF MATERIALS:           |
| The HCl solns were satd by shak  | ing them with |   |
| •  | -             | 1   |
| an excess of solid sulfadiazine  |               |   |
| 3 h. They were then quickly filtered. The                                    |               | specified) from water.                    |
| sulfadiazine concn was detd by   | the method of | Purity of the remaining materials was not |
| Bratton and Marshall (1), and t  | he pH values: | specified.                                |
| were measured with the glass el  | ectrode.      |   |
| which was standardized in terms  | -             |   |
| fer solns recommended by Hitche  |               |   |
| •  | ock and       |   |
| Taylor (2).  |               | ESTIMATED ERROR:                          |
|  |               | Nothing specified.                        |
|  |               | [   |
|  |               |   |
|  |               | REFERENCES:                               |
|  |               | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|  |               | J. Biol. Chem. <u>1939</u> , 128, 537.    |
|  |               | 2. Hitchcock, D. I.; Taylor, A. C.        |
|  |               | J. Am. Chem. Soc. <u>1937</u> , 59, 181   |
|  |               |   |
|  |               |   |
|  |               |   |



| (1) | pyrimidiny1- (a<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [ | de, 4-amino-N-2-<br>sulfadiazine);<br>68-35-9]<br>; NaOH; [1310-73-2]              | ORIGINAL MEASUREMENTS:<br>Holz, E.; Garcia Onandia, A.; Holz, S.<br>Acta Cient. Venezolana <u>1955</u> , 6(2), 68-73. |
|-----|---|--|---|
|     | Water; H <sub>2</sub> 0; [  |  |   |
| VAR | IABLES:   |  | PREPARED BY:  |
|     | Concentrati   | on of NaOH   | R. Piekos   |
| EXP | ERIMENTAL VALUES:   | <u> </u>   |   |
|     | Concentration<br>of NaOH soln   | Volume of NaOH soln requ<br>to dissolve 1 g of sulfa<br>azine at 26 <sup>0</sup> C | iired Solubility of sulfadiazine<br>di- at 26°C   |
|     | N   | cm <sup>3</sup>  | mol dm <sup>-3</sup> NaOH soln <sup>a</sup>   |
|     | 1/10  | 43.3   | 0.0923  |
|     | 1/4   | 17.3   | 0.231   |
|     | 1/2   | 8.35   | 0.478   |
|     | 1   | 4.5  | 0.89  |
|     | 1.5   | 2.8  | 1.4   |
|     | 2   | 2.1  | 1.9   |
|     | 2.5   | 1.65   | 2.42  |
|     | 3   | 1.4  | 2.8   |
|     | 3.5   | 1.2  | 3.3   |
|     | 3.75  | 1.2  | 3.3   |
| -   | 4   | 101  | 0.0396  |
|     | <sup>a</sup> Calculate  | d by compiler  |   |
|     |   | AUXILIARY  | INFORMATION   |
| MET | HOD/APPARATUS/PRO   | CEDURE :   | SOURCE AND PURITY OF MATERIALS:   |
| N   | othing specified.   |  | Nothing specified. Distd water was used.  |
|     |   |  |   |
|     |   |  |   |
|     |   |  | ESTIMATED ERROR:  |
|     |   |  | Nothing specified.  |
|     |   |  | REFERENCES:   |
|     |   |  |   |
|     |   |  |   |

| A0/70/00100   |   |
|---|---|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2- | ORIGINAL MEASUREMENTS:                          |
| pyrimidinyl- (sulfadiazine);                        | Nogami, H.; Nagai, T.; Suzuki, A.               |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]                    | Chem. Pharm. Bull. <u>1966</u> , 14(4), 339-50. |
| (2) Sodium hydroxide; NaOH; [1310-73-2]             |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]            |   |
| VARIABLES:  | PREPARED BY:                                    |
| Concentration of sodium hydroxide                   | R. Piekos                                       |
|   |   |
| EXPERIMENTAL VALUES:                                |   |
| Concentration of NaOH Solub:                        | lity of sulfadiazine at 37 <sup>0</sup> C       |
| 10 <sup>3</sup> mol dm <sup>-3</sup> mg/3           | 100 ml 10 <sup>3</sup> mol dm <sup>-3</sup>     |
| 1 35.   | .2 1.41   |
| 1.4 46  | .9 1.88   |
| 2 68  | .1 2.72   |
| 3 96  | .0 3.84   |
| 4 118   | 4.72  |
| 5 153   | 6.12  |
| 10 272  | 10.9  |
| 30 760  | 30.4  |
| 50 1270   | 50.8  |
| 100 2520  | 100.8   |
|   |   |
| AUXILIARY   | INFORMATION                                     |
| METHOD /APPARATUS / PROCEDURE :                     | SOURCE AND PURITY OF MATERIALS:                 |
| Soly of sulfadiazine was detd from dissoln          | Commercial sulfadiazine J. P. was used.         |
| rate data obtained by the rotating disk             | Purity of the remaining materials was not       |
| method.   | specified.                                      |
|   |   |
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|   |   |
|   |   |
|   | ESTIMATED ERROR:                                |
|   | Nothing specified.                              |
|   | NOCHINE OPECITICA.                              |
|   |   |
|   |   |
|   | REFERENCES:                                     |
|   |   |
|   |   |
|   |   |

| pyrin<br>C <sub>10</sub> H <sub>1</sub><br>(2) Potas | :<br>enesulfonamide, 4-amino-N-2<br>hidinyl- (sulfadiazine);<br>LO <sup>N</sup> 4 <sup>0</sup> 2 <sup>S</sup> ; [68-35-9]<br>ssium hydroxide; KOH; [13]<br>; H <sub>2</sub> 0; [7732-18-5] |           | ORIGINAL MEASUREMENTS:<br>Nogami, H.; Nagai, T.; Suzuki, A.<br>Chem. Pharm. Bull. <u>1966</u> , 14(4), 339-50. |
|--|--|-----------|--|
| VARIABLES  |  |           | DEDIDED DY.  |
|  | oncentration of KOH  |           | PREPARED BY:<br>R. Piekos  |
| EXPERIMENT   | TAL VALUES:  |           |  |
|  |  |           |  |
|  | Concentration of KOH   | Solubili  | ty of sulfadiazine at 37 <sup>0</sup> C  |
|  | 10 <sup>2</sup> mol dm <sup>-3</sup>   | mg/100    | m1 10 <sup>2</sup> mol dm <sup>-3</sup>  |
|  | 0.1  | 35        | 0.141  |
|  | 0.5  | 131       | 0.524  |
|  | 1.0  | 326       | 1.30   |
|  | 5.0  | 1350      | 5.40   |
|  | 10.0   | 2710      | 1.08 <sup>a</sup>  |
|  |  |           |  |
|  |  | AUXILIARY | INFORMATION  |
| METHOD/API   | PARATUS/PROCEDURE:   |           | SOURCE AND PURITY OF MATERIALS;  |
|  | sulfadiazine was detd from   | diccoln   | Commercial sulfadiazine J. P. was used.  |
| -  | a obtained by the rotating   |           | Purity of the remaining materials was not  |
| method.  | obtained by the lotating   | ulon      | specified.   |
|  |  |           |  |
|  |  |           |  |
|  |  |           |  |
|  |  |           | ESTIMATED ERROR:   |
|  |  |           | Nothing specified.   |
|  |  |           | REFERENCES:  |
|  |  |           |  |
|  |  |           |  |
|  |  |           |  |
|  |  |           |  |

| COME<br>(1)<br>(2)<br>(3) | PONENTS:<br>Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfadiazine);<br>$C_{10}H_{10}N_4O_2S$ ; [68-35-9]<br>Carbonic acid, disodium salt;<br>$Na_2CO_3$ ; [497-19-8]<br>Water; $H_2O$ ; [7732-18-5] | ORIGINAL MEASUREMENTS:<br>Takubo, T.; Matsumaru, H.; Tsuchiya, S.;<br>Hiura, M. Chem. Pharm. Bull.<br><u>1973</u> , 21(7), 1440-5. |
|---------------------------|--|--|
|                           | IABLES:<br>temperature: 37 <sup>0</sup> C; one pH: 11.3  | PREPARED BY:<br>R. Piekos  |

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in a  $Na_2CO_3$  solution ( 2.120 g  $Na_2CO_3/100$  ml water ) of pH 11.3 at  $37^{\circ}C$  is 29.12 mg/ml solution<sup>a</sup> ( 0.1163 mol dm<sup>-3</sup> solution, compiler ).

<sup>a</sup>Numerical value to the graphical data given by one of the authors ( S.T. ) in personal communication.

### AUXILIARY INFORMATION

| METHOD /APPARATUS / PROCEDURE:                                      | SOURCE AND PURITY OF MATERIALS;   |
|---|---|
| Aliquots of the Na <sub>2</sub> CO <sub>3</sub> soln were placed in | The sulfadiazine was of pharmaceutical  |
| glass-stoppered flasks with excess of sulfa-                        | purity. The source and purity of $Na_2CO_3$   |
| diazine. The flasks were allowed to stand                           | were not specified.   |
| at 37±1°C and shaken vigorously for 4 h un-                         | Distd water was used.   |
| til equilibrium was established. One ml of                          |   |
| the supernatant was removed by means of a                           |   |
| filter pipet and sulfadiazine was assayed                           |   |
| by the previously reported method (1).                              |   |
|   | ESTIMATED ERROR:  |
|   | ESTIMATED ERROR:  |
|   | Soly and pH: not specified.   |
|   |   |
|   | Soly and pH: not specified.<br>Temp: ±1 <sup>0</sup> C (authors).   |
|   | Soly and pH: not specified.<br>Temp: ±1 <sup>O</sup> C (authors).<br>REFERENCES:                              |
|   | Soly and pH: not specified.<br>Temp: ±1°C (authors).<br>REFERENCES:<br>1. Takubo, T.; Tsuchiya, S.; Hiura, M. |
|   | Soly and pH: not specified.<br>Temp: ±1 <sup>O</sup> C (authors).<br>REFERENCES:                              |
|   | Soly and pH: not specified.<br>Temp: ±1°C (authors).<br>REFERENCES:<br>1. Takubo, T.; Tsuchiya, S.; Hiura, M. |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Takubo, T.; Matsumaru, H.; Tsuchiya, S.;                            |
| pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | Hiura, M. Chem. Pharm. Bull.  |
| (2) Carbonic acid, monosodium salt;  | <u>1973</u> , 21(7), 1440-5.  |
| NaHCO <sub>3</sub> ; [144-55-8]  |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>o</sup> C; one pH: 8.4  | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of culfadianing in a N-NCO  |   |
| Solubility of sulfadiazine in a NaHCO <sub>3</sub>   | ,   |
| water ) of pH 8.4 at 37 <sup>o</sup> C is 8.06 mg/m  | L solution <sup>a</sup> ( $3.22 \times 10^{-2} \text{ mol dm}^{-3}$ |
| solution, compiler ).  |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                                     |
| Aliquots of the NaHCO3 soln were placed in   | The sulfadiazine was of pharmaceutical                              |
| glass-stoppered flasks with excess of sulfa-   | 1 1   |
| diazine. The flasks were allowed to stand  | was not specified.  |
| at 37±1°C and shaken vigorously for 4 h un-  | Distd. water was used.  |
| til equilibrium was established. One ml of   | bista, water was used.  |
| the supernatant was removed by means of a  |   |
| filter pipet and sulfadiazine was assayed  |   |
| by the previously reported method (1).   |   |
| by the previously reported method (1).   | ESTIMATED ERROR:  |
|  | Soly and pH: not specified.   |
|  | Temp: ±1 <sup>°</sup> C (authors).                                  |
|  |   |
|  | REFERENCES:   |
|  | l. Takubo, T.; Tsuchiya, S.;  |
|  | Hiura, M. Yakuzaigaku, <u>1971</u> , 31,                            |
|  | 298.  |
|  |   |
|  |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                         |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                              | Langecker, H.                                  |
| pyrimidinyl- (sulfadiazine);<br>$C_{10}H_{10}N_4O_2S$ ; [68-35-9] | Arch. Exptl. Path. Pharmakol. 1948,            |
| (2) Sodium chloride; NaCl; [7647-14-5]                            | 205, 291-301.                                  |
| (3) Water; H <sub>2</sub> O; [7732-18-5]                          |  |
| (,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,                           |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 37 <sup>0</sup> C                                | R. Piekos                                      |
| one temperature. 57 C   | R. FIEKOS                                      |
| EXPERIMENTAL VALUES:  | ······································         |
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| Solubility of sulfadiazine in a 0.9 %                             | $x/x$ NoCl colution of $27^{\circ}$ C to 16 mc |
|   | w/w Naci Solucion at 57 C 18 10 mg/            |
| $(6.4 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler}).$     |  |
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|   | INFORMATION                                    |
|   |  |
| METHOD/APPARATUS/PROCEDURE:                                       | SOURCE AND PURITY OF MATERIALS:                |
| An excess of sulfadiazine in a 0.9% w/w NaCl                      | Source and purity of the materials were        |
| soln was boiled for 1 h in a sealed ampul                         | not specified.                                 |
| followed by keeping the ampul at 37 <sup>o</sup> C. The           |  |
| sulfadiazine concn was detd colorimetrically                      |  |
| by the method of Bratton and Marsahll (1)                         |  |
| using a Havemann colorimeter (2), and by mi-                      |  |
| croanal detn of the solid residue.                                |  |
|   |  |
|   | ESTIMATED ERROR:                               |
|   | Nothing specified.                             |
| · · ·   |  |
|   | REFERENCES:                                    |
|   | 1. Bratton, A. G.; Marshall, E. K., Jr.        |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.         |
|   | 2. Havemann, R. Klin. Wochenschr.              |
|   | <u>1940,</u> p. 503.                           |
|   |  |

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|----------|---|----------|---|
| COMPONEI |   |          | ORIGINAL MEASUREMENTS:                          |
|          | enzenesulfonamide, 4-amino-N-2-<br>vrimidinyl- (sulfadiazine);            | -        | Nogami, H.; Nagai, T.; Suzuki, A.               |
| C1       | 10 <sup>H</sup> 10 <sup>N</sup> 4 <sup>0</sup> 2 <sup>S</sup> ; [68-35-9] |          | Chem. Pharm. Bull. <u>1966</u> , 14(4), 339-50. |
| (2) Sc   | odium chloride: NaCl; [7647-]   | 14-5]    |   |
| (3) Wa   | ater; H <sub>2</sub> 0; [7732-18-5]                                       |          |   |
|          |   |          |   |
| VARIABL  | ES:   |          | PREPARED BY:                                    |
| Co       | oncentration of sodium chloride   | e        | R. Piekos                                       |
|          |   |          |   |
| EXPERIM  | ENTAL VALUES:   |          |   |
|          |   |          |   |
|          |   |          |   |
|          | Concentration of NaCl   | Solubi   | lity of sulfadiazine at 37 <sup>0</sup> C       |
|          | mol $dm^{-3}$   | mg/100   | $10^4 \text{ mol dm}^{-3} \text{ a}$            |
|          | 10 <sup>-3</sup>  | 12.1     | 4.83  |
|          | 10 <sup>-2</sup>  | 11.3     | 4.51  |
|          | 10 <sup>-1</sup>  | 10.2     |   |
|          |   |          | 4.07  |
|          | 1   | 9.0      | 3.6   |
|          |   |          |   |
|          | A   | UXILIARY | INFORMATION                                     |
| METHOD/  | APPARATUS/PROCEDURE:  |          | SOURCE AND PURITY OF MATERIALS:                 |
| Soly     | of sulfadiazine was detd from   | dissoln  | Commercial sulfadiazine J. P. was used.         |
| rate     | data obtained by the rotating   | disk     | Purity of the remaining materials was not       |
| metho    | d.  |          | specified.                                      |
|          |   |          |   |
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|          |   |          |   |
|          |   |          |   |
|          |   |          | ESTIMATED ERROR:                                |
|          |   |          | Nothing specified.                              |
|          |   |          |   |
|          |   |          | REFERENCES :                                    |
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| COMP         | DNENTS:  |             |                 | ORIGINAL MEASUREMENTS:                       |          |
|--------------|--|-------------|-----------------|--|----------|
|              | Benzenesulfonam  | ide, 4-ami  | no-N-2-         |  | _        |
| -            | pyrimidinyl-   | (sulfadiaz  |                 | Avico, U.; Cavazuti, G.; di Frances          | co, R.   |
| / <b>^</b> ` | C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; |             |                 | Signoretti Ciranni, E.; Zuccaro, P.          |          |
|              | Sodium chloride  |             |                 | Farmaco, Ed. Practica <u>1975</u> , 30(1),   | 40-6.    |
| (3)          | Water; H <sub>2</sub> 0;   | [7732-18-   | 5]              |  |          |
| VARI         | ABLES:   |             |                 | PREPARED BY:                                 | <u> </u> |
|              | Temperatur   | e           |                 | R. Piekos                                    |          |
|              |  |             |                 |  |          |
| EXPE         | RIMENTAL VALUES:   |             |                 |  |          |
|              |  |             |                 |  |          |
|              |  |             |                 |  |          |
|              |  |             |                 |  |          |
|              |  |             |                 |  |          |
|              |  | .0          | -               | amorphous sulfadiazine                       |          |
|              |  | t/°C        | in equimolal    | NaCl solutions                               |          |
|              |  |             | g/100 g water   | $10^3 \text{ mol kg}^{-1} \text{ water}^{a}$ |          |
|              |  | 25          | 0.151           | 6.03   |          |
|              |  | 35          | 0.151           | 6.03   |          |
|              |  | 40          | 0.151           | 6.03   |          |
|              |  |             |                 |  |          |
|              | -  |             |                 | ······································       |          |
|              |  | а           | Calculated by   | compiler                                     |          |
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|              |  |             |                 |  |          |
|              |  |             | AUXILIARY       | INFORMATION                                  |          |
| METH         | OD/APPARATUS/PRO   | CEDURE:     |                 | SOURCE AND PURITY OF MATERIALS:              |          |
| A            | soln of Na salt o  | of sulfadia | azine was added | Source and purity of sulfadiazine was        | not      |
| to           | a HC1 soln contg   | g stoichion | netric quantity | specified. The mp of crystalline sulf        | Ea-      |
| of           | the acid to neut   | ralize the  | e salt. The     | diazine was 253-6 <sup>0</sup> C.            |          |
| ner          | utralization was   | carried ou  | it in a ther-   | Purity of the water was not specified.       |          |
| mo           | stat and the pH o  | of the mixi | t was maintain- |  |          |
| ed           | close to that of   | a satd su   | ılfadiazine     |  |          |
| SO           | ln. The procedur   | e was rep   | eated using     |  |          |
| va           | rious initial cor  | icns of the | e reagents to   |  |          |
| fi           | nd the max concn   | of sulfad   | lazine at which | ESTIMATED ERROR:                             | <u></u>  |
|              | pptn occurred.   |             |                 | Nothing specified.                           |          |
|              |  |             |                 |  |          |
|              |  |             |                 | PEEPENCES.                                   |          |
|              |  |             |                 | REFERENCES:                                  |          |
|              |  |             |                 |  |          |
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|              |  |             |                 |  |          |
| -            | <u> </u>   |             |                 |  | _        |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-                                       | ORIGINAL MEASUREMENTS:                                   |
|---|--|
| pyrimidinyl- (sulfapyrimidine);   | Krüger-Thiemer, E.                                       |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]  | Arch. Dermatol. Syphilis <u>1942</u> , 183,              |
| (2) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0] | 90-116.  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: ca 20 <sup>0</sup> C; one pH: 4.37                                       | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfapyrimidine in a 0.7  | 35M (10%) KH <sub>2</sub> PO <sub>4</sub> solution of pH |
| 4.37 at room temperature (about 20 <sup>0</sup> C)  | is 0.0070 g% ( 2.8 x 10 <sup>-4</sup> mol                |
| $dm^{-3}$ solution, compiler ).   |  |
| um Boracion, compiler ).  |  |
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|   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                          |
| Sulfapyrimidine (0.5 g) was dissolved in 10   | Sulfapyrimidine was manufd by Schering                   |
| $cm^3$ of a 0.735M (10%) KH <sub>2</sub> PO <sub>4</sub> soln of pH 4.37,                 | (purity not specified). The source and                   |
| shaken for 2 h at room temp (about 20 <sup>0</sup> C),                                    | purity of the remaining materials were not               |
| and filtered. A 1-cm <sup>3</sup> aliquot of the fil-                                     | specified.   |
| trate was withdrawn, cooled, acifified with   |  |
| 1 cm <sup>3</sup> of 2N HCl, and the sulfapyrimidine                                      |  |
| content was detd colorimetrically by the  |  |
| method of Marshall modified by Kimmig (1)   |  |
| using an Authenrieth colorimeter. The pH  | ESTIMATED ERROR:   |
| was detd on an ultraionograph using a glass   | Soly: precision ±5% (author).                            |
| electrode.  | Temp: not specified.                                     |
|   | pH : ±0.05 pH unit (author).                             |
|   | REFERENCES:  |
|   | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> ,              |
|   | 176, 722; Erg. Hyg. <u>1941,</u> 24,                     |
|   | 398.   |
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|   | 149  |
|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                         |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);</li> </ol> | Nogami, H.; Nagai, T.; Suzuki, A.              |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]  | Chem. Pharm. Bull. <u>1966</u> , 14(4),        |
| (2) Phosphoric acid; disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] | 339-50.  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                   |
| Concentration of $Na_2HPO_4$  | R. Piekos                                      |
| EXPERIMENTAL VALUES:  |  |
|   |  |
| Concentration of Na <sub>2</sub> HPO <sub>4</sub> So                                  | olubility of sulfadiazine at 37 <sup>0</sup> C |
| mol dm <sup>-3</sup>  | $mg/100 m1$ $10^{-3} mo1 dm^{-3}$              |
| 10 <sup>-4</sup>  | 15.8 0.63                                      |
| 10 <sup>-3</sup>  | 33.1 1.3                                       |
| 10 <sup>-2</sup>  | 104 4.2  |
| 10-1  | 242 9.7  |
|   |  |
|   |  |
| AUXILIARY   | INFORMATION                                    |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                |
| Soly of sulfadiazine was detd from dissoln  | Commercial sulfadiazine J. P. was used.        |
| rate data obtained by the rotating disk   | Purity of the remaining materials was          |
| method.   | not specified.                                 |
|   |  |
|   |  |
|   |  |
|   | ESTIMATED ERROR:                               |
|   | Nothing specified.                             |
| · ·   |  |
|   | REFERENCES :                                   |
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| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfapyrimidine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</li> <li>Hydrochloric acid; HCl; [7647-01-0]</li> </ol> | ORIGINAL MEASUREMENTS:<br>Stricker, H.<br>Pharm. Ind. <u>1971</u> , 33(7), 446-54. |
|--|--|
| <ul> <li>(3) Phosphoric acid, trisodium salt;<br/>Na<sub>3</sub>PO<sub>4</sub>; [7601-54-9]</li> <li>(4) Water; H<sub>2</sub>O; [7732-18-5]</li> </ul>   |  |
| VARIABLES:   | PREPARED BY:<br>R. Piekos  |
|  |  |

| -11 | Solubility at 37 <sup>0</sup> C |                               |  |
|-----|---------------------------------|-------------------------------|--|
| рН  | g/100 m1                        | $10^3$ mol dm <sup>-3 a</sup> |  |
| 5.7 | ca 0.03                         | 1.2                           |  |
| 7.5 | ca 0.11                         | 4.4                           |  |
|     |                                 |                               |  |

<sup>a</sup> Calculated by compiler

| AUXILIARY   | INFORMATION   |
|---|---|
| METHOD/APPARATUS/PROCEDURE:<br>Soly was detd in a Sartorius-Loesemodell SM  | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor the purity of the |
| 16 751 soly apparatus contg 100 ml of sol-<br>vent. The solvent consisted of $0.06\underline{N}$ HC1<br>whose pH was adjusted to the desired value<br>by addn of a concd $Na_3PO_4$ soln.<br>Aliquots of solns were acidifed, diazotized<br>and coupled with <u>N</u> -(1-naphthyl)-ethylene-<br>diammonium chloride. After subsequent addn | materials was specified.  |
| of an acetate buffer soln of pH 5 and ace-  | ESTIMATED ERROR:  |
| tone, extinction of the solns was measured at 500 nm.   | Soly: not specified.<br>Temp: ±0.5 <sup>0</sup> C (authors).            |
|   | REFERENCES:   |

|  |  |         |   |  | 151      |  |
|--|--|---------|---|--|----------|--|
| COMPONENTS:                                      |  |         | ORIGINAL MEASUR   | EMENTS:  | <u> </u> |  |
| (1) Benzenesulfonamide, 4-amino-N-2-             |  |         | Takubo, T.; Matsumaru, H.;  |  |          |  |
|  | pyrimidinyl- (sulfadiazine);<br>C10H10N4O2S; [68-35-9] |         |   | Tsuchiya, S.; Hiura, M.                                |          |  |
| (2) Carbonic acid,                               | _  |         |   | Bull. 1973, 21(7),                                     | 1//0 5   |  |
| Na <sub>2</sub> CO <sub>3</sub> ; [497-          |  |         | chem. Phaim.  | Bull. <u>1975</u> , 21(7),                             | 1440-5.  |  |
| (3) Carbonic acid,<br>NaHCO <sub>3</sub> ; [144- | monosodium salt;<br>55-81                              |         |   |  |          |  |
| (4) Water; H <sub>2</sub> O;                     | [7732-18-5]  |         |   |  |          |  |
| VARIABLES:                                       |  |         | PREPARED BY:  |  |          |  |
|  | рН   |         |   | R. Piekos  |          |  |
| EXPERIMENTAL VALUES:                             | <u></u> .  |         |   |  |          |  |
|  |  |         |   |  |          |  |
| Na2C03   | NaHC03   | - PH    | ······  | .ity at 37°C   |          |  |
| g/100 ml water `                                 | g/100 ml water   |         | mg/m1 soln <sup>a</sup>   | 10 <sup>2</sup> mol dm <sup>-3</sup> soln <sup>b</sup> |          |  |
| 0.212  | 1.512  | 9.1     | 9.32  | 3.724  |          |  |
| 0.848  | 1.008  | 9.8     | 18.82   | 7.520  |          |  |
| 1.908  | 0.168  | 10.7    | 26.94   | 10.764   |          |  |
|  |  |         |   |  |          |  |
| <sup>a</sup> Numerical value:                    | s to the graphical                                     | ones w  | ere given by one  | of the authors ( S. T                                  | • )      |  |
| in personal com                                  | munication.  |         |   |  |          |  |
|  |  |         |   |  |          |  |
| <sup>b</sup> Calculated by                       | compiler   |         |   |  |          |  |
|  |  |         |   |  | •        |  |
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|  |  |         |   |  |          |  |
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|  |  |         |   |  |          |  |
|  |  |         | INFORMATION   |  |          |  |
| METHOD/APPARATUS/PRO                             |  |         |   | TY OF MATERIALS:                                       |          |  |
| Aliquots of the carl                             |  |         |   | ne was of pharmaceutic                                 | -        |  |
| placed in glass-stop                             |  |         |   | purity of Na <sub>2</sub> CO <sub>3</sub> and 1        | NaHC03   |  |
| of sulfadiazine. Th                              |  |         |   | fied.  |          |  |
| stand at 37±1°C and                              | d shaken vigorously                                    | y for 4 | Distd water wa  | s used.  |          |  |
| h until equilibrium                              |  |         |   |  |          |  |
| of the supernatant w                             | was removed by mean                                    | ns of a |   |  |          |  |
| filter pipet and su                              |  | aved hv | 1   |  |          |  |
| the previously report                            | lfadiazine was assa                                    | ayeu by |   |  |          |  |
|  |  | ijcu bj |   |  |          |  |
|  |  | ayeu by | ESTIMATED ERRO  | R:   |          |  |
|  |  | ijcu bj | ESTIMATED ERRO  | R:<br>not specified.                                   |          |  |
|  |  | ijcu by | ESTIMATED ERRO  |  |          |  |
|  |  |         | ESTIMATED ERRO<br>Soly and pH:  |  |          |  |
| 1  |  | .,      | ESTIMATED ERRO<br>Soly and pH:  |  |          |  |
|  |  | .,      | ESTIMATED ERRO<br>Soly and pH:<br>Temp: ±1°C<br>REFERENCES:               | not specified.   | iura. M  |  |
|  |  | .,      | ESTIMATED ERRO<br>Soly and pH:<br>Temp: ±1°C<br>REFERENCES:<br>1. Takubo, | not specified.<br>T.; Tsuchiya, S.; H                  |          |  |
|  |  | .,      | ESTIMATED ERRO<br>Soly and pH:<br>Temp: ±1°C<br>REFERENCES:<br>1. Takubo, | not specified.   |          |  |
|  |  | .,      | ESTIMATED ERRO<br>Soly and pH:<br>Temp: ±1°C<br>REFERENCES:<br>1. Takubo, | not specified.<br>T.; Tsuchiya, S.; H                  |          |  |
|  |  | .,      | ESTIMATED ERRO<br>Soly and pH:<br>Temp: ±1°C<br>REFERENCES:<br>1. Takubo, | not specified.<br>T.; Tsuchiya, S.; H                  |          |  |

| COMP(<br>(1)<br>(2)<br>(3) | DNENTS:<br>Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfapyrimidine);<br>$C_{10}H_{10}N_40_2S$ ; [68-35-9]<br>Phosphoric acid, disodium salt;<br>$Na_2HPO_4$ ; [7558-94-4]<br>Phosphoric acid, monopotassium salt;<br>$KH_2PO_4$ ; [7778-77-0] | ORIGINAL MEASUREMENTS:<br>Krüger-Thiemer, E.<br>Arch. Dermatol. Syphilis <u>1942</u> , 183,<br>90-116. |
|----------------------------|---|--|
| (4)                        | Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:   |
| VARIABLES: pH              |   | R. Piekos  |

| Composition of 1/15M phosphate<br>buffer solutions |   | рН а  |  | Solubility<br>at room temperature (about 20 <sup>0</sup> C)   |  |
|--|---|---|--|---|--|
| кн <sub>2</sub> р0 <sub>4</sub>                    | %Content  |   | g%   | $10^3$ mol dm <sup>-3</sup> solution <sup>a</sup>   |  |
| 99.0   | 0.91  | 4.944   | 0.0087   | 0.35  |  |
| 90.0   | 0.91  | 5.906   | 0.0101   | 0.403   |  |
| 38.9   | 0.93  | 7.005   | 0.033  | 1.3   |  |
| 0.5  | 0.733 <sup>b</sup>  | 7.51  | 0.065  | 2.6   |  |
| 5.3  | 0.95  | 8.018   | 0.127  | 5.07  |  |
|  | r solutions<br>KH <sub>2</sub> PO <sub>4</sub><br>99.0<br>90.0<br>38.9<br>0.5 | r solutions       XContent         KH2P04       XContent         99.0       0.91         90.0       0.91         38.9       0.93         0.5       0.733 <sup>b</sup> | r solutions     pH       KH <sub>2</sub> PO <sub>4</sub> %Content       99.0     0.91       4.944       90.0     0.91       5.906       38.9     0.93       0.5     0.733 <sup>b</sup> | r solutions       pH       at room t         KH2P04       %Content       g%         99.0       0.91       4.944       0.0087         90.0       0.91       5.906       0.0101         38.9       0.93       7.005       0.033         0.5       0.733 <sup>b</sup> 7.51       0.065 |  |

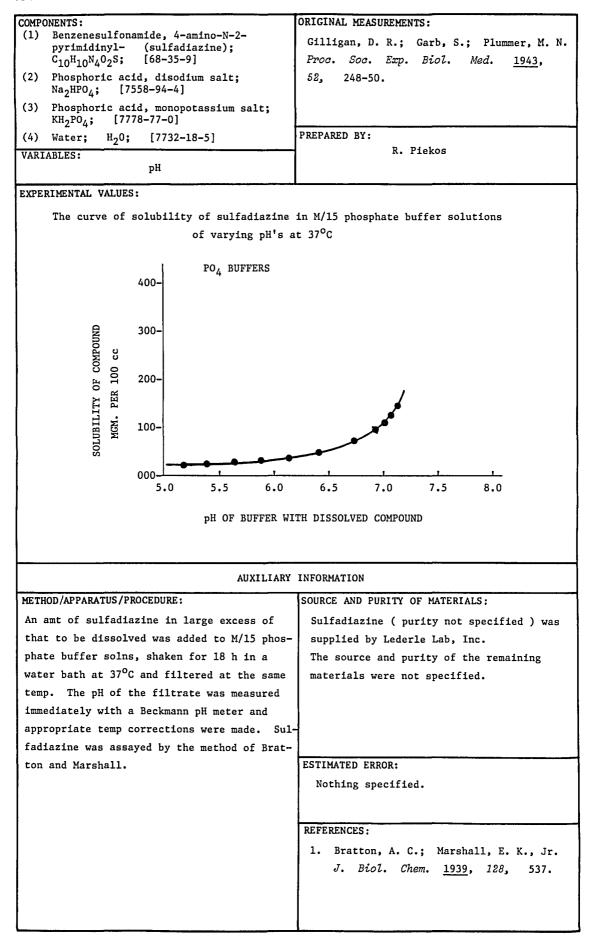
<sup>a</sup>Calculated by compiler

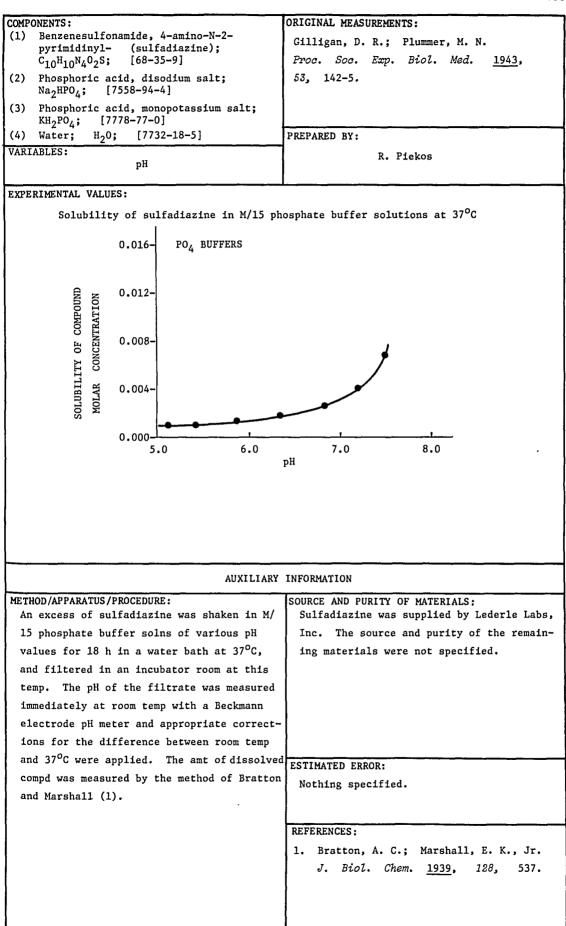
<sup>b</sup>Molar content; 10% buffer solution

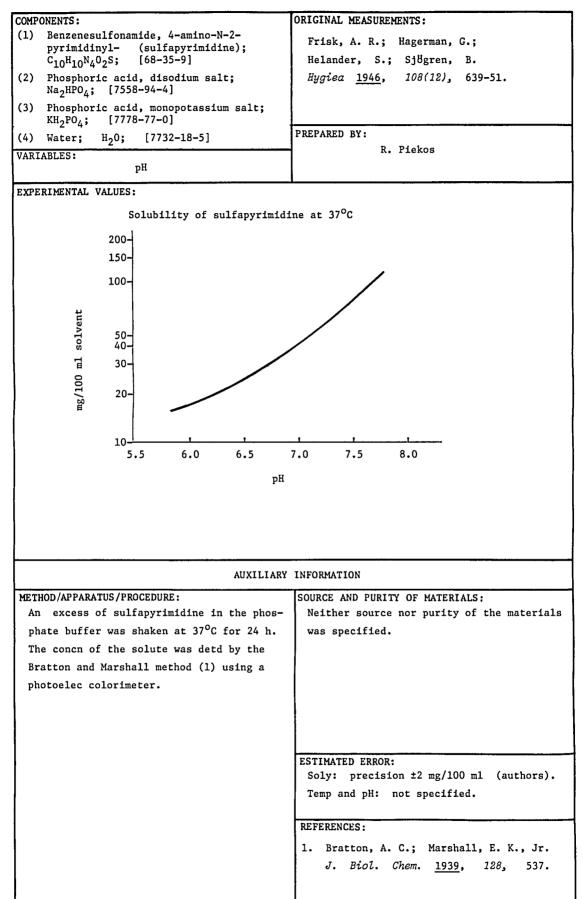
| AUXILIARY  | INFORMATION   |
|--|---|
| METHOD/APPARATUS/PROCEDURE:<br>Sulfapyrimidine (0.5 g) was dissolved in 10   | SOURCE AND PURITY OF MATERIALS:<br>Sulfapyrimidine was manufd by Schering   |
| $cm^3$ of the buffer soln, shaken for 2 h at<br>room temp (about 20 <sup>o</sup> C), and filtered. A<br>1-cm <sup>3</sup> aliquot of the filtrate was withdrawn,<br>cooled, acidified with 1 cm <sup>3</sup> of 2N HCl, and<br>the sulfapyrimidine content was detd colori-<br>metrically by the method of Marshall modi-<br>fied by Kimmig (1) using an Authenrieth co- |   |
| lorimeter. The pH was detd on an ultraiono-<br>graph using a glass electrode.  | ESTIMATED ERROR:<br>Soly: precision ±5% (author).<br>Temp: not specified.<br>pH : ±0.05 pH unit (author).<br>REFERENCES:<br>1. Kimmig, J. Arch. Dermatol.<br>176, 722; Erg. Hyg. <u>1941</u> , 24, 398. |

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|   |          |  |   | 153     |
|---|----------|--|---|---------|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidiny1- (sulfadiazine);<br>$C_{10}H_{10}N_4O_2S$ ; [68-35-9]<br>(2) Phosphoric acid, disodium salt;<br>$Na_2HPO_4$ ; [7558-94-4]<br>(3) Phosphoric acid, monopotassium salt;<br>$KH_2PO_4$ ; [7778-77-0]<br>(4) Water; $H_2O$ ; [7732-18-5] |          | ORIGINAL MEASUREMENTS:<br>Pulver, R.; Suter, R.<br>Schweiz. Med. Wochenschr.<br>73(13), 403-8.<br>PREPARED BY: | <u>1943,</u>  |         |
| VARIABLES:  | рH       |  | R. Piekos   |         |
| EXPERIMENTAL VALUES   | :        | Solubility of su   | lfadiazine in M/15 phosphate                          |         |
|   | рН       | buffers (accordi   | ng to Sørensen) at 20 <sup>0</sup> C                  |         |
|   |          | mg%  | $10^3 \text{ mol } dm^{-3} a$                         |         |
|   | 6.0      | 13   | 0.52  |         |
|   | 7.0      | 45   | 1.80  |         |
|   | 8.0      | 191  | 7.63  |         |
|   |          | <sup>a</sup> Calculated by   | compiler  |         |
|   |          | AUXILIARY  | INFORMATION   | <u></u> |
| METHOD/APPARATUS/PR   | OCEDURE: | <u>,</u>   | SOURCE AND PURITY OF MATERIALS:                       |         |
| Nothing specified   |          |  | Nothing specified.                                    |         |
|   |          |  | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES: |         |
|   |          |  |   |         |







| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-                                       | ORIGINAL MEASUREMENTS:   |
|---|--|
| pyrimidinyl- (sulfadiazine);  | Langecker, H.  |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]  | Arch. Exptl. Path. Pharmakol. 1948,                                      |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]     | 205, 291-301.  |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0] |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:   |
| VARIABLES:<br>pH  | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
|   |  |
| pH of the 1/15M   | Solubility at 37 <sup>0</sup> C  |
| phosphate buffer  | $mgZ$ $10^4 mol dm^{-3} a$   |
| 4.9   | 16 6.4   |
| 5.9   | 21 8.4   |
| 6.9   | 29 12  |
| 7.0   | 54 22  |
| 7.5   | 81 32  |
| ······································  |  |
| <sup>a</sup> Calculated by c  | ompiler  |
|   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| An excess of sulfadiazine was added to a buffer soln and boiled for 1 h in a sealed       | Source and purity of the materials were<br>not specified.                |
| ampul followed by keeping the ampul at 37°C   | -  |
| The concn of sulfadiazine was detd colori-  |  |
| metrically by the method of Bratton and   |  |
| Marshall (1) using a Havemann colorimeter   |  |
| (2), as well as by microanal detn of the  |  |
| solid residue.  |  |
|   | ESTIMATED ERROR:   |
|   | Nothing specified.   |
|   | DEPEDENCUS.  |
|   | REFERENCES:  |
|   | 1. Bratton, A. G.; Marshall, E. K, Jr.<br>J. Biol. Chem. 1939, 128, 537. |
|   | 2. Havemann, R. Klin. Wochenschr.  |
|   | <u>1940,</u> p. 503.   |
|   |  |

| 1 | 58 |
|---|----|
|---|----|

| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>0<sub>2</sub>S; [68-35-9]<br/>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]<br/>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]<br/>(4) Water; H<sub>2</sub>0; [7732-18-5]<br/>VARIABLES:<br/>One temperature: 20°C; one pH: 7.4<br/>EXPERIMENTAL VALUES:</pre> | ORIGINAL MEASUREMENTS:<br>Riess, W.<br>Intern. Congr. Chemotherapy, Proc.,<br>3rd, Stuttgart <u>1963</u> , 1, 627-32.<br>PREPARED BY:<br>R. Piekos |
|---|--|
| Solubility of sulfadiazine in a M/15 S<br>at 20 <sup>0</sup> C is 65 mg% ( 2.6 x 10 <sup>-3</sup> mol dm <sup>-3</sup>  | · · · · · · · · · · · · · · · · · · ·  |
|   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| Surensen buffer solns of pH varying between   |  |
| 7 and 8 were prepd, satd with sulfadiazine  | Nothing specified.   |
| at 20°C, their pH was measured at equilibri-  | }  |
| um, and the sulfadiazine was assayed colori-  |  |
| metrically. The measured pH values were   |  |
| then plotted against concn and the soly at  |  |
| pH 7.4 was detd by interpolation (personal communication).  |  |
|   | ESTIMATED ERROR:   |
|   | Nothing specified.   |
|   | REFERENCES:  |
|   |  |
|   |  |
|   |  |
|   |  |
|   |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                    |  |
|--|---|--|
| <ol> <li>Benzensulfonamide, 4-amino-N-2-</li> </ol>  | ONTOTINAL MEASUREMENTS:                                   |  |
| <pre>pyrimidiny1- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</pre> | Yamazaki, M.; Aoki, M.; Kamada, A.;                       |  |
| <ul> <li>Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>             | Yata, N. <i>Yakuzaigaku <u>1967</u>, 27(1),</i><br>37-40. |  |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                      |   |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:  |  |
| VARIABLES:<br>One temperature: 30 <sup>0</sup> C; one pH: 7.4  | R. Piekos   |  |
| EXPERIMENTAL VALUES:   |   |  |
| Solubility of sulfadiazine in a phospha<br>(μ = 0.17) at 30 <sup>0</sup> C is 2.70 mmol/L ((                   | -   |  |
|  | ·····   |  |
| AUXILIARY  | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                           |  |
| Sulfadiazine (0.5 g) was placed in an L-   | Nothing specified.  |  |
| shaped tube together with 20 ml of the buffer  |   |  |
| soln. The mixt was shaken in a thermostat  |   |  |
| until equilibrium was attained. The sulfa-   |   |  |
| diazine was assayed in the supernatant spec-   |   |  |
| trophotometrically at 545 nm on a Beckmann   |   |  |
| DU spectrophotometer. The results were ta-   | ESTIMATED ERROR:  |  |
| ken from a calibration graph.  | Soly and pH: not specified.                               |  |
| ken from a caribración graph.  | Temp: ±1 <sup>0</sup> C (authors).                        |  |
|  | REFERENCES:   |  |
|  |   |  |
|  |   |  |
|  |   |  |
|  |   |  |
|  |   |  |

#### ORIGINAL MEASUREMENTS: COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-Hekster, Y. A.; Vree, T. B.; pyrimidinyl- (sulfadiazine); C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]

(2) Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]

pН

KH<sub>2</sub>PO<sub>4</sub>; (4) Water; H<sub>2</sub>0; [7732-18-5] Damsma, J. E.; Friesen, W. T.

J. Antimicrob. Chemother. <u>1981</u>, 8, 133-44.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

VARIABLES:

| рН  | Solubility at 25 <sup>0</sup> C |                               |  |
|-----|---------------------------------|-------------------------------|--|
|     | mg/1                            | $10^3$ mol dm <sup>-3</sup> a |  |
| 5.5 | 265                             | 1.06                          |  |
| 7.5 | 950                             | 3.80                          |  |
|     |                                 |                               |  |

<sup>a</sup>Calculated by compiler

| AUXILIARY INFORMATION   |  |  |  |  |
|---|--|--|--|--|
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns of sulfadiazine were prepd in<br>phosphate buffers of pH 5.5 and 7.5 at room<br>temp (25°C). The concn of the solute was<br>measured by means of a Spectra Physics<br>3500B high-performance liquid chromatograph<br>equipped with a column oven (Model 748) and<br>a Pye-Unicam LC-UV spectrophotometric de-<br>tector. The detector was connected to a<br>1-mV recorder. A stainless steel column<br>(10 cm x 4.6 mm i.d.) was packed with Li-<br>chrosorb RPS, 5 μm, obtained from Chrom-<br>pack. An injection loop of 100 μl was used. | ESTIMATED ERROR:<br>The detection limit of the solute by HPLC<br>was 0.5 mg/l (authors).<br>The error in temperature and pH was not<br>specified.<br>REFERENCES: |  |  |  |

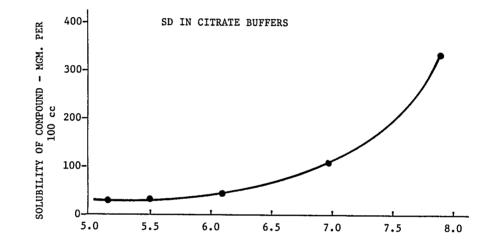
| COMPONENTS :   |                                      |                       | ORIGINAL MEASUREMENTS:                    |
|--|--------------------------------------|-----------------------|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-2-     pyrimidinyl- (sulfadiazine);</pre> |                                      | 4-amino-N-2-          | Hawking, F.                               |
|  | $C_{10}H_{10}N_4O_2S;$ [68-35-9]     |                       | -   |
| (2) Calcium chloride; CaCl <sub>2</sub> ; [10043-52-4]                           |                                      |                       | Lancet <u>1941</u> , 240, 786-8.          |
| 1  |                                      | KC1; [7447-40-7]      |   |
|  |                                      | aC1; [7647-14-5]      |   |
| (5) Water;   |                                      |                       |   |
|  | <sup>n</sup> 2 <sup>0</sup> ; [7732- | -10-01                | PREPARED BY:                              |
| VARIABLES:   | Temperatu                            | ıre                   | R. Piekos                                 |
| EXPERIMENTAL   | VALUES:                              |                       |   |
|  |                                      |                       |   |
|  | t/ <sup>o</sup> C                    | Solubility in bicard  | ponate-free Locke's solution <sup>a</sup> |
|  | £/-C                                 | mg/100 ml             | $10^4 \text{ mol } dm^{-3} b$             |
|  | 17                                   | 7.8                   | 3.12                                      |
|  | 36                                   | 18.0                  | 7.19                                      |
|  |                                      |                       |   |
|  | <del></del>                          |                       |   |
|  | arhe col                             | lution contained NaCl | 9 g, KC1 0.2 g, CaCl <sub>2</sub> 0.2 g,  |
|  |                                      |                       | -   |
|  | water 1                              | l liter, and had a pH | of 6.8.                                   |
|  | <sup>b</sup> Calcula                 | ated by compiler      | · · · · · ·                               |
|  | Galcula                              | ited by complifier    |   |
|  |                                      |                       |   |
|  |                                      |                       |   |
|  |                                      |                       |   |
|  |                                      |                       |   |
|  |                                      | AUXILIARY             | INFORMATION                               |
| METHOD/APPARA  | TUS/PROCEDUR                         | Æ:                    | SOURCE AND PURITY OF MATERIALS:           |
| Sulfadiazin  | e was shaker                         | n up with the bicar-  | Nothing specified.                        |
| bonate-free  | Locke's so                           | oln for many hours in |   |
| a tube whic  | h was corked                         | i to prevent loss of  |   |
|  |                                      | was filtered through  |   |
| -  |                                      | room to prevent pptn, |   |
|  |                                      |                       |   |
| and sulfadiazine was detd by the method of                                       |                                      |                       |   |
| Marshall an  | d Litchfield                         | 1 (1).                |   |
|  |                                      |                       |   |
| ł  |                                      |                       | ESTIMATED ERROR:                          |
|  |                                      |                       | Soly: average of 3 detns has been given   |
|  |                                      |                       | (authors).                                |
|  |                                      |                       | Temp: not specified.                      |
|  |                                      |                       | REFERENCES:                               |
| 1  |                                      |                       | 1. Marshall, E. K., Jr.; Litchfield,      |
| 1  |                                      |                       | J. T., Jr. Science <u>1938</u> , 88, 85.  |
|  |                                      |                       |   |
|  |                                      |                       |   |
|  |                                      |                       |   |

| COMPONENTS:   |  |  |
|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-  | 2-   | RIGINAL MEASUREMENTS:<br>Krebs, H. A.; Speakman, J. C.   |
| pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]  |  | J. Chem. Soc. <u>1945</u> , 42, 593-5.   |
| <pre>(2) Boric acid, disodium salt;<br/>Na<sub>2</sub>B<sub>4</sub>0<sub>7</sub>; [1330-43-4]</pre>   |  |  |
| (3) Phosphoric acid; H <sub>3</sub> PO <sub>4</sub> ; [766  | 4-38-2]  |  |
| (4) Phosphoric acid; monosodium sa<br>NaH <sub>2</sub> PO <sub>4</sub> ; [7558-80-7]  |  | REPARED BY:  |
| (5) Sodium chloride; NaCl; [7647-14-5]  |  | R. Piekos  |
| (6) Water; H <sub>2</sub> 0; [7732-18-5]  |  |  |
| VARIABLES: pH   |  |  |
| EXPERIMENTAL VALUES:  |  |  |
| pH Sol<br>at saturation in  | ubility of su<br>phosphate — b   | ulfadiazine at 25.0 <sup>0</sup> C<br>borate buffer solutions <sup>a</sup>   |
|   | mg/100 ml  | $10^3 \text{ mol } \text{dm}^{-3} \text{ b}$   |
| 6.01  | 8.5  | 0.34   |
| 6.35  | 11.1   | 0.443  |
| 6.82  | 19.4   | 0.775  |
| 7.23  | 43.5   | 1.74   |
| 7.56  | 86   | 3.4  |
| 7.67  | 114  | 4.56   |
| 8.00  | 229  | 9.15   |
| total concentration of each ac  | -  | t 0.1M. After dilution, the final<br>8M.   |
|   | AUXILIARY IN   | ΕΟΡΜΑΤΙΟΝ  |
|   |  | FORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>The buffer solns were satd by shaki  |  |  |
|   | -  | DURCE AND PURITY OF MATERIALS:<br>The sulfadiazine, mp 256 <sup>0</sup> C, was obtained  |
| vigorously with an excess of solid  | sulfadi- ł   | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.   |
| azine for at least 3 h. They were   | sulfadi- H<br>then N   | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine   | sulfadi- H<br>then N<br>concn was n  | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M  | sulfadi- h<br>then N<br>concn was m<br>arshall   | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure   | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with   | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan  | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized                                 | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized                                 | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan  | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by                     | The sulfadiazine, mp 256 <sup>0</sup> C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by                     | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.  |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by                     | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.<br>STIMATED ERROR:   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by                     | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.<br>STIMATED ERROR:<br>Nothing specified.   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by<br>ES<br>N<br>RI    | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.<br>STIMATED ERROR:<br>Nothing specified.<br>EFERENCES:   |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by                     | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.<br>STIMATED ERROR:<br>Nothing specified.<br>EFERENCES:<br>. Bratton, A. C.; Marshall, E. K., Jr. |
| azine for at least 3 h. They were<br>quickly filtered. The sulfadiazine<br>detd by the method of Bratton and M<br>(1), and the pH values were measure<br>the glass electrode, which was stan<br>in terms of the buffer solns recomm | sulfadi- h<br>then N<br>concn was m<br>arshall<br>d with<br>dardized<br>ended by ES<br>N<br>RI<br>1. | The sulfadiazine, mp 256°C, was obtained<br>by recrystg a common specimen from water.<br>Neither source nor purity of the remaining<br>materials was specified.<br>STIMATED ERROR:<br>Nothing specified.<br>EFERENCES:   |

| COMP<br>(1) | ONENTS:<br>Benzenesulfonamide, 4-amino-  |                    | ORIGINAL MEÀSUREMENTS:  |
|-------------|--|--------------------|---|
| (1)         | pyrimidiny1- (sulfadiazine $C_{10}H_{10}N_4O_2S$ ; [68-35-9]   |                    | Krebs, H. A.; Speackman, J. C.<br><i>J. Chem. Soc.</i> 1945, <i>42</i> , 593-5.                       |
| (2)         | Acetic acid; C <sub>2</sub> H <sub>4</sub> O <sub>2</sub> ; [64-   | -19-7]             |   |
| (3)         | Acetic acid, sodium salt; (  | 2H3Na02;           |   |
| (4)         | [127-09-3]<br>Phosphoric acid; H <sub>3</sub> PO <sub>4</sub> ; [7   | 7664-38-21         |   |
|             | Phosphoric acid, monosodium  | 1                  | PREPARED BY:  |
| (6)<br>(7)  | NaH <sub>2</sub> PO <sub>4</sub> ; [7558-80-7]<br>Sodium chloride; NaCl; [76<br>Water; H <sub>2</sub> O; [7732-18-5] | 547 <b>-1</b> 4-5] | R. Piekos   |
|             | IABLES: pH   |                    |   |
| EXF         | PERIMENTAL VALUES:   |                    |   |
|             | pH<br>at saturation  |                    | of sulfadiazine at 25.0 <sup>0</sup> C<br>- phosphate buffer solutions <sup>a</sup>                   |
|             |  | mg/100 1           | nl $10^4$ mol dm <sup>-3</sup> a  |
|             | 2.31   | 9.3                | 3.7   |
|             | 2.69   | 7.5                | 3.0   |
|             | 3.06   | 6.9                | 2.8   |
|             | 4.89   | 6.3                | 2.5   |
|             | amba buffan anluttana mana   |                    | dding NaOH to a solution of 0.0375M   |
|             | <sup>b</sup> Calculated by compiler.   |                    |   |
|             |  | AUXILIARY          | INFORMATION   |
| MET         | HOD/APPARATUS/PROCEDURE:   |                    | SOURCE AND PURITY OF MATERIALS:   |
|             | e buffer solns were satd by a  | shaking them       | The sulfadiazine, mp 256 <sup>o</sup> C, was obtained   |
|             | gorously with an excess of so  |                    | by recrystg a common specimen from water.   |
|             | ine for at least 3 h. They w   |                    | Neither source nor purity of the remaining  |
|             | ickly filtered. The sulfadia   |                    | materials was specified.  |
| -           | s detd by the method of Bratt  |                    | materials was specified.  |
|             | all (1), and the pH values we  |                    |   |
|             | th the glass electrode, which  |                    |   |
|             | ed in terms of the buffer sol  |                    |   |
|             | by Hitchcock and Taylor (2).   |                    | ESTIMATED ERROR:  |
|             | by mitcheoler and rayior (2).  |                    | Nothing specified.  |
|             |  |                    |   |
|             |  |                    | REFERENCES:<br>1. Bratton, A. C.; Marshall, E.K., Jr.<br><i>L. Biol. Cham.</i> 1939, 129, 537         |
|             |  |                    | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|             |  |                    | <ol> <li>Hitchcock, D. I.; Taylor, A. C.</li> <li>J. Am. Chem. Soc. <u>1937</u>, 59, 1812.</li> </ol> |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfadiazine);<br>$C_{10}H_{10}N_4O_2S$ ; [68-35-9]<br>(2) 1,2,3-Propanetricarboxylic acid, 2-<br>hydroxy, disodium salt; (Na citrate);<br>$C_6H_6Na_2O_7$ ; [144-33-2]<br>(3) Sodium hydroxide; NaOH; [1310-73-2] | Gilligan, D. R.; Garb, S.; Plummer, M. N.<br>Proc. Soc. Exp. Biol. Med. <u>1943</u> , 52,<br>248-50. |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:   |
| VARIABLES: pH  | R. Piekos  |

The curve of solubility of sulfadiazine in M/10 citrate plus NaOH buffer solutions at  $37^{\circ}C$ .



pH OF BUFFER WITH DISSOLVED COMPOUND

### AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: An amt of sulfadiazine in large excess of that to be dissolved was added to M/10 citrate plus NaOH buffers, shaken for 18 h in a water bath at 37°C and filtered at the same temp. The pH of the filtrate was measured immediately with a Beckmann pH meter and appropriate corrections were made. Sulfadiazine was assayed by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

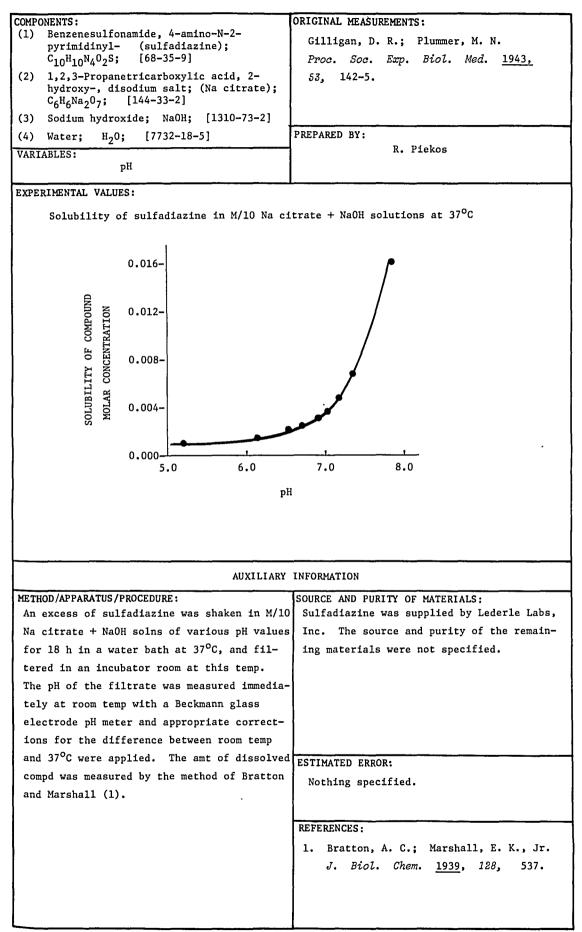
Sulfadiazine (purity not specified) was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

**REFERENCES:** 

 Bratton, A. C.; Marshall, E. K., Jr. J. Biol. Chem. 1939, 128, 537.



| 166   |  |
|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]<br>(2) 1,2,3-Propanetricarboxylic acid, 2-<br>hydroxy- (citric acid); C <sub>6</sub> H <sub>8</sub> 0 <sub>7</sub> ; [77-92-9]<br>(3) Water; H <sub>2</sub> 0; [7732-18-5]  | ORIGINAL MEASUREMENTS:<br>Takubo, T.; Matsumaru, H.;<br>Tsuchiya, S.; Hiura, M.<br><i>Chem. Pharm. Bull.</i> <u>1973</u> , 21(7),<br>1440-5. |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C; one pH: 2.1   | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
| Solubility of sulfadiazine in a citric a<br>per 100 ml water ) of pH 2.1 at 37°C is<br>mol dm <sup>-3</sup> solution, compiler ).<br><sup>a</sup> Numerical value to the graphical data<br>in personal communication.   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Aliquots of the citric acid soln were placed<br>in glass-stoppered flasks with excess of<br>sulfadiazine. The flasks were allowed to<br>stand at $37\pm1^{\circ}$ C and shaken vigorously for<br>4 h until equilibrium was established. One<br>ml of the supernatant was removed by means<br>of a filter pipet and sulfadiazine was assay<br>ed by the previously reported method (1). | grade. The source and purity of the citric<br>acid was not specified.<br>Distd water was used.   |
|   | <ul> <li>1. Takubo, T.; Tsuchiya, S.; Hiura, M.</li> <li>Yakuzaigaku <u>1971</u>, 31, 298.</li> </ul>  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |
|---|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);</pre>  | Nogami, H.; Nagai, T.; Suzuki, A.           |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]  |   |
| (2) Phosphoric acid, disodium salt;   | Chem. Pharm. Bull. <u>1966</u> , 14(4),     |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | 339-50.                                     |
| (3) 1,2,3-Propanetricarboxylic acid, 2-<br>hydroxy- (citric acid); C <sub>6</sub> H <sub>8</sub> O <sub>7</sub> ; [77-92-9] |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:                                |
| VARIABLES:  | R. Piekos                                   |
| рН  |   |
| EXPERIMENTAL VALUES:  |   |
| pH of Mc'Ilvaine buffer   |   |
| solutions <sup>a</sup> at constant<br>ionic strength of 0.35. Solu  | bility of sulfadiazine at 37 <sup>0</sup> C |
| at the begin- at the end  |   |
| ning of the of the run<br>run   | $mg/100 m1 10^3 mo1 dm^{-3} b$              |
| 4.17 4.19   | 10.7 0.4275                                 |
| 5.06 5.09   | 11.0 0.4395                                 |
| 6.56 6.59   | 93.0 3.716                                  |
| 7.23 7.10   | 175 6.992                                   |
|   | 242 9.669                                   |
| 8.14 7.30   | 242 9.009                                   |
|   |   |
|   | INFORMATION                                 |
|   |   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| Soly of sulfadiazine was detd from dissoln  | Commercial sulfadiazine J. P. was used.     |
| rate data obtained by the rotating disk   | Purity of the remaining materials was not   |
| method.   | specified.                                  |
|   |   |
|   |   |
|   |   |
|   |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                            |
|   | Nothing specified.                          |
|   |   |
|   | REFERENCES:                                 |
|   |   |
|   |   |
|   |   |
|   | 1   |
|   |   |
|   |   |

| 10 10 12 12       11 12 12         Phosphoric acid, disodium salt; $Na_2HPO_4$ ; [7558-94-4]         1 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (citric acid); $C_6H_80_7$ ; [77-92-9]       PREPARED BY:         Nater; $H_20$ ; [7732-18-5]       R. Piekos         RIABLES: pH       PH         Citric acid       Na2HPO4       pH         /100 ml water       g/100 ml water       pH         1.680       0.572       3.1       0.13         0.840       1.716       5.8       0.16       0.639         0.420       2.228       6.8       0.49       1.96   | pyrimidinyl-<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;<br>) Phosphoric aci  | (sulfadiazine);<br>[68-35-9]                              |        |  | ents:   |
|--|---|---|--------|--|---|
| ) Phosphoric acid, disodium salt;<br>$Na_2HPO_4$ ; [7558-94-4]<br>) 1,2,3-Propanetricarboxylic acid, 2-<br>hydroxy- (citric acid); $C_6H_8O_7$ ;<br>[77-92-9]<br>) Water; $H_2O$ ; [7732-18-5]<br>RIABLES: pH<br>ERIMENTAL VALUES:<br>Citric acid $Na_2HPO_4$ pH Solubility at $37^{\circ}C$<br>1.680 0.572 3.1 0.13 0.519<br>1.260 1.144 4.2 0.11 0.439<br>0.840 1.716 5.8 0.16 0.639<br>0.420 2.228 6.8 0.49 1.96<br>Aumerical values to the graphical data were given by one of the authors (S. T. )<br>in personal communication.  | ) Phosphoric aci  | d. disodium salt:   |        |  |   |
| hydroxy-       (citric acid); $C_6H_80_7$ ;         [77-92-9]       PREPARED BY:         Nater; $H_20$ ; [7732-18-5]       R. Piekos         RIABLES:       pH         ERIMENTAL VALUES:       R. Piekos         Citric acid       Na2HPO4       pH         g/100 ml water       pH       Solubility at $37^{\circ}C$ 1.680       0.572       3.1         1.680       0.572       3.1         0.840       1.716       5.8         0.420       2.228       6.8       0.49         aNumerical values to the graphical data were given by one of the authors (S. T. )       in personal communication.                    | Na <sub>2</sub> HPO <sub>4</sub> ; [755   |   |        | 21(7), 1440-5.   |   |
| B)       Water; $H_20$ ; $[7732-18-5]$ R. Piekos         RIABLES:       pH       PH       R. Piekos         VERIMENTAL VALUES:       Solubility at $37^{\circ}C$ mg/ml soln <sup>a</sup> $10^3 \text{ mol dm}^{-3} \text{ soln}^b$ 5/100 ml water       g/100 ml water       pH       Solubility at $37^{\circ}C$ mg/ml soln <sup>a</sup> $10^3 \text{ mol dm}^{-3} \text{ soln}^b$ 1.680       0.572       3.1       0.13       0.519         1.260       1.144       4.2       0.11       0.439         0.840       1.716       5.8       0.16       0.639         0.420       2.228       6.8       0.49       1.96 | hydroxy- (cit   |   | L -    | DDEDADEN DV.   |   |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $   | ) Water; H <sub>2</sub> 0;  | [7732-18-5]   | ľ      |  | Piekos  |
| PERIMENTAL VALUES:         Citric acid       Na2HPO4       Solubility at $37^{\circ}C$ g/100 ml water       pH       Solubility at $37^{\circ}C$ 1.680       0.572       3.1       0.13       0.519         1.260       1.144       4.2       0.11       0.439         0.840       1.716       5.8       0.16       0.639         0.420       2.228       6.8       0.49       1.96  | RIABLES:  | Hα  |        | к.   | TIERUS  |
| $\frac{2}{g/100 \text{ ml water}}  pH \qquad mg/ml \ soln^a \qquad 10^3 \ mol \ dm^{-3} \ soln^b}$ 1.680 0.572 3.1 0.13 0.519 1.260 1.144 4.2 0.11 0.439 0.840 1.716 5.8 0.16 0.639 0.420 2.228 6.8 0.49 1.96<br><sup>a</sup> Numerical values to the graphical data were given by one of the authors (S. T. ) in personal communication.  |   |   |        |  |   |
| $\frac{g/100 \text{ ml water } g/100 \text{ ml water } mg/m1 \text{ soln}^{a} 10^{3} \text{ mol } dm^{-3} \text{ soln}^{b}}{1.680 \\ 1.680 \\ 0.572 \\ 3.1 \\ 0.13 \\ 0.439 \\ 0.840 \\ 1.716 \\ 5.8 \\ 0.16 \\ 0.639 \\ 0.420 \\ 2.228 \\ 6.8 \\ 0.49 \\ 1.96 \\ \hline \\ \hline \\ a_{\text{Numerical values to the graphical data were given by one of the authors ( S. T. )}}{a_{\text{Numerical values to the graphical data were given by one of the authors ( S. T. )}}$   | Citric acid   | Na2HPO4   | - 11   | Solubi   | lity at 37 <sup>0</sup> C   |
| 1.260       1.144       4.2       0.11       0.439         0.840       1.716       5.8       0.16       0.639         0.420       2.228       6.8       0.49       1.96 <sup>a</sup> Numerical values to the graphical data were given by one of the authors (S. T. ) in personal communication.   | g/100 ml water  | g/100 ml water  | - рн   | mg/ml soln <sup>a</sup>  | 10 <sup>3</sup> mol dm <sup>-3</sup> soln <sup>b</sup>  |
| 0.840       1.716       5.8       0.16       0.639         0.420       2.228       6.8       0.49       1.96 <sup>a</sup> Numerical values to the graphical data were given by one of the authors (S. T. ) in personal communication.  | 1.680   | 0.572   | 3.1    | 0.13   | 0,519   |
| 0.420 2.228 6.8 0.49 1.96<br><sup>a</sup> Numerical values to the graphical data were given by one of the authors (S. T. )<br>in personal communication.   | 1.260   | 1.144   | 4.2    | 0.11   | 0.439   |
| <sup>a</sup> Numerical values to the graphical data were given by one of the authors ( S. T. )<br>in personal communication.   | 0.840   | 1.716   | 5.8    | 0.16   | 0.639   |
| in personal communication.   | 0.420   | 2 228   | 6.8    | 0.49   | 1.96  |
|  |   |   |        | e given by one of  | the authors ( S. T. )   |
|  | <sup>a</sup> Numerical values<br>in personal comm   | to the graphical dat                                      |        | e given by one of  | the authors ( S. T. )   |
| AUXILIARY INFORMATION  | <sup>a</sup> Numerical values<br>in personal comm   | to the graphical day<br>nunication.                       | ta wer |  | the authors ( S. T. )   |
| AUXILIARY INFORMATION THOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS:  | <sup>a</sup> Numerical values<br>in personal comm<br><sup>b</sup> Calculated by c   | to the graphical day<br>nunication.<br>compiler.<br>AUXII | La wer | INFORMATION  |   |
|  | <sup>a</sup> Numerical values<br>in personal comm<br><sup>b</sup> Calculated by c<br>THOD/APPARATUS/PRC   | to the graphical day<br>nunication.<br>compiler.<br>AUXII | LIARY  | INFORMATION<br>SOURCE AND PURITY   | OF MATERIALS;   |
| THOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS:  | <sup>a</sup> Numerical values<br>in personal comm<br><sup>b</sup> Calculated by c<br>THOD/APPARATUS/PRC<br>Liquots of the buf<br>Lass-stoppered fla | AUXII<br>CEDURE:  | JARY 1 | INFORMATION<br>SOURCE AND PURITY<br>The sulfadiazine<br>The source and p | OF MATERIALS:<br>was of pharmaceutical gr<br>urity of Na <sub>2</sub> HPO <sub>4</sub> and citr |

ESTIMATED ERROR: Solv and pH: not specifie

Soly and pH: not specified. Temp: ±1°C (authors).

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#### **REFERENCES:**

equilibrium was established. One ml of the supernatant was removed by means of a filter

pipet and sulfadiazine was assayed by the

.

previously reported method (1).

 Takubo, T.; Tsuchiya, S.; Hiura, M. Yakuzaigaku <u>1971</u>, 31, 298.

| COMPONENTS:   |   | ODICINAL MEACUDEMENTS.   |  |
|---|---|--|--|
| DMPONENTS:<br>1) Benzenesulfonamide, 4-amino-N-2-   |   | ORIGINAL MEASUREMENTS:   |  |
| <pre>pyrimidinyl- (sulfadiazine);</pre>   |   | Gasco, M. R.; Aimonetto, S.  |  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]  |   | Atti Accad. Sci. Torino, Cl. Sci. Fis.   |  |
| <ul> <li>(2) Ethanesulfonic acid, 2-[[3α, 5β, 7<br/>-3,7,12-trihydroxy-24-oxocholan-24<br/>amino]-, monosodium salt (Na taura<br/>ate); C<sub>26</sub>H<sub>45</sub>NO<sub>7</sub>S·Na; [145-42-6]</li> </ul>   | 4-y1]-<br>ochol-  | Mat. Nat. <u>1979</u> , <i>113(1-2)</i> , 119-22.  |  |
| (3) Phosphoric acid, disodium salt;   | '   | PREPARED BY:   |  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]<br>(4) Phosphoric acid, monosodium salt;<br>NaH <sub>2</sub> PO <sub>4</sub> ; [7558-80-7]<br>(5) Water; H <sub>2</sub> O; [7732-18-5]   |   | R. Piekos  |  |
| VARIABLES:<br>Concentration of Na taurocholate; pH  |   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
| Concentration of<br>Na taurocholate   | Solubil   | lity of sulfadiazine at 25 <sup>0</sup> C<br>μM/ml solution <sup>a</sup>   |  |
| mM/l solution <sup>a</sup>  | рН 6.3  | 3 рН 7.2   |  |
| 2.25  | 0,52  | 1.43   |  |
| 4.50  | 0.47  |  |  |
| 6.00  | 0.47  | 1.39   |  |
| 8.00  | 0.47  |  |  |
| 12.00   | 0.47  |  |  |
| 16.00   | 0.47  |  |  |
| 10.00   |   | •  |  |
| 20.00<br><sup>a</sup> Numerical values given by the fi  | 0.47<br>rst autl  | 1.43   |  |
| 20.00   | <u> </u>  | ······   |  |
| 20.00<br><sup>a</sup> Numerical values given by the fi  | rst aut   | ······   |  |
| 20.00<br><sup>a</sup> Numerical values given by the finance of t | rst aut   | hor in personal communication.   |  |
| 20.00<br><sup>a</sup> Numerical values given by the finance<br>AUX<br>METHOD/APPARATUS/PROCEDURE:   | rst aut)<br>KILIARY   | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by   | rst aut<br>KILIARY<br>the   | hor in personal communication.   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series o   | rst aut<br>KILIARY<br>the<br>f 15-ml  | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50  | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series o   | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of  | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of  |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing b  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>1 of<br>Na  | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of  |  |
| 20.00<br><sup>a</sup> Numerical values given by the fit<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series o<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>1 of<br>Na<br>were                                    | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.  |  |
| 20.00<br><sup>a</sup> Numerical values given by the fination<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing by  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The                          | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.  |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions of<br>agitated for 20 h at 25°C and filtered  | rst aut<br>KILIARY<br>the<br>f 15-m1<br>rs, 50<br>1 of<br>Na<br>were<br>d. The<br>s detd                | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:  |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by a<br>method of Hofmann (1). In a series o<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing a<br>taurocholate concn. The suspensions a<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a        | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).  |  |
| 20.00<br><sup>a</sup> Numerical values given by the fine<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions of<br>agitated for 20 h at 25°C and filterer<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means   | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).<br>pH : precision ±0.02 pH unit (authors).   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions of<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means<br>Dognon-Abribat (Prolabo) tensiometer  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).  |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means<br>Dognon-Abribat (Prolabo) tensiometer<br>spectrophotometrically on a Perkin E   | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).<br>pH : precision ±0.02 pH unit (authors).<br>Temp: ±0.5°C (authors).<br>REFERENCES:   |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means<br>Dognon-Abribat (Prolabo) tensiometer<br>spectrophotometrically on a Perkin E   | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).<br>pH : precision ±0.02 pH unit (authors).<br>Temp: ±0.5°C (authors).  |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing is<br>taurocholate concn. The suspensions<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means<br>Dognon-Abribat (Prolabo) tensiometer<br>spectrophotometrically on a Perkin E   | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).<br>pH : precision ±0.02 pH unit (authors).<br>Temp: ±0.5°C (authors).<br>REFERENCES:<br>1. Hofmann, A. F., Biochem. J. <u>1963</u> , |  |
| 20.00<br><sup>a</sup> Numerical values given by the final<br>AUX<br>METHOD/APPARATUS/PROCEDURE:<br>The soly of sulfadiazine was detd by a<br>method of Hofmann (1). In a series of<br>glass cylinders with ground-in stopper<br>mg of sulfadiazine was placed in 15 m<br>phosphate buffer solns of increasing a<br>taurocholate concn. The suspensions a<br>agitated for 20 h at 25°C and filtered<br>quantity of sulfadiazine dissolved wa<br>by measuring surface tension by means<br>Dognon-Abribat (Prolabo) tensiometer<br>spectrophotometrically on a Perkin E  | rst aut<br>KILIARY<br>the<br>f 15-ml<br>rs, 50<br>l of<br>Na<br>were<br>d. The<br>s detd<br>of a<br>and | hor in personal communication.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials<br>was specified.<br>The phosphate buffer was 0.3M in respect of<br>the Na <sup>+</sup> ion concentration.<br>ESTIMATED ERROR:<br>Soly: precision ±2% (authors).<br>pH : precision ±0.02 pH unit (authors).<br>Temp: ±0.5°C (authors).<br>REFERENCES:<br>1. Hofmann, A. F., Biochem. J. <u>1963</u> , |  |

| COMPONENTS:   | ORIGINAL MEA            | SUREMENTS:  |
|---|-------------------------|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);</li> </ol>   | -                       | .; Aimonetto, S.  |
| <ul> <li>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</li> <li>(2) Ethanesulfonic acid, 2-[[[[(3α,5β,7α<br/>12α)-3,7,12-trihydroxy-24-oxacholan-'<br/>yl]amino]acetyl]amino]-, sodium salt<br/>(Na tauroglycocholate);</li> </ul> | Mat. Nat.               | l. Sci. Torino, Cl. Sci. Fi.<br><u>1979</u> , 113(1–2), 119–22. |
| C <sub>28</sub> H <sub>48</sub> N <sub>2</sub> O <sub>8</sub> S·Na [11006-55-6]   |                         |   |
| (3) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | PREPARED BY:            | R. Piekos   |
| (4) Phosphoric acid, monosodium salt;<br>NaH <sub>2</sub> PO <sub>4</sub> ; [7558-80-7]   |                         |   |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]  |                         |   |
| ARIABLES:<br>Concentration of Na tauroglycochlolate;  | рH                      |   |
| XPERIMENTAL VALUES:   |                         |   |
| Concentration of Na S   | -1-1414                 | fadiazine at 25 <sup>0</sup> C                                  |
| tauroglycocholate   | -                       | olution <sup>a</sup>  |
| mM/1 solution   | ······                  |   |
|   | рН 6.3                  | pH 7.2  |
| 2.25  | 0.43                    | 1.34  |
| 4.50  | 0.39                    | 1.21  |
| 6.00  | 0.41                    | 1.26  |
| 8.00  | 0.41                    | 1.26  |
| 12.00   | 0.43                    | 1.26  |
| 16.00   | 0.43                    | 1.28  |
| 20.00   | 0.47                    | 1.30  |
| <sup>a</sup> Numerical values given by the first  | author in perso         | onal communication.   |
| AUXILIA   | ARY INFORMATION         |   |
| ETHOD/APPARATUS/PROCEDURE:  |                         | URITY OF MATERIALS:   |
| The soly of sulfadiazine was detd by the  | 1                       | rce nor purity of the material                                  |
| method of Hofmann (1). In a series of 15  |                         |   |
| glass cylinders with ground-in stoppers,  |                         | te buffer was 0.3M in respect                                   |
|   | the Na <sup>+</sup> ion | concn.  |
| - ·   |                         |   |
| phosphate buffer solns of increasing Na   |                         |   |
| phosphate buffer solns of increasing Na tauroglycocholate concn. The suspensions  |                         |   |
| were agitated for 20 h at 25°C and filter   | ed.                     |   |
| phosphate buffer solns of increasing Na tauroglycocholate concn. The suspensions  | ed.<br>s                |   |
| nosphate buffer solns of increasing Na  |                         |   |

and spectrophotometrically on a Perkin Elmer pH : precision ±0.02 pH unit (authors).

Soly: precision ±2% (authors).

1. Hofmann, A. F.; Biochem. J. <u>1963</u>,

Temp: ±0.5°C (authors).

**REFERENCES:** 

*89*, 57.

of a Dognon-Abribat (Prolabo) tensiometer

EPS-35 spectrophotometer.

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-1   | N-2-          | DRIGINAL MEASUREMENTS:  |  |
|--|---------------|---|--|
| pyrimidinyl- (sulfadiazine)  |               | Watari, N.; Kaneniwa, N.  |  |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]   |               | Chem. Pharm. Bull. 1976, 24(11),  |  |
| (2) Sulfuric acid monododecyl est<br>salt (Na lauryl sulfate);<br>C <sub>12</sub> H <sub>25</sub> Na0 <sub>4</sub> S; [151-21-3] | er, sodium    | 2577-84.  |  |
| Water; H <sub>2</sub> O; [7732-18-5]   |               |   |  |
| VARIABLES:   |               | PREPARED BY:  |  |
| Concentration of Na lauryl sulfat  |               | R. Piekos   |  |
| soncentration of na facily suffa   |               |   |  |
| EXPERIMENTAL VALUES:   | l             |   |  |
| Concentration  | Tetel -       |   |  |
| Concentration<br>of Na lauryl  | Total s       | olubility of sulfadiazine at 37°C   |  |
| sulfate  | mg/ml s       | solution $10^4$ mol dm <sup>-3 a</sup>  |  |
| % w/v  |               |   |  |
| 0.01   | 0.124         | 4 4.954   |  |
| 0.05   | 0.13          | 2 5.274   |  |
| 0.10   | 0.15          |   |  |
| 0.25   | 0.16          |   |  |
| 0.50   | 0.17          |   |  |
| 1.00   | 0.20          |   |  |
| 2.00   | 0.258         |   |  |
| 3.00   | 0.309         |   |  |
| 4.00   | 0.36          |   |  |
| 5.00   | 0.30          | •   |  |
| 6.00   | 0.41          |   |  |
|  |               |   |  |
| <sup>a</sup> Calculated by   | compiler.     |   |  |
|  | AUXILIARY I   | INFORMATION   |  |
| MERIOD ADDADATUS (DDOGEDUDE -  |               |   |  |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of sulfadiazine was ad  |               | SOURCE AND PURITY OF MATERIALS:<br>Commercial sulfadiazine of the Japanese              |  |
| of the Na lauryl sulfate soln contained in a   |               | Pharmacopeia grade and distd water were   |  |
| 50-ml flask and the flask was shaken ( 2   |               | used.   |  |
|  |               |   |  |
| strokes/s at the amplitude of 3 cm ) in a  |               | Na lauryl sulfate was of the reagent grade  |  |
| thermostatically controlled water bath at  |               | (Wako Pure Chemical Industries Ltd, lot No<br>PA10233) and used without further purifi- |  |
| 37°C. One-ml sample was removed every 6 h  |               | •   |  |
| (total equilibration period was 3-5 days)  |               | cation.   |  |
| using a warmed Millipore filter syringe with   |               |   |  |
| a filter pore size of 0.45 $\mu$ (Mi   | -             | ESTIMATED ERROR:  |  |
| HAWP 01300) and the filtrate was   |               | Soly: not specified.  |  |
| water and assayed spectrophotome   | trically (1). | Temp: ±0.05 <sup>0</sup> C (authors).   |  |
|  | ŀ             | REFERENCES :  |  |
|  |               |   |  |
|  |               | 1. Kaneniwa, N.; Watari, N.   |  |
|  |               | Chem. Pharm. Bull. <u>1974</u> , 22, 1699   |  |
|  |               |   |  |
|  | ]             |   |  |
|  |               |   |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |
|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);</li> </ol> |  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]            | Dolique, R.; Foucault, J.                    |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> 0; [64-17-5]                               | Trav. soc. pharm. Montpellier <u>1952</u> ,  |
| (3) 1,2,3-Propanetriol; C <sub>3</sub> H <sub>8</sub> O <sub>3</sub> ; [56-81-5]      | 12, 145-53.                                  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 26-28°C  | R. Piekos                                    |
| •   |  |
| EXPERIMENTAL VALUES:  | 1  |
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|   |  |
|   |  |
| Solubility of sulfadiazine in a mixtu   | re of 1,2,3-propanetriol and 95 <sup>0</sup> |
| ethanol ( 2:1 by wt ) at 26-28 <sup>0</sup> C is O                                    | .27% ( 1.1 x $10^{-2}$ mol kg <sup>-1</sup>  |
|   | , C  |
| solvent, compiler ).  |  |
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| AUXILIARY   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| The sulfadiazine content was detd by diazo-   | Nothing specified.                           |
| tization of the amine group in a cold aci-  |  |
| dified 0.1N KNO <sub>2</sub> soln. An excess of KNO <sub>3</sub>                      |  |
| was detected by using iodinated starch.   |  |
|   |  |
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|   | ESTIMATED ERROR:                             |
|   | Nothing specified.                           |
|   |  |
|   | REFERENCES :                                 |
|   | NET ERENCES ;                                |
|   |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-  | ORIGINAL MEASUREMENTS:                     |
|--|--|
| pyrimidinyl- (sulfadiazine):   | Dolique, R.; Foucault, J.                  |
| pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | Trav. soc. pharm. Montpellier 1952,        |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [64-17-5]  | 12, 145-53.                                |
| (3) 1,2,3-Propanetriol; C <sub>3</sub> H <sub>8</sub> O <sub>3</sub> ; [56-81-5]                           |  |
| (4) Urea; $CH_4N_2O$ ; [57-13-6]   |  |
| 4  |  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                               |
| VARIABLES:<br>One temperature: 26-28 <sup>o</sup> C  | R. Piekos                                  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfadiazine at 26-28 <sup>0</sup> C   |  |
| Solubility of sulfadiazine at 26-28°C  | in a saturated solution of urea in a       |
| mixture of 1,2,3-propanetriol and 95 <sup>0</sup>  | C ethanol (2:1 by wt), containing          |
|  | · · · · · · · · · · · · · · · · · · ·      |
| 54.5 g of urea per 100 g of the mixtu  | re, is $0.26\%$ ( $1.1 \times 10^{-2}$ mol |
| kg <sup>-1</sup> solvent, compiler ).  |  |
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| AUXILIARY  | INFORMATION                                |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:            |
| The sulfadiazine content was detd by diazo-  |  |
|  |  |
| tization of the amine group in a cold acidi-   | · [ .                                      |
| fied 0.1N KNO2 soln. An excess of KNO3 was   |  |
| detected by using iodinated starch.  |  |
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|  | ESTIMATED ERROR:                           |
|  | Nothing specified                          |
|  | Nothing specified.                         |
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|  | REFERENCES :                               |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                          |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-   |   |
| pyrimidinyl- (sulfadiazine);   | Nogami, H.; Nagai, T.; Suzuki, A.               |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]   | Chem. Pharm. Bull. <u>1966</u> , 14(4), 339–50. |
| <pre>(2) Ethanol; 2,2'-iminobis- (diethanolamine);<br/>C<sub>4</sub>H<sub>11</sub>NO<sub>2</sub>; [111-42-2]</pre> |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:                                    |
| Concentration of diaethanolamine   | R. Piekos                                       |
|  |   |
| EXPERIMENTAL VALUES:   |   |
| EARENIMENTAL VALUES.   |   |
|  |   |
|  |   |
|  |   |
|  |   |
|  | bility of sulfadiazine at 37 <sup>0</sup> C     |
| diethanolamine mg  | $/100 \text{ ml}$ $10^2 \text{ mol dm}^{-3}$    |
| mol dm <sup>-3</sup>   |   |
| 10 <sup>-3</sup> 3   | 3.8 0.135                                       |
| 10 <sup>-2</sup> 26  | 6.0 1.06  |
| 10 <sup>-1</sup> 2510  | 0.0 10.0  |
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| AUXILIARY  | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                 |
| Soly of sulfadiazine was detd from dissoln   | Commercial sulfadiazine J. P. was used.         |
| rate data obtained by the rotating disk  | Purity of the remaining materials was not       |
| method.  | specified.                                      |
|  | apecified.                                      |
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|  |   |
|  | ESTIMATED ERROR:                                |
|  |   |
|  | Nothing specified.                              |
|  |   |
|  | REFERENCES:                                     |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                             |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Nogami, H.; Nagai, T.; Suzuki, A.                  |
| pyrimidinyl; (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |  |
| (2) Ethanol, 2,2',2''-nitrilotris-   | Chem. Pharm. Bull. <u>1966</u> , 14(4),<br>339-50. |
| (triethanolamine); C <sub>6</sub> H <sub>15</sub> NO <sub>3</sub> ;<br>[102-71-6]                          |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:                                       |
| Concentration of triethanolamine   | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
|  |  |
|  |  |
| · · · · · · · · · · · · · · · · · · ·  | lity of sulfadiazine at 37 <sup>0</sup> C          |
| triethanolamine mg/100   | ml $10^2 \text{ mol } \text{dm}^{-3}$              |
| mol dm <sup>-3</sup>   |  |
| 10 <sup>-3</sup> 31.4  | 0.15   |
| 10 <sup>-2</sup> 286.0   | 1.10   |
| 10 <sup>-1</sup> 2550.0  | 10.0   |
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| AUXILIAR   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                    |
| Soly of sulfadiazine was detd from dissoln   | Commercial sulfadiazine J. P. was used.            |
| rate data obtained by the rotating disk  | Purity of the remaining materials was              |
| method.  | not specified.                                     |
|  |  |
|  |  |
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|  |  |
|  |  |
|  | ESTIMATED ERROR:                                   |
|  | Nothing specified.                                 |
|  |  |
|  | REFERENCES:  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl-; (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</li> <li>Formamide, N, N-dimethyl- (DMF);<br/>C<sub>3</sub>H<sub>7</sub>NO; [68-12-2]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Elworthy, P. H.; Worthington, H. E. C.<br>J. Pharm. Pharmac. <u>1968</u> , 20, 830-5. |
| VARIABLES:  | PREPARED BY:  |
| Temperature: Concentration of DMF   | R. Piekos   |

| % w/w | Sulfadi         | ated solution |         |
|-------|-----------------|---------------|---------|
| DMF   | 20 <sup>0</sup> | 30°C          | 40°C    |
| 0.5   | 0.00490         | 0.00828       | 0.0138  |
| 1.0   | 0.00520         | 0.00881       | 0.0147  |
| 2.0   | 0.00598         | 0.00987       | 0.0166  |
| 3.0   | 0.00679         | 0.01110       | 0.0187  |
| 5.0   | 0.00861         | 0.01410       | 0.0233  |
| 10.0  | 0.01700         | 0.02520       | 0.0410  |
| 20.0  | 0.03950         | 0.05790       | 0.0968  |
| 30.0  | 0.08500         | 0.12300       | 0.1880  |
| 50.0  | 0.35200         | 0.50200       | 0.7580  |
| 70.0  | 1.90000         | 2.40000       | 3.5000  |
| 78.0  | 4.28000         | 4.85000       | 6.2000  |
| 89.0  | 9.80000         | 10.90000      | 12.0000 |

#### AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:<br>Solns were presatd by shaking with powd sul-<br>fadiazine for 24 h, and transferred to a soly<br>app which was of the percolation type and a<br>modification of that used by Davies and Grif-<br>fiths (1). The soln was recycled in the app<br>until satd (7-14 days). The solute concn was<br>detd by one of the three methods: (a) concn<br>1.5%, by evapn of solvent and drying the re-<br>sidue to const wt; (b) concn 0.02 to 1.5%,<br>samples were dild to give a 70% DMF solvent<br>mixt and assayed spectrophotometrically at<br>270 nm; (c) concn < 0.02%, samples were dild<br>with water and assayed as in (b). In all spec<br>trophotometric assays suitable calibration<br>lines were prepd.<br>SOURCE AND PURITY OF MATERIALS:<br>Source (and pressure and gave 100.0% pu-<br>rity calcd with reference to the material<br>dried at 105°C. DMF (May and Baker Ltd)<br>was distd under reduced pressure and gave<br>$n_D^{-25} = 1.4283$ . Purity of the water was not spe-<br>given (authors).<br>Temp: $\pm 0.05^{\circ}C$ (authors).<br>Temp: $\pm 0.05^{\circ}C$ (authors). |
|--|
| 1405.  |

| ton, H. E. C.<br><u>8</u> , <i>20</i> , 830-5. |
|--|
|  |
|  |

| % w∕w DMF |                   | $10^{\circ}$ mol kg <sup>-1</sup> | water <sup>a</sup> |
|-----------|-------------------|-----------------------------------|--------------------|
|           | 20 <sup>0</sup> C | 30 <sup>0</sup> C                 | 40 <sup>0</sup> C  |
| 0.5       | 0.0196            | 0.0331                            | 0.0551             |
| 1.0       | 0.0208            | 0.0352                            | 0.0587             |
| 2.0       | 0.0239            | 0.0394                            | 0.0663             |
| 3.0       | 0.0271            | 0.0443                            | 0.0747             |
| 5.0       | 0.0344            | 0.0563                            | 0.0931             |
| 10.0      | 0.0679            | 0.1010                            | 0.1640             |
| 20.0      | 0.1580            | 0.2310                            | 0.3870             |
| 30.0      | 0.3400            | 0.4920                            | 0.7520             |
| 50.0      | 1.4100            | 2.0200                            | 3.0500             |
| 70.0      | 7.7400            | 9.8200                            | 14.5000            |
| 78.0      | 17.900            | 20.4000                           | 26.4000            |
| 89.0      | 42.900            | 48.9000                           | 54.5000            |

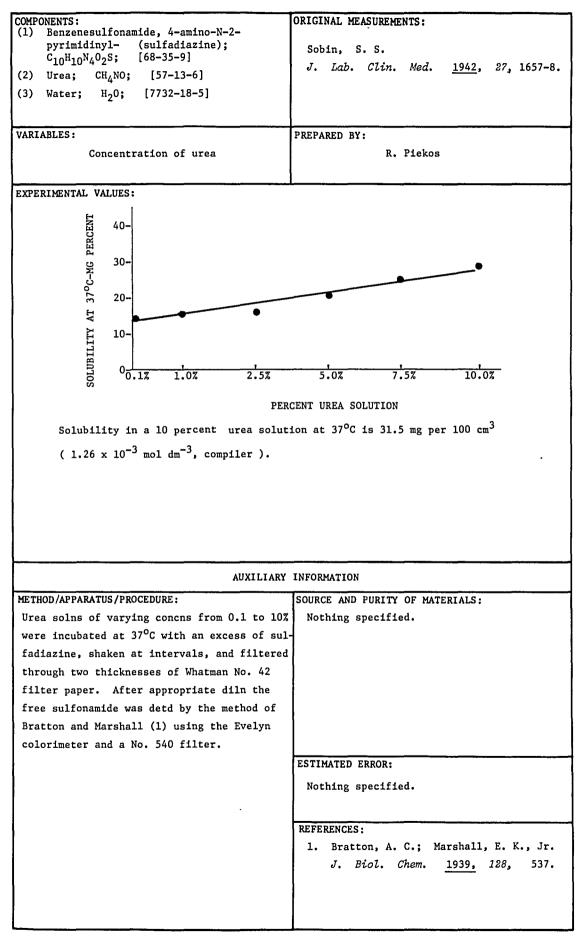
<sup>a</sup>Calculated by compiler.

|                             | • • • • • • • • • • • • • • • • • • • |
|-----------------------------|---------------------------------------|
| AUXILIARY                   | INFORMATION                           |
| METHOD/APPARATUS/PROCEDURE: | SOURCE AND PURITY OF MATERIALS:       |
|                             |                                       |
|                             |                                       |
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|                             |                                       |
|                             | ESTIMATED ERROR:                      |
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|                             |                                       |
|                             |                                       |
|                             | REFERENCES:                           |
|                             |                                       |
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|                             |                                       |
|                             |                                       |

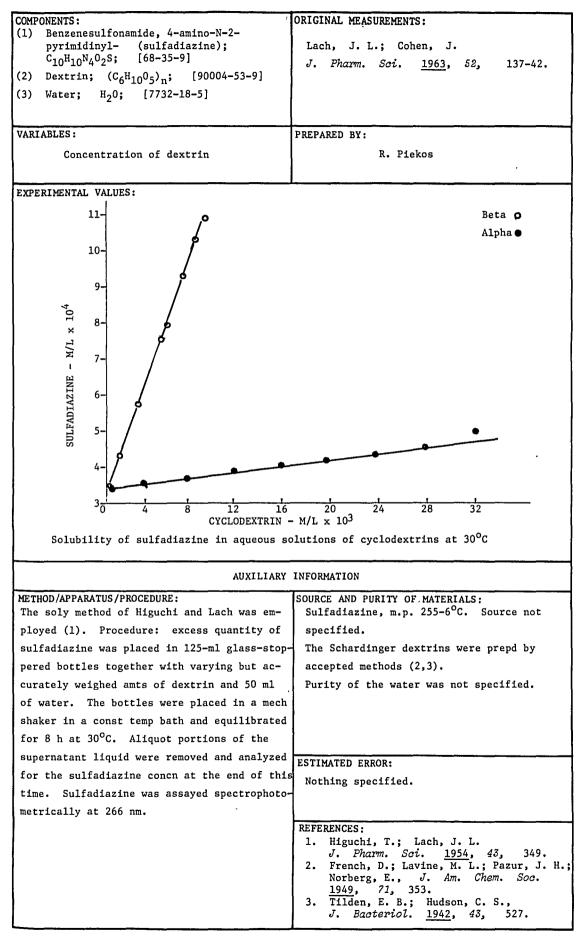
| Continued         | from previous page      | J. Pharm               | P. H.; Worthington, H. E. C.<br>. <i>Pharmac</i> . <u>1968</u> , <i>20</i> , 830-5. |
|-------------------|-------------------------|------------------------|---|
| VARIABLES:        |                         | PREPARED B             | Y:  |
| Temperature: (    | Concentration of D      | MF                     | R. Piekos   |
| EXPERIMENTAL VALU | JES:                    | I                      |   |
| % w/w             | Мо                      | le fraction sulfadiaz: | ine in solution   |
| DMF               | 20 <sup>°</sup> C       | 30 <sup>0</sup>        | 40°C  |
| 0.5               | $3.54 \times 10^{-6}$   | $5.47 \times 10^{-6}$  | 9.97 x 10 <sup>-6</sup>   |
| 1.0               | $3.78 \times 10^{-6}$   | $6.39 \times 10^{-6}$  | $1.07 \times 10^{-5}$   |
| 2.0               | $4.37 \times 10^{-6}$   | $7.21 \times 10^{-6}$  | $1.21 \times 10^{-5}$   |
| 3.0               | $5.00 \times 10^{-6}$   | $8.18 \times 10^{-6}$  | $1.38 \times 10^{-5}$   |
| 5.0               | $6.44 \times 10^{-6}$   | $1.06 \times 10^{-5}$  | $1.74 \times 10^{-5}$   |
| 10.0              | $1.33 \times 10^{-5}$   | $1.97 \times 10^{-5}$  | $3.19 \times 10^{-5}$   |
| 20.0              | $3.35 \times 10^{-5}$   | $4.87 \times 10^{-5}$  | $8.21 \times 10^{-5}$   |
| 30.0              | 7.91 x 10 <sup>-5</sup> | $1.14 \times 10^{-4}$  | $1.75 \times 10^{-4}$   |
| 50.0              | $4.08 \times 10^{-4}$   | 5.84 x $10^{-4}$       | $8.81 \times 10^{-4}$   |
| 70.0              | $2.94 \times 10^{-3}$   | $3.73 \times 10^{-3}$  | $5.50 \times 10^{-3}$   |
| 78.0              | $7.75 \times 10^{-3}$   | $8.84 \times 10^{-3}$  | $1.14 \times 10^{-2}$   |
| 89.0              | $2.32 \times 10^{-2}$   | $2.60 \times 10^{-2}$  | $2.90 \times 10^{-2}$   |
| a                 | Calculated by comp      | iler                   |   |
|                   |                         | AUXILIARY INFORMATION  | N   |
| METHOD/APPARATUS  | /PROCEDURE:             | SOURCE AND             | PURITY OF MATERIALS:  |
|                   |                         |                        |   |
|                   |                         | ESTIMATED              |   |
|                   |                         |                        |   |

ORIGINAL MEASUREMENTS:

COMPONENTS:



| COMPONENTS:  |                  |   | ORIGINAL MEASU           | REMENTS :          |                        |                    |
|--|------------------|---|--------------------------|--------------------|------------------------|--------------------|
| (1) Benzenesulfonamide, 4-amino-N-2-   |                  | Narand II a Narad T a Curulad A   |                          |                    |                        |                    |
| pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9] |                  | Nogami, H.; Nagai, T.; Suzuki, A.<br>Chem. Pharm. Bull. <u>1966,</u> 14(4), |                          |                    |                        |                    |
| (2) Urea; $CH_4N_20$ ; [57-13-   | -61              |   |                          | . Bull.            | <u>1966,</u> <i>14</i> | ر (4)              |
| (3) Water; H <sub>2</sub> 0; [7732-18-   |                  |   | 339-50.                  |                    |                        |                    |
|  | -                |   |                          |                    |                        |                    |
| VARIABLES:   |                  |   | PREPARED BY:             | <b></b>            |                        |                    |
| Concentration of urea; temp  | erature          |   | 1                        | R. Piekos          |                        |                    |
|  |                  |   |                          |                    |                        |                    |
| EXPERIMENTAL VALUES:   |                  | ······  |                          |                    |                        |                    |
| Concentration  |                  |   | Solubility of a          | sulfadiaz          | ine                    |                    |
| of urea  | 25               | i <sup>o</sup> C  | 37                       |                    |                        | 0°c                |
| mol dm <sup>-3</sup>   | mg/100 ml        | concr   | n <sup>a</sup> mg/100 ml | concn <sup>b</sup> | mg/100m1               | concn <sup>b</sup> |
| 10 <sup>-3</sup>   |                  |   | 15.9                     | 0.635              |                        | ·····              |
| 10 <sup>-2</sup>   |                  |   | 20.2                     | 0.807              |                        |                    |
| 10 <sup>-1</sup>   | 10.2             | 4.07  | 28.8                     | 1.150              | 34.4                   | 1.37               |
| $5 \times 10^{-1}$   |                  |   | 31.4                     | 1.250              |                        |                    |
| 1  |                  |   | 42.3                     | 1.690              |                        |                    |
|  |                  |   |                          | <u> </u>           |                        |                    |
| Note: molar concent:   | rations of       | the so  | olute calculate          | d by comp          | iler.                  |                    |
| $a - 10^4 \text{ mol}$   | dm <sup>-3</sup> |   |                          |                    |                        |                    |
| $b - 10^3 mol$   | dm <sup>-3</sup> |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  | AUXI             | LIARY   | INFORMATION              |                    |                        |                    |
| METHOD/APPARATUS/PROCEDURE:  |                  |   | SOURCE AND PUR           | TTY OF MA          | TEDTAIC.               |                    |
| Soly of sulfadiazine was det   | rd from die      | soln  | Commercial su            |                    |                        | s used.            |
|  |                  |   |                          |                    |                        |                    |
| rate data obtained by the ro   | otating dis      | k   | Purity of the            | e remainin         | ng materials           | s was not          |
| method.  |                  |   | specified.               |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   | ESTIMATED ERRO           | )R:                |                        | _                  |
|  |                  |   | Nothing spect            | ified.             |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   | REFERENCES:              |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |
|  |                  |   |                          |                    |                        |                    |



| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>0<sub>2</sub>S; [68-35-9]</li> <li>Poly(oxy-1,2-ethanediyl), α - hexadecyl-<br/>ω-hydroxy-, mixt with α- octadecyl-ω -<br/>hydroxypoly(oxy-1,2-ethanediyl) (ceto-<br/>macrogol) [8065-80-3]</li> <li>Watana W 0. [7722 18 5]</li> </ol> | ORIGINAL MEASUREMENTS:<br>Corby, T. C.; Elworthy, P. H.<br>J. Pharm. Pharmac. <u>1971,</u> 23, Suppl.<br>395-485.<br>PREPARED BY:<br>R. Piekos |
|---|--|
| Concentration of Max  | imum additive concentration  |
| cetomacrogol  | of sulfadiazine at 20 <sup>0</sup> C   |
|   | 1 kg <sup>-1</sup> % by wt <sup>a</sup>  |
|   | vent   |
|   |  |
| 1 0.  | 272 0.0680   |
| 8 0.  | 535 0.134  |
| 10 1.   | 01. 0.252  |
|   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadiazine (Macarthy's Ltd, Romford) was a  |
| The soly was detd in an app where the aqueous   | i i i i i i i i i i i i i i i i i i i  |
| soln of cetomacrogol was percolated through   | British Pharmacopeia product. It was recry-<br>std twice from a DMF-EtOH mixt (1:3) and dri-   |
| a plug of sulfadiazine supported on a 5/3   | ed at 40°C over P <sub>2</sub> 0 <sub>5</sub> . Its mp was $254^{\circ}$ C (de-  |
| sintered glass disc. The percolation was  | compn). Cetomacrogol 1000 B.P.C. was of the  |
| continued until the soln was satd (5-6 days).   | same origin and was used as received. Tap wa-  |
| The concn of sulfadiazine was detd spectro-<br>photometrically from a calibration curve   | ter once distd from glass was used.  |
| using a Uvispek spectrophotometer (1).  | -  |
| using a ovisper spectrophotometer (1).  |  |
|   | ESTIMATED ERROR:<br>Soly: nothing specified.   |
|   | Temp: ±0.05°C (authors).   |
|   |  |
|   | REFERENCES:  |
|   | 1. Elworthy, P. H.; Lipscomb, F. J.  |
|   | J. Pharm. Pharmac. <u>1968</u> , 20, 790.  |
|   |  |
|   |  |
|   |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| <pre>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>0<sub>2</sub>S; [68-35-9]</pre>        | Corby, T. C.; Elworthy, P. H.<br>J. Pharm. Pharmac. <u>1971</u> , 23, Suppl. |
| <pre>(2) Poly(oxy-1,2-ethanediy1), α -hydro- ω -<br/>hydroxy- (PEG 1000); (C<sub>2</sub>H<sub>4</sub>0)<sub>n</sub>H<sub>2</sub>0;<br/>[25322-68-3] 1000</pre> | 395-485.   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:   |
|  | R. Piekos  |

| Concentration of PEG 1000 | Solubility of sulfadiazine at 20 <sup>0</sup> C |                      |  |
|---------------------------|---|----------------------|--|
| % w/v                     | mmol kg <sup>-1</sup> solvent                   | % by wt <sup>a</sup> |  |
| 10                        | 0.719   | 0.180                |  |
| 30                        | 2.11  | 0.525                |  |
| 50                        | 4.20  | 1.04                 |  |
| 50                        | 4.20  | 1.04                 |  |

<sup>a</sup> Calculated by compiler

| AUXILIARY  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:  |
|--|---|
| METHOD/APPARATUS/PROCEDURE:<br>The soly was detd in an app where the a-<br>queous soln of PEG 1000 was percolated<br>through a plug of sulfadiazine supported on<br>a 5/3 sintered glass disc. The percolation<br>was continued until the soln was satd (5 - 6<br>days). The concn of sulfadiazine was detd<br>spectrophotometrically from a calibration<br>curve using a Uvispek spectrophotometer (1). | Sulfadiazine (MaCarthy's Ltd, Romford) was<br>British Pharmacopeia product. It was recry-<br>std twice from a DMF-EtOH mixt (1:3) and<br>dried at $40^{\circ}$ C over P <sub>2</sub> 0 <sub>5</sub> . Its mp was 254°C<br>(decompn). PEG 1000 was a B.D.H. Laboratory<br>Reagent and was used as received. Tap water<br>once distd from glass was used. |
| ·  | ESTIMATED ERROR:<br>Soly: nothing specified.<br>Temp: ±0.05°C (authors).<br>REFERENCES:<br>1. Elworthy, P. H.; Lipscomb, F. J.<br>J. Pharm. Pharmac. <u>1968</u> , 20, 790.   |

#### COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-ORIGINAL MEASUREMENTS: pyrimidinyl- (sulfadiazine); Higuchi, T.; Lach, J. L. [68-35-9] C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S;

(2) 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (caffeine); C<sub>8</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>; [58-08-2] (3) Water; н<sub>2</sub>0; [7732-18-5]

J. Amer. Pharm. Assoc., Sci. Ed.

PREPARED BY:

<u>1954,</u> 43, 349-54.

VARIABLES:

Concentration of caffeine

R. Piekos

## EXPERIMENTAL VALUES:

Total solubility of sulfadiazine in water containing caffeine at  $30^{\circ}C$ 

| Caffeine                    | Sulfadiazi                  | ne                   | Caffeine                            | Sulfad                      | liazine              |
|-----------------------------|-----------------------------|----------------------|-------------------------------------|-----------------------------|----------------------|
| $10^2$ mol dm <sup>-3</sup> | $10^4$ mol dm <sup>-3</sup> | g dm <sup>-3 a</sup> | $10^2 \text{ mol } \text{dm}^{-3}$  | $10^4$ mol dm <sup>-3</sup> | g dm <sup>-3</sup> a |
| 0.000                       | 3.64                        | 0.091                | 10.470                              | 6.47                        | 0.162                |
| 1.454                       | 3.80                        | 0.095                | 10.742                              | 6.36                        | 0.159                |
| 1.467                       | 3.77                        | 0.094                | 12.410                              | 6.64                        | 0.166                |
| 3.716                       | 4.51                        | 0.113                | 12.865                              | 7.04                        | 0.176                |
| 3.728                       | 4.50                        | 0.113                | 14.556                              | 7.69                        | 0.192                |
| 5.285                       | 4.84                        | 0.121                | 14.957                              | 7.51                        | 0.188                |
| 5.964                       | 5.04                        | 0.126                | ······                              |                             |                      |
| 7.356                       | 5.32                        | 0.133                | <sup>a</sup> Calculated by compiler |                             |                      |
| 7.703                       | 5.55                        | 0.139                |                                     |                             |                      |

| AUXILIARY INFORMATION   |  |  |  |
|---|--|--|--|
| METHOD/APPARATUS/PROCEDURE:<br>Excess quantities of sulfadiazine (25 mg)<br>were placed in 125-ml glass-stoppered bot-<br>tles together with varying but accurately<br>weighed amts of caffeine and 50-ml portion of<br>water. The bottles were placed in a mech<br>shaker in a const temp bath and equilibrated<br>for 8 h at 30°C. Aliquots of the superna-<br>tant liquid were analyzed for the sulfadi- |  |  |  |
| azine content by the method of Bratton and<br>Marshall (1).   | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537. |  |  |

|   | I   |  |  |
|---|---|--|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |  |  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);</li> </ol>                                     | Nogami, H.; Nagai, T.; Suzuki, A.               |  |  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]  | Chem. Pharm. Bull. <u>1966</u> , 14(4),         |  |  |
| (2) α-D-Glucopyranoside, β-D-fructofuranos-<br>y1- (sucrose); C <sub>12</sub> H <sub>22</sub> O <sub>11</sub> ; [57-50-1] | 339-50.   |  |  |
| (3) Water; $H_20$ ; [7732-18-5]   |   |  |  |
|   |   |  |  |
| VARIABLES:  | PREPARED BY:                                    |  |  |
| Concentration of sucrose  | R. Piekos                                       |  |  |
| EXPERIMENTAL VALUES:  | L   |  |  |
| Concentration of sucrose  | Solubility of sulfadiazine at 37 <sup>0</sup> C |  |  |
| mol dm <sup>-3</sup>  | $mg/100 ml$ $10^4 mol dm^{-3} a$                |  |  |
|   |   |  |  |
| 10 <sup>-3</sup>  | 10.9 4.35                                       |  |  |
| 10 <sup>-2</sup>  | 11.0 4.39                                       |  |  |
| 10 <sup>-1</sup>  | 12.0 4.79                                       |  |  |
| 1   | 12.9 5.15                                       |  |  |
|   |   |  |  |
|   |   |  |  |
| AUXILIARY   | INFORMATION                                     |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                 |  |  |
| Soly of sulfadiazine was detd from dissoln  | Commercial sulfadiazine J. P. was used.         |  |  |
| rate data obtained by the rotating disk   | Purity of the remaining materials was not       |  |  |
| method.   | specified.                                      |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |
|   | ESTIMATED ERROR:                                |  |  |
|   | Nothing specified.                              |  |  |
|   |   |  |  |
|   | REFERENCES :                                    |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |

| 180   |   |  |
|---|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Paruta, A. N.;<br>Gerraughty, R. J. J. Pharm. Sci.<br><u>1972</u> , 61(1), 97-7. |  |
| (2) Methanol; CH <sub>4</sub> 0; [67-56-1]  |   |  |
| VARIABLES:  | PREPARED BY:  |  |
| Temperature   | R. Piekos   |  |
| EXPERIMENTAL VALUES:  |   |  |
|   |   |  |
| t/ <sup>o</sup> C Mole fracti   | on solubility (x 10 <sup>5</sup> )  |  |
| 25  | 19.3  |  |
| 30  | 22.9  |  |
| 37  | 29.9  |  |
|   |   |  |
|   |   |  |
|   |   |  |
|   |   |  |
|   |   |  |
|   |   |  |
| AUXILIA   | RY INFORMATION  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |  |
| A const temp bath contg screw-capped bott<br>with sulfadiazine in excess and methanol v   |   |  |
| rotated for 24 h. Samples were withdrawn  | Methanol was a spectrophotometric grade   |  |
| through a pledget of glass wool into a pip  |   |  |
| which was wiped clean and allowed to drain  | Works.  |  |
| into a volumetric flask. Solute concns we   | ere   |  |
| detd by spectrophotometric assay at predet  |   |  |
| wavelengths using a Cary model 16 spectro-  |   |  |
| photometer (1).   | ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).   |  |
|   | Temp: ±0.1 <sup>0</sup> C (authors).  |  |
|   | REFERENCES:   |  |
|   | <ol> <li>Paruta, A. N.; Mauger, J. W.</li> <li>J. Pharm. Sci. 1971, 60, 432.</li> </ol>                                   |  |
|   | <u>, , , , , , , , , , , , , , , , , , , </u>   |  |
|   |   |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</li> <li>Methanol; CH<sub>4</sub>O; [67-56-1]</li> </ol> | Mauger, J. W.; Petersen, H., Jr.<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),<br>163-83. |
| VARIABLES:<br>Temperature  | PREPARED BY:<br>R. Piekos  |

EXPERIMENTAL VALUES:

| t/ <sup>o</sup> C |       | Solubili                       | ty                                     |
|-------------------|-------|--------------------------------|--|
|                   | mg/ml | 10 <sup>5</sup> x <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3 b</sup> |
| 25                | 1.18  | 19.3                           | 4.71                                   |
| 30                | 1.40  | 22.9                           | 5.59                                   |
| 37                | 1.82  | 29.9                           | 7.27                                   |
|                   |       |                                |  |

<sup>a</sup> X = mole fraction

<sup>b</sup> Calculated by compiler

| AUXILIARY                                     | INFORMATION                                |
|---|--|
| ETHOD/APPARATUS/PROCEDURE:                    | SOURCE AND PURITY OF MATERIALS:            |
| A const temp bath contg screw-capped bottles  | Sulfadiazine: lot W02235, Eli Lilly and Co |
| with sulfadiazine in excess and methanol was  | Its mp agreed with the literature value.   |
| rotated for 24 h. Samples were withdrawn      | Methanol was a spectrograde solvent from   |
| through a pledget of glass wool into a pipet, | Mallinckrodt Chemical Works.               |
| which was wiped clean and allowed to drain    |  |
| into a volumetric flask. Soly was detd from   |  |
| absorbance and previously ascertained Beer's  |  |
| law plots detd on a Cary model 6 spectropho-  |  |
| tometer (1).                                  | ESTIMATED ERROR:                           |
|   | Soly: av of at least 3 detns is reported   |
|   | (authors).                                 |
|   | Temp: ±0.1 <sup>0</sup> C (authors).       |
|   | REFERENCES:                                |
|   | 1. Mauger, J.W.; Paruta, A. N.;            |
|   | Gerraughty, R. J. J. Pharm. Sci.           |
|   | <u>1972</u> , <i>61(1)</i> , 94.           |
|   |  |

| • | 188   |                                  |  |
|---|-------|----------------------------------|--|
|   | COMPO | NENTS:                           |  |
|   | (1)   | Benzenesulfonamide, 4-amino-N-2- |  |
|   |       | pyrimidinyl- (sulfadiazine);     |  |

ORIGINAL MEASUREMENTS: Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. J. Pharm. Sci. <u>1972</u>, 61(1), 94-7.

(2) Ethanol; C<sub>2</sub>H<sub>6</sub>0; [64-17-5]

C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]

| VARIABLES:  | PREPARED BY: |       |
|-------------|--------------|-------|
| Temperature | R. P         | lekos |

EXPERIMENTAL VALUES:

| t/ <sup>o</sup> C | Mole fraction solubility (x 10 <sup>5</sup> ) |
|-------------------|---|
| 25                | 7.68  |
| 30                | 9.36  |
| 37                | 12.4  |

| AUXILIARY   | INFORMATION   |
|---|---|
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfadiazine in excess and ethanol was<br>rotated for 24 h. Samples were withdrawn<br>through a pledget of glass wool into a pipet,<br>which was wiped clean and allowed to drain<br>into a volumetric flask. Solute concns were<br>detd by spectrophotometric assay at predetd<br>wavelengths using a Cary model 16 spectro- | SOURCE AND PURITY OF MATERIALS:<br>Sulfadiazine: lot W02235 from Eli Lilly<br>and Co.<br>Ethanol was from the U. S. Industrial<br>Chemicals Co.   |
| photometer (1).   | ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.<br>J. Pharm. Sci. <u>1971</u> , 60, 432. |

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| COMPONENTS:                                      |                    |             | ORIGINAL ME                    | ASUREMENTS .  |
|--|--------------------|-------------|--------------------------------|---|
| (1) Benzenesulfonamide,                          | 4-amino-N-         | -2-         |                                | ASUREMENTS:<br>J. W.; Petersen, H., Jr.;                              |
| <pre>pyrimidinyl- (sulfadiazine);</pre>          |                    |             | -                              | , K. S.; Paruta, A. N.  |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]                 |                    |             |                                | . Ind. Pharm. <u>1977</u> , 3(2),                                     |
| (2) Ethanol, C <sub>2</sub> H <sub>6</sub> 0;    |                    |             | 163-83.                        |   |
| (2) Lenanor, 32160,                              |                    |             |                                |   |
| VARIABLES:                                       |                    |             | PREPARED BY                    | :   |
| Temperature                                      |                    |             |                                | R. Piekos   |
| EXPERIMENTAL VALUES:                             |                    |             | I                              |   |
|  |                    |             |                                |   |
|  |                    |             |                                |   |
|  | .0                 | S           | olubility                      |   |
|  | t/ <sup>o</sup> C  | mg/ml       | 10 <sup>5</sup> x <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3</sup> b                                |
|  | 25                 | 0.33        | 7.68                           | 1.32  |
|  | 30                 | 0.40        | 9.36                           | 1.60  |
|  | 37                 | 0.53        | 12.40                          | 2.12  |
|  |                    |             |                                |   |
|  | a <sub>X =</sub>   | mole frac   | tion                           |   |
|  | <sup>b</sup> Calcu | ilated by c | ompiler                        |   |
|  |                    |             |                                |   |
|  |                    |             |                                |   |
|  |                    | AUXILIARY   | INFORMATION                    |   |
| METHOD/APPARATUS/PROCEDU                         |                    |             |                                | PURITY OF MATERIALS:  |
| A const temp bath cont<br>with sulfadiazine in e | -                  | -           | 1                              | ine: lot WO2235, Eli Lilly and Co.<br>reed with the literature value. |
| rotated for 24 h. Sam                            |                    |             |                                | as from the U.S. Industrial Chem-                                     |
| through a pledget of g                           |                    |             | 1                              | . Its refractive index value and                                      |
| pipet, which was wiped                           |                    |             | density a                      | greed with literature values.   |
| drain into a volumetric flask. Soly was          |                    |             |                                |   |
| detd from absorbance an                          | nd previous        | ly ascer-   |                                |   |
| tained Beer's law plot:                          | s detd on a        | a Cary Mo-  |                                |   |
| del 16 spectrophotomete                          | er (1).            |             | ESTIMATED E                    | ERROR:  |
|  |                    |             | 1                              | of at least 3 detns is reported                                       |
|  |                    |             | -                              | uthors).  |
|  |                    |             |                                | .1 <sup>o</sup> C (authors).  |
|  |                    |             | REFERENCES                     |   |
|  |                    |             | -                              | r, J. W.; Paruta, A. N.   |
|  |                    |             |                                | ughty, R. J. J. Pharm. Sci.<br>61(1), 94.                             |
|  |                    |             | <u>1972,</u>                   | . 74.   |
|  |                    |             |                                |   |

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| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       | Mauger, J. W.; Paruta, A. N.;  |
| pyrimidinyl- (sulfadiazine);   | Gerraughty, R. J. J. Pharm. Sci.   |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | <u>1972,</u> 61(1), 94-7.  |
| (2) 1-Propanol; $C_{3}H_{8}O;$ [71-23-8]                                   | <u>19729</u> 01(17) 9407.  |
| (2) 1-110pano1, 03ng0, $[71-25-0]$   |  |
| VARIABLES:   | PREPARED BY:   |
| Temperature  | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
|  | on solubility ( X 10 <sup>5</sup> )  |
| 25   | 4.32   |
| 30   | 5.45   |
| 37   | 7.44   |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
| AUXILIARY  | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS;  |
| A const temp bath contg screw-capped bottle                                |  |
| with excess and 1-propanol was rotated for                                 |  |
| 24 h. Samples were withdrawn through a                                     | 1-Propanol was a Baker Analyzed Reagent  |
| pledget of glass wool into a pipet, which                                  | from J. T. Baker Chemical Co.  |
| was wiped clean and allowed to drain into                                  |  |
| a volumetric flask. Solute concns were                                     |  |
| detd by spectrophotometric assay at predete                                | 4  |
| wavelengths using a Cary model 16 spectro-                                 |  |
| photometer (1).  | ESTIMATED ERROR:   |
|  | Soly: av values of 3 runs are given  |
|  | (authors).   |
|  | Temp: ±0.1 <sup>0</sup> C (authors).   |
|  | REFERENCES:  |
|  | <ol> <li>Paruta, A. N.; Mauger, J. W.</li> <li>J. Pharm. Sci. <u>1971</u>, 60, 432.</li> </ol> |
|  |  |

| COMPONE  | NTS:  |                   |                              |                   | ORIGINAL MEAS                  | UREMENTS :                       |                   |       |
|--|---|-------------------|------------------------------|-------------------|--------------------------------|----------------------------------|-------------------|-------|
| (1) Benzenesulfonamide, 4-amino-N-2-   |   |                   |                              |                   |                                | W.; Petersen                     | , H., Jr.,        |       |
| pyrimidinyl- (sulfadiazine);   |   |                   |                              |                   | Alexander, H                   | K. S.; Paruta                    | , A. N.           |       |
| С  | 10 <sup>H</sup> 10 <sup>N</sup> 4 <sup>0</sup> 2 <sup>S</sup> | ; [68-            | -35-9]                       |                   | Drug Dev.                      | Ind. Pharm.                      | <u>1977</u> , 3(2 | 2),   |
|  |   |                   | ); [71-23-8                  | 31                | 163-83.                        |                                  |                   |       |
| (-) _  |   | -3-8              | , [ <i>i</i> =               |                   |                                |                                  |                   |       |
| VARIABL  | ES:   |                   |                              |                   | PREPARED BY:                   |                                  |                   |       |
|  | Tempe   | rature            |                              |                   | R. Piekos                      |                                  |                   |       |
| EXPERIM  | ENTAL VALU  | ES:               |                              |                   |                                | <u> </u>                         |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   | t/ <sup>o</sup> C |                              | Solub             | ility                          |                                  |                   |       |
|  |   |                   | mg/ml                        | 10 <sup>5</sup> X | ( <sup>a</sup> 10 <sup>4</sup> | mol dm <sup>-3 b</sup>           |                   |       |
|  |   | 25                | 0.14                         | 4.32              | ! !                            | 5.59                             |                   |       |
|  |   | 30                | 0.18                         | 5.45              | ;                              | 7.19                             |                   |       |
|  |   | 37                | 0.25                         | 7.44              | • !                            | 9.99                             |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   | <sup>a</sup> x =  | mole fraction                | on                |                                |                                  |                   | •     |
|  |   | Þ. c. 1.          | culated by c                 |                   |                                |                                  |                   |       |
|  |   | Cal               | culated by c                 | ompiler           |                                |                                  |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   |                   |                              | AUXILIARY         | INFORMATION                    |                                  |                   |       |
|  | APPARATUS/  |                   |                              | - 1 1 - 4 4 1 - 4 | 1                              | URITY OF MATER<br>e: lot WO2235, |                   | ad Co |
|  |   |                   | g screw-capp                 |                   |                                | e: 10t w02233,<br>ed with the li |                   |       |
|  |   |                   | scess and 1-;<br>Samples wer |                   |                                | was a Baker An                   |                   |       |
|  |   |                   | -                            |                   |                                | r Chemical Co.                   |                   |       |
|  | -   |                   | t of glass w                 |                   |                                | and density a                    |                   |       |
| a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Soly was |   |                   | ture values                  |                   |                                |                                  |                   |       |
|  |   |                   | nd previously                | -                 |                                |                                  |                   |       |
|  |   |                   | s detd on a (                | •                 |                                |                                  |                   |       |
|  | .6 spectrop   | -                 |                              | <b>,</b>          | ESTIMATED ER                   |                                  |                   |       |
|  |   |                   |                              |                   |                                | f at least 3 d                   | letns is repor    | rted  |
|  |   |                   |                              |                   |                                | hors).                           | -                 |       |
|  |   |                   |                              |                   |                                | <sup>o</sup> C (authors).        |                   |       |
|  |   |                   |                              |                   | REFERENCES:                    |                                  | -                 |       |
|  |   |                   |                              |                   | 1. Mauger,                     | J. W.; Parut                     | a, A. N.;         |       |
|  |   |                   |                              |                   | Gerraug                        | hty, R. J. J                     | . Pharm. So       | ci.   |
|  |   |                   |                              |                   | <u>1972,</u>                   | 61(1), 94.                       |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |
|  |   |                   |                              |                   |                                |                                  |                   |       |

| 192  |  |
|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-<br>pyrimidiny1- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]<br>(2) 2-Propano1; C <sub>3</sub> H <sub>8</sub> 0; [67-63-0]  | ORIGINAL MEASUREMENTS:<br>Burlage, H. M.<br>J. Am. Pharm. Assoc., Sci. Ed.<br>1948, 37, 345.   |
| VARIABLES:<br>One temperature: 25 <sup>0</sup> C   | PREPARED BY:<br>R. Piekos  |
| EXPERIMENTAL VALUES:<br>Solubility of sulfadiazine in 2-propano<br>solution ( 1.72 x 10 <sup>-3</sup> mol dm <sup>-3</sup> , comp  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns of sulfadiazine in 2-propanol<br>were prepd at 25°C and definite vols of the<br>solns were measured into tared dishes by<br>means of standard pipets. The alcohol was<br>allowed to evap at room temp and the resi-<br>due was dried at 105°C. In the case of<br>losses due to apparent decompn, the residue<br>was dried in a desiccator (1). | SOURCE AND PURITY OF MATERIALS:<br>The sulfadiazine was manufd by Squibb and<br>was of the U.S.P. purity. The source and<br>purity of 2-propanol were not specified. |
|  | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Burlage, H. M.<br>J. Am. Pharm. Assoc., Sci. Ed.<br><u>1947</u> , 36(1), 16.                             |

| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl- (sulfadiazine);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>0<sub>2</sub>S; [68-35-9]</li> <li>(2) 1-Butanol; C<sub>4</sub>H<sub>10</sub>0; [71-36-3]</li> <li>VARIABLES:<br/>Temperature</li> <li>Mauger, J. W.; Paruta, A. N.;<br/>Gerraughty, R. J. J. Pharm. Sci.<br/>1972, 61(1), 94-7.</li> </ul>  | 001/001/01/01  |                                      |
|--|--|--------------------------------------|
| Auger, J. W. Frauda, A. W.;<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]<br>(2) 1-Butanol; C <sub>4</sub> H <sub>10</sub> O; [71-36-3]<br>VARIABLES:<br>Temperature<br>EXPERIMENTAL VALUES:   | COMPONENTS:  | ORIGINAL MEASUREMENTS:               |
| C10H10V4025:       (68-35-9)         (2) 1-Butanol; C4H100; (71-36-3)       (97-36-3)         VARIABLES:       R. Piekos         Temperature       R. Piekos         EXPERIMENTAL VALUES:       R. Piekos         EXPERIMENTAL VALUES:       25         25       3.18         30       4.09         37       5.66         ENTHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS;         A const temp bath contg screw-capped bottles       SUICE AND PURITY OF MATERIALS;         Variant through a pledget of glass wool into       and co.         1-Butanol into a volumetric flask. Solute       Soluce Stromether is assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         16 spectrophotometer (1).       Solute Stromes).         REFERENCES:       I. Paruta, A. N.; Mauger, J. W.  |  | Mauger, J. W.; Paruta, A. N.;        |
| (2) 1-Butanol; C <sub>4</sub> U <sub>10</sub> 0; [71-36-3]         VARIABLES:         Temperature         R. Piekos         EXPERIMENTAL VALUES:         EXPERIMENTAL VALUES:         t/°C       Mole fraction solubility (x 10 <sup>5</sup> )         25       3.18         30       4.09         37       5.66         EXPERIMENTAL VALUES:         AUXILIARY INFORMATION         RETROD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles         with sulfadiazine in excess and 1-butanol         was rotated for 24 h. Samples were with-         drawn through a pledget of glass wool into         a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute         Conces were lead by spectrophotometer (1).         ESTIMATED ERROR:         Soly: av values of 3 runs are given (authors).         REFERENCES:         1. Paruta, A. N.; Mauger, J. W.  | -  | Gerraughty, R. J. J. Pharm. Sci.     |
| VARIABLES:<br>Temperature PREPARED BY: R. Piekos EXPERIMENTAL VALUES:  | $c_{10}H_{10}N_4O_2S;$ [68-35-9]                           | <u>1972</u> , <i>61(1)</i> , 94-7.   |
| R. Piekos         EXPERIMENTAL VALUES:         Importance of the solubility (x 10 <sup>5</sup> )         25         3.18         30         AUXILLARY INFORMATION         Solution of the solubility (x 10 <sup>5</sup> )         25         37         Solution of the solut            | (2) 1-Butanol; C <sub>4</sub> H <sub>10</sub> 0; [71-36-3] |                                      |
| R. Piekos         EXPERIMENTAL VALUES:         Importance of the solubility (x 10 <sup>5</sup> )         25         3.18         30         AUXILLARY INFORMATION         Solution of the solubility (x 10 <sup>5</sup> )         25         37         Solution of the solut            |  |                                      |
| EXPERIMENTAL VALUES:         t/°C       Mole fraction solubility (x 10 <sup>5</sup> )         25       3.18         30       4.09         37       5.66         MUTILIARY INFORMATION         SUBJECTION COLDIES:         A const temp bath contg screw-capped bottles         SUBJECTION COLDIES:   | VARIABLES:   | PREPARED BY:                         |
| t/°C       Mole fraction solubility (x 10 <sup>5</sup> )         25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         RETHOD/APPARATUS/FROCEDURE:         A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-butanol Was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped cleen and allowed to drain into a volumetric flask. Solute concess were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).       Soly: av values of 3 runs are given (authors).         ESTIMATED ERROR:       I. Paruta, A. N.; Mauger, J. W.   | Temperature  | R. Piekos                            |
| t/°C       Mole fraction solubility (x 10 <sup>5</sup> )         25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         RETHOD/AFPARATUS/FROCEDURE:         A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-butanol Was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped cleen and allowed to drain into a volumetric flask. Solute concess were detd by spectrophotometric assay at predetd wavelengths using a Cary model l6 spectrophotometer (1).       SOURCE AND FURITY OF MATERIALS: Sulfadiazine: lot W02235 from Eli Lilly and Co.         ISURGE SCIENCE:         Source AND PURITY OF MATERIALS:         Sulfadiazine: lot W02235 from Eli Lilly and Co.         ISURATION Was from the Mallinckrodt Chemical Works.         Soly: av values of 3 runs are given (authors).         Temp: 5.01°C (authors).         REFERENCES:         I. Paruta, A. N.; Mauger, J. W.  |  |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles         with sulfadiazine in excess and 1-butanol         was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Solute<br>Concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model       SOURCE AND PURITY OF MATERIALS:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).         REFERENCES:       1. Paruta, A. N.; Mauger, J. W.   | EXPERIMENTAL VALUES:                                       |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles         with sulfadiazine in excess and 1-butanol         Was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Solute<br>Concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model       SOURCE AND PURITY OF MATERIALS:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: 10.1 <sup>Q</sup> C (authors).         FEFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles       SOURCE AND PURITY OF MATERIALS:         Source AND PURITY OF MATERIALS:       Sulfadiazine: lot W02235 from Eli Lilly and Co.         uss rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute Concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model       Io Super Third DERROR: Soly: av values of 3 runs are given (authors).         I6 spectrophotometer (1).       REFERENCES:       I. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles       SOURCE AND PURITY OF MATERIALS:         Source AND PURITY OF MATERIALS:       Sulfadiazine: lot W02235 from Eli Lilly and Co.         Was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute Concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model       Io String a Cary model         I6 spectrophotometer (1).       ESTIMATED ERROR: Soly: av values of 3 runs are given (authors).       Soly: av values of 3 runs are given (authors).         REFERENCES:       1. Paruta, A. N.; Mauger, J. W.       REFERENCES:   |  |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles       SOURCE AND PURITY OF MATERIALS:         Source AND PURITY OF MATERIALS:       Sulfadiazine: lot W02235 from Eli Lilly and Co.         Was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute Concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model       Io String a Cary model         I6 spectrophotometer (1).       ESTIMATED ERROR: Soly: av values of 3 runs are given (authors).       Soly: av values of 3 runs are given (authors).         REFERENCES:       1. Paruta, A. N.; Mauger, J. W.       REFERENCES:   |  |                                      |
| 25       3.18         30       4.09         37       5.66         AUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         A const temp bath contg screw-capped bottles       SOURCE AND PURITY OF MATERIALS:         Source AND PURITY OF MATERIALS:       Sulfadiazine: lot W02235 from Eli Lilly and Co.         Was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute Concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model       Io String a Cary model         I6 spectrophotometer (1).       ESTIMATED ERROR: Soly: av values of 3 runs are given (authors).       Soly: av values of 3 runs are given (authors).         REFERENCES:       1. Paruta, A. N.; Mauger, J. W.       REFERENCES:   |  |                                      |
| 30       4.09         37       5.66         MUXILIARY INFORMATION         MUXILIARY INFORMATION         Source and Purity OF MATERIALS:         A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-butanol was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a volumetric flask. Solute Conens were detd by spectrophotometric assay at predetd wavelengths using a Cary model l6 spectrophotometer (1).       Source AND PURITY OF MATERIALS: Sulfadiazine: lot W02235 from Eli Lilly and Co.         ESTIMATED ERROR:         Soly: av values of 3 runs are given (authors).         Temp: ±0.1°C (authors).         REFERENCES:         1. Faruta, A. N.; Mauger, J. W.  | t/ <sup>0</sup> C Mole frac                                | tion solubility (x 10 <sup>5</sup> ) |
| 30       4.09         37       5.66         MUXILIARY INFORMATION <b>AUXILIARY INFORMATION SURCE AND PURITY OF MATERIALS:</b> A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-butanol was rotated for 24 h. Samples were with-drawn through a pledget of glass wool into a spiet, which was wiped clean and allowed to drain into a volumetric flask. Solute Conens were detd by spectrophotometric assay at predetd wavelengths using a Cary model l6 spectrophotometer (1).       Source AND PURITY OF MATERIALS: Soly: Soly: av values of 3 runs are given (authors). Temp: ±0.1°C (authors). <b>ESTIMATED ERKOR:</b> Soly: av values of 3 runs are given (authors).         Temp: ±0.1°C (authors). <b>REFERENCES:</b> 1. Paruta, A. N.; Mauger, J. W.  |  |                                      |
| 37       5.66         MUXILIARY INFORMATION         METHOD/APPARATUS/PROCEDURE:         SOURCE AND PURITY OF MATERIALS:         Source And Purity OF MATERIALS:         Sulfadiazine: lot W02235 from Eli Lilly and Co.         House wore with-drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concess were detd by spectrophotometric assay at predetd wavelengths using a Cary model lo spectrophotometer (1).       SUITATED ERROR: Soly: av values of 3 runs are given (authors).         ESTIMATED ERROR: Soly: av values of 3 runs are given (authors).         REFERENCES:         I. Paruta, A. N.; Mauger, J. W.  | 25   | 3.18                                 |
| AUXILIARY INFORMATION<br>METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfadiazine in excess and 1-butanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Solute<br>concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model<br>16 spectrophotometer (1).<br>ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.  | 30   | 4.09                                 |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       Weight of the second sec | 37   | 5.66                                 |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       Soly: av values of 3 runs are given (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       I-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       I-Butanol was from the Mallinckrodt Chem-         a pipet, which was wiped clean and allowed       to drain into a volumetric flask. Solute         concns were detd by spectrophotometric assay       at predetd wavelengths using a Cary model         16 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         1. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       I-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       I-Butanol was from the Mallinckrodt Chem-         a pipet, which was wiped clean and allowed       to drain into a volumetric flask. Solute         concns were detd by spectrophotometric assay       at predetd wavelengths using a Cary model         16 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         1. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       I-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       I-Butanol was from the Mallinckrodt Chem-         a pipet, which was wiped clean and allowed       to drain into a volumetric flask. Solute         concns were detd by spectrophotometric assay       at predetd wavelengths using a Cary model         16 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         1. Paruta, A. N.; Mauger, J. W.       W.   |  | •                                    |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       Soly: av values of 3 runs are given (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       Soly: av values of 3 runs are given (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       W.  |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       a pipet, which was wiped clean and allowed         to drain into a volumetric flask. Solute       Concns were detd by spectrophotometric assay         at predetd wavelengths using a Cary model       ESTIMATED ERROR:         l6 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         l. Paruta, A. N.; Mauger, J. W.       Weight of the second sec |  |                                      |
| METHOD/APPARATUS/PROCEDURE:       SOURCE AND PURITY OF MATERIALS:         A const temp bath contg screw-capped bottles       Sulfadiazine: lot W02235 from Eli Lilly         with sulfadiazine in excess and 1-butanol       and Co.         was rotated for 24 h. Samples were with-       1-Butanol was from the Mallinckrodt Chem-         drawn through a pledget of glass wool into       1-Butanol was from the Mallinckrodt Chem-         a pipet, which was wiped clean and allowed       to drain into a volumetric flask. Solute         concns were detd by spectrophotometric assay       at predetd wavelengths using a Cary model         16 spectrophotometer (1).       ESTIMATED ERROR:         Soly: av values of 3 runs are given       (authors).         Temp: ±0.1°C (authors).       REFERENCES:         1. Paruta, A. N.; Mauger, J. W.       W.   |  |                                      |
| A const temp bath contg screw-capped bottles<br>with sulfadiazine in excess and 1-butanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Solute<br>concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model<br>16 spectrophotometer (1).  | AUXILIAR   | Y INFORMATION                        |
| A const temp bath contg screw-capped bottles<br>with sulfadiazine in excess and 1-butanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Solute<br>concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model<br>16 spectrophotometer (1).  | METHOD /ADDADATUS /DDOCEDUDE                               | COURCE AND BUDTTY OF MATERIALC.      |
| <pre>with sulfadiazine in excess and 1-butanol was rotated for 24 h. Samples were with- drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1). ESTIMATED ERROR: Soly: av values of 3 runs are given</pre>   |  |                                      |
| <pre>was rotated for 24 h. Samples were with-<br/>drawn through a pledget of glass wool into<br/>a pipet, which was wiped clean and allowed<br/>to drain into a volumetric flask. Solute<br/>concns were detd by spectrophotometric assay<br/>at predetd wavelengths using a Cary model<br/>16 spectrophotometer (1).</pre> ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| <pre>drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model l6 spectrophotometer (1). ESTIMATED ERROR: Soly: av values of 3 runs are given</pre>  |  |                                      |
| <pre>a pipet, which was wiped clean and allowed<br/>to drain into a volumetric flask. Solute<br/>concns were detd by spectrophotometric assay<br/>at predetd wavelengths using a Cary model<br/>16 spectrophotometer (1).<br/>ESTIMATED ERROR:<br/>Soly: av values of 3 runs are given<br/>(authors).<br/>Temp: ±0.1°C (authors).<br/>REFERENCES:<br/>1. Paruta, A. N.; Mauger, J. W.</pre>  | · · ·  |                                      |
| to drain into a volumetric flask. Solute<br>concns were detd by spectrophotometric assay<br>at predetd wavelengths using a Cary model<br>16 spectrophotometer (1).<br>ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  | Ical Works.                          |
| <pre>concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model l6 spectrophotometer (1). ESTIMATED ERROR: Soly: av values of 3 runs are given</pre>   |  |                                      |
| at predetd wavelengths using a Cary model<br>16 spectrophotometer (1).<br>ESTIMATED ERROR:<br>Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| <pre>16 spectrophotometer (1). 16 spectrophotometer (1). ESTIMATED ERROR: Soly: av values of 3 runs are given</pre>  | 1  | <sup>1</sup> y                       |
| Soly: av values of 3 runs are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| (authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   | 10 spectrophotometer (1).                                  |                                      |
| Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   |  |                                      |
| REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.   | · ·  |                                      |
|  | 1  |                                      |
|  |  | 1. Paruta, A. N.; Mauger, J. W.      |
|  |  |                                      |
|  | 1  |                                      |
|  | 1  |                                      |
|  |  |                                      |

| COMP                                 | ONENTS:  |                                       |                                    | ORIGINAL N                        | ÆASUREMENTS :  |       |
|--------------------------------------|--|---------------------------------------|------------------------------------|-----------------------------------|--|-------|
| (1) Benzenesulfonamide, 4-amino-N-2- |  |                                       |                                    | Mauger, J. W.; Petersen, H., Jr.; |  |       |
|                                      | pyrimidinyl-   |                                       |                                    | 1 -                               | r, K. S.; Paruta, A. N.  |       |
|                                      | c <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> s; | [68-35-9                              | ]                                  | Drug De                           | v. Ind. Pharm. <u>1977,</u> 3(2                                | 2),   |
| (2)                                  | 1-Butanol;   | C <sub>4</sub> H <sub>10</sub> 0;     | [71-36-3]                          | 163-83.                           |  |       |
| VARI                                 | ABLES:   |                                       |                                    | PREPARED                          |  |       |
|                                      | Temper   | ature                                 |                                    |                                   | R. Piekos  |       |
| EXPE                                 | RIMENTAL VALU  | ES:                                   |                                    |                                   |  |       |
|                                      |  |                                       |                                    |                                   |  |       |
|                                      |  | t/ <sup>o</sup> C                     |                                    | Solubility                        |  |       |
|                                      |  |                                       | mg/ml                              | 10 <sup>5</sup> x <sup>a</sup>    | $10^4$ mol dm <sup>-3</sup> a                                  |       |
|                                      |  | 25                                    | 0.087                              | 3.18                              | 3.48   |       |
|                                      |  | 30                                    | 0.111                              | 4.09                              | 4.43   |       |
|                                      |  | 37                                    | 0.153                              | 5.66                              | 6.11   |       |
|                                      |  | a x                                   | mole fraction                      |                                   |  |       |
|                                      |  | <sup>b</sup> Cal                      | culated by compil                  | ler                               |  |       |
|                                      |  |                                       |                                    |                                   |  |       |
|                                      |  | · · · · · · · · · · · · · · · · · · · | AUXILIARY                          | INFORMATIC                        | DN   |       |
|                                      | HOD/APPARATUS/   |                                       |                                    | 1                                 | D PURITY OF MATERIALS:   |       |
|                                      | -  |                                       | ew-capped bottles<br>and 1-butanol |                                   | zine: lot W02235, Eli Lilly a                                  |       |
|                                      |  |                                       | les were with-                     | -                                 | greed with the literature val<br>1 was from the Mallinckrodt ( |       |
|                                      |  | •                                     | glass wool into                    |                                   | Its refractive index value an                                  |       |
|                                      | _  |                                       | ean and allowed                    | density                           | agreed with literature values                                  | 5.    |
| to                                   | drain into a   | volumetric                            | flask. Soly was                    |                                   |  |       |
|                                      |  |                                       | eviously ascer-                    |                                   |  |       |
|                                      |  |                                       | d on a Cary mo-                    |                                   |  |       |
| de.                                  | l 16 spectroph   | otometer (J                           | .).                                | ESTIMATED                         | ) ERROR:<br>v of at least 3 detns is repo                      | orted |
|                                      |  |                                       |                                    | 1 -                               | authors).  |       |
|                                      |  |                                       |                                    | -                                 | 0.1 <sup>o</sup> C (authors).                                  |       |
|                                      |  |                                       |                                    | REFERENCE                         | S:   |       |
| Į                                    |  |                                       |                                    | 1 -                               | r, J. W.; Paruta, A. N.;                                       | ~ ·   |
| 1                                    |  |                                       |                                    | 1                                 | ughty, R. J. J. Pharm. 5<br>61(1), 94.                         | 501.  |
|                                      |  |                                       |                                    | <u>1772</u> ,                     | 01(1/3 )7.   |       |
|                                      |  |                                       |                                    |                                   |  |       |

| COMPONENTS :   | OPICINAL AT CURRENTING                                      |
|--|---|
| (1) Benzanesulfonamide, 4-amino-N  | ORIGINAL MEÀSUREMENTS:<br>-2- Mauger, J. W.; Paruta, A. N.; |
| pyrimidinyl- (sulfadiazine)  |   |
|  | 1972, 61(1), 94-7.  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |   |
| (2) 1-Pentanol; C <sub>5</sub> H <sub>12</sub> 0; [71-41                   | -0]   |
|  |   |
| VARIABLES:   | PREPARED BY:  |
| Temperature  | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
|  |   |
|  |   |
|  |   |
|  |   |
|  | 5.  |
| t/ <sup>o</sup> C  | Mole fraction solubility ( x 10 <sup>5</sup> )              |
| 25   | 2.63  |
| 30   | 3.31  |
|  |   |
| 37   | 4.61  |
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|  | AUXILIARY INFORMATION                                       |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                             |
| A const temp bath contg screw-cap  |   |
| with sulfadiazine in excess and 1  |   |
| was rotated for 24 h. Samples we   |   |
| drawn through a pledget of glass   |   |
| a pipet, which was wiped clean an  |   |
| to drain into a volumetric flask.  |   |
| concus were detd by spectrophotom  |   |
| at predetd wavelengths using a C   |   |
| 16 spectrophotometer (1).  |   |
| spectrophotometer (1).   | ESTIMATED ERROR:<br>Soly: av values of 3 runs are given     |
|  |   |
|  | (authors).  |
|  | Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:         |
|  |   |
| 1  | 1. Paruta, A. N.; Mauger, J. W.                             |
|  | J. Pharm. Sci. <u>1971</u> , 60, 432.                       |
|  |   |
|  |   |
|  |   |

| 196          |  |                    |
|--------------|--|--------------------|
| COMP(<br>(1) | NENTS:<br>Benzenesulfona   | mide, 4-amino-N-2- |
|              | pyrimidinyl-   | (sulfadiazine);    |
|              | c <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> s; | [68-35-9]          |

(2) 1-Pentanol; C<sub>5</sub>H<sub>12</sub>0; [71-41-0]

ORIGINAL MEASUREMENTS: Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. Drug Dev. Ind. Pharm. <u>1977</u>, 3(2), 163-83.

R. Piekos

PREPARED BY:

Temperature

EXPERIMENTAL VALUES:

VARIABLES:

|   | t/ <sup>o</sup> C | Solubility |  |                                     |  |
|---|-------------------|------------|--|-------------------------------------|--|
|   |                   | mg/ml      | 10 <sup>5</sup> x <sup>a</sup> 10 <sup>6</sup> | <sup>4</sup> mol dm <sup>-3</sup> b |  |
| - | 25                | 0.061      | 2.63   | 2.437                               |  |
|   | 30                | 0.076      | 3.31   | 3.036                               |  |
|   | 37                | 0.106      | 4.61   | 4.235                               |  |
|   |                   |            |  |                                     |  |

a X = mole fraction

<sup>b</sup> Calculated by compiler

| AUXILIARY INFORMATION                        |  |  |  |
|--|--|--|--|
| METHOD / APPARATUS / PROCEDURE :             | SOURCE AND PURITY OF MATERIALS;                              |  |  |
| A const temp bath contg screw-capped bottles | Sulfadiazine: lot WO2235, Eli Lilly and Co.                  |  |  |
| with sulfadiazine in excess and 1-pentanol   | Its mp agreed with the literature value.                     |  |  |
| was rotated for 24 h. Samples were with-     | 1-Pentanol was from Fisher Scientific Co.                    |  |  |
| drawn through a pledget of glass wool into a | Its refractive index value and density                       |  |  |
| pipet, which was wiped clean and allowed to  | agreed with literature values.                               |  |  |
| drain into a volumetric flask. Soly was      |  |  |  |
| detd from absorbance and previously ascer-   |  |  |  |
| tained Beer's law plots detd on a Cary mo-   |  |  |  |
| del 16 spectrophotometer (1)                 | ESTIMATED ERROR:<br>Soly: av of at least 3 detns is reported |  |  |
|  | (authors).   |  |  |
|  | Temp: 0.1 <sup>0</sup> C (authors).                          |  |  |
|  | REFERENCES:  |  |  |
|  | 1. Mauger, J. W.; Paruta, A. N.;                             |  |  |
|  | Gerraughty, R. J. J. Pharm. Sci.                             |  |  |
|  | <u>1972</u> , 61(1), 94                                      |  |  |
|  |  |  |  |
|  |  |  |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-2-  | Mauger, J. W.; Paruta, A. N.;            |
| pyrimidinyl- (sulfadiazine);  | Gerraughty, R. J. J. Pharm. Sci.         |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]              | <u>1972</u> , 61(1), 94-7.               |
| (2) 1-Octanol; C <sub>8</sub> H <sub>18</sub> O; [111-87-5]                             |  |
|   |  |
| VARIABLES:  | PREPARED BY:<br>R. Piekos                |
| Temperature   | K. Flekos                                |
| EXPERIMENTAL VALUES:  |  |
| t/ <sup>0</sup> C Mole fract:   | ion solubility (x 10 <sup>5</sup> )      |
| 25  | 1.41                                     |
| 30  | 1.76                                     |
| 37  | 2.65                                     |
|   |  |
| AUXILIARY   | INFORMATION                              |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:          |
| A const temp bath contg screw-capped bottles  |  |
| with sulfadiazine in excess and 1-octanol   | and Co.                                  |
| was rotated for 24 h. Samples were with-  | 1-Octanol was from Mallinckrodt Chemical |
| drawn through a pledget of glass wool into  | Works.                                   |
| a pipet , which was wiped clean and allowed<br>to drain into a volumetric flask. Solute |  |
| concns were detd by spectrophotometric assay  |  |
| at predetd wavelengths using a Cary model   |  |
| 16 spectrophotometer (1).   | ESTIMATED ERROR:                         |
|   | Soly: av values of 3 runs are given      |
|   | (authors).                               |
|   | Temp: ±0.1 <sup>0</sup> C (authors).     |
|   | REFERENCES:                              |
|   | 1. Paruta, A. N.; Mauger, J. W.          |
|   | J. Pharm. Sci. <u>1971</u> , 60, 432.    |
|   |  |
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ENTS: enzenesulfonamide, 4-amir

| COMPONENTS:  |   |                      | ORIGINAL MEASUREMENTS:  |  |  |
|--|---|----------------------|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       |   |                      | Mauger, J. W.; Petersen, H., Jr.;                               |  |  |
| pyrimidinyl- (sulfadiazine);   |   |                      | Alexander, K. S.; Paruta, A. N.                                 |  |  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] |   |                      | Drug Dev. Ind. Pharm. <u>1977</u> , 3(2),                       |  |  |
|  |   |                      | 163-83.   |  |  |
| (2) 1-06   | anol; C <sub>8</sub> H <sub>18</sub> 0; | [111-8/-5]           |   |  |  |
| VARIABLES:   |   |                      | PREPARED BY:  |  |  |
|  | Temperature                             |                      | R. Piekos   |  |  |
| EXPERIMENT   | AL VALUES:                              | ·····                |   |  |  |
|  |   |                      |   |  |  |
|  |   |                      |   |  |  |
|  | t/ <sup>o</sup> C                       | Solu                 | bility  |  |  |
|  |   | mg/ml 1              | $10^5  \mathrm{x}^{a}  10^4  \mathrm{mol}  \mathrm{dm}^{-3  a}$ |  |  |
|  | 25                                      | 0.022                | 0.879   |  |  |
|  | 30                                      | 0.028 1              | 1.76 1.118  |  |  |
|  | 37                                      | 0.042 2              | 2.65 1.678  |  |  |
|  |   |                      |   |  |  |
|  | a <sub>x =</sub>                        | mole fraction        |   |  |  |
| <sup>b</sup> Calculated by compiler  |   |                      |   |  |  |
| calculated by compiler   |   |                      |   |  |  |
|  |   |                      |   |  |  |
|  |   |                      |   |  |  |
|  | ••••••••••••••••••••••••••••••••••••••  | <u> </u>             | INFORMATION   |  |  |
|  | ARATUS / PROCEDURE                      |                      | SOURCE AND PURITY OF MATERIALS:                                 |  |  |
|  | -                                       | screw-capped bottles |   |  |  |
|  |   | ess and 1-octanol    | Its mp agreed with the literature value.                        |  |  |
|  |   | amples were with-    | 1-Octanol was from Fisher Scientific Co.                        |  |  |
| 1  |   | of glass wool into   | Its refractive index and density agreed with                    |  |  |
|  | -                                       | clean and allowed    | literature values.  |  |  |
|  |   | ic flask. Soly was   |   |  |  |
|  |   | previously ascer-    |   |  |  |
|  | -                                       | detd on a Cary mo-   | ESTIMATED ERROR:  |  |  |
| del 16 sp  | ectrophotometer                         | (1).                 | Soly: av of at least 3 detns is reported                        |  |  |
|  |   |                      | (authors).  |  |  |
|  |   |                      | Temp: ±0.1 <sup>0</sup> C (authors).                            |  |  |
| 1  |   |                      | REFERENCES:   |  |  |
|  |   |                      | 1. Mauger, J. W.; Paruta, A. N.;                                |  |  |
|  |   |                      | Gerraughty, R. J. J. Pharm. Sci.                                |  |  |
|  |   |                      | <u>1972,</u> <i>61(1)</i> , 94.                                 |  |  |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                             |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-</li> </ol>                       | Mauger, J. W.; Paruta, A. N.;                      |
| pyrimidinyl- (sulfadiazine);   | Gerraughty, R. J. J. Pharm. Sci.                   |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | <u>1972</u> , <i>61(1)</i> , 94-7.                 |
| (2) 1-Decanol; C <sub>10</sub> H <sub>2</sub> 0; [112-30-1]                |  |
| 10 2 7 1   |  |
| VARIABLES:   | PREPARED BY:                                       |
| Temperature  | R. Piekos  |
| Purpose and the second   |  |
| EXPERIMENTAL VALUES:   |  |
|  |  |
|  |  |
| t/ <sup>0</sup> C Mole fraction  | solubility ( $x \ 10^5$ )                          |
| 25   | 7.40   |
| 30   | 8.04   |
| 37   | 9.47   |
| 5,   | J • 47   |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                    |
| A const temp bath contg screw-capped bottles                               |  |
| with sulfadiazine in excess and 1-decanol                                  | and Co.  |
| was rotated for 24 h. Samples were with-                                   | 1-Decanol was from Matheson, Coleman and           |
| drawn through a pledget of glass wool into a                               | Bell.  |
| pipet, which was wiped clean and allowed to                                |  |
| drain into a volumetric flask. Solute                                      |  |
| concns were detd by spectrophotometric assay                               |  |
| at predetd wavelengths using a Cary model 16                               |  |
| spectrophotometer (1).   | ESTIMATED ERROR:                                   |
|  | Soly: av values of 3 runs are given                |
|  | (authors).<br>Temp: ±0.1 <sup>0</sup> C (authors). |
|  | REFERENCES:  |
|  | 1. Paruta, A. N.; Mauger, J. W.                    |
|  | J. Pharm. Sci. <u>1971</u> , 60, 432.              |
|  | · · · · · · · · · · · · · · · · · · ·              |
|  |  |
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COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2pyrimidinyl- (sulfadiazine);  $C_{10}H_{10}N_4O_2S;$  [68-35-9] (2) 1-Decanol; C<sub>10</sub>H<sub>22</sub>O; [112-30-1] 163-83.

ORIGINAL MEASUREMENTS: Mauger, J. W.; Petersen, H., Jr. Alexander, K. S.; Paruta, A. N. Drug Dev. Ind. Pharm. 1977, 3(2),

VARIABLES: PREPARED BY: R. Piekos Temperature

EXPERIMENTAL VALUES:

| t/ <sup>o</sup> C | Solubility |                                |  |  |
|-------------------|------------|--------------------------------|--|--|
|                   | mg/ml      | 10 <sup>5</sup> x <sup>a</sup> | 10 <sup>4</sup> mol dm <sup>-3 a</sup> |  |
| 25                | 0.097      | 7.40                           | 3.875                                  |  |
| 30                | 0.105      | 8.04                           | 4.195                                  |  |
| 37                | 0.123      | 9.47                           | 4.914                                  |  |
|                   |            |                                |  |  |

 $a_X = mole fraction$ 

<sup>b</sup> Calculated by compiler

## AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: Sulfadiazine: lot W02235, Eli Lilly and Co. A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-decanol Its mp agreed with the literature value. 1-Decanol was from Matheson, Coleman and was rotated for 24 h. Samples were with-Bell. Its refractive index and density drawn through a pledget of glass wool into a pipet, which was wiped clean and allowed agreed with literature values. to drain into a volumetric flask. Soly was detd from absorbance and previously ascertained Beer's law plots detd on a Cary mo-ESTIMATED ERROR: del 16 spectrophotometer (1). Soly: av of at least 3 detns is reported (authors). Temp: ±0.1°C (authors). **REFERENCES:** 1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. J. Pharm. Sci. 1972, 61(1), 94.

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                       |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-               |  |
| pyrimidinyl- (sulfadiazine);                       | Sunwoo, C.; Eisen, H.                        |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]                   | J. Pharm. Sci. <u>1971</u> , 60, 238-44.     |
| (2) Acetamide, N,N-dimethy1-;                      |  |
| C <sub>4</sub> H <sub>9</sub> NO; [127-19-5]       |  |
| VARIABLES:   | PREPARED BY:                                 |
| One temperature: 25 <sup>0</sup> C                 | R. Piekos                                    |
|  |  |
| EXPERIMENTAL VALUES:                               |  |
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|  |  |
| The mole fraction solubility of sulfa              | diazine in N.N-dimethylacetamide             |
|  | -  |
| at 25 <sup>0</sup> C is 0.0239 ( 6.57 g/100 g solu | tion, compiler ).                            |
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| AUXILIARY  | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:                        | SOURCE AND PURITY OF MATERIALS:              |
|  |  |
| Soly was detd by the method reported by            | A USP sulfadiazine (American Cyanamide) Co., |
| Restaino and Martin (1). Sulfadiazine was          | Pearl River, N. Y.) was recrystd from warm   |
| assayed on a Coleman-Hitachi 124 double-           | acetone. N,N-Dimethylacetamide was of        |
| beam spectrophotometer at 270 nm after diln        | technical grade.                             |
| of a sample with 95% alcohol or water.             |  |
|  |  |
|  |  |
|  |  |
|  | ESTIMATED ERROR:                             |
|  | Temp: ±1.0° (authors).                       |
|  | Soly: the mean of 3 runs was given           |
|  | (authors).                                   |
|  | REFERENCES:                                  |
|  | 1. Restaino, F. A.; Martin, A. N.            |
| 1  | J. Pharm. Sci. <u>1964</u> , 53, 636.        |
|  |  |
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| COMPON                                     | ENTS:  |                                   |                                   | ORIGINAL MEASUREMENTS:                                     |  |  |
|--|--|-----------------------------------|-----------------------------------|--|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-       |  |                                   |                                   | Elworthy, P. H.; Worthington, H. E. C.                     |  |  |
| 1  | pyrimidinyl-   | (sulfadiazin                      | e);                               | J. Pharm. Pharmac. 1968, 20, 830-5.                        |  |  |
| (  | C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; | [68-35-9]                         |                                   | <u> </u>   |  |  |
| (2)  | Formamide, N,1   | N-dimethyl-;                      | с <sub>3</sub> н <sub>7</sub> NO; |  |  |  |
|  | [68-12-2]  |                                   |                                   |  |  |  |
| VARIAE                                     | BLES:  | <u></u>                           |                                   | PREPARED BY:   |  |  |
|  | Tempeı   | ature                             |                                   | R. Piekos  |  |  |
|  |  |                                   |                                   |  |  |  |
| EXPERI                                     | MENTAL VALUES  | :                                 | I                                 |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  | SoJ  |                                   |                                   | ubility  |  |  |
|  | t/ <sup>o</sup> C  | Weight % 10 <sup>2</sup> mole fra |                                   | raction mole kg <sup>-1</sup> water <sup>a</sup>           |  |  |
|  | 20   | 18.0                              | 6.02                              | 0.782  |  |  |
|  | 30   | 18.7                              | 6.29                              | 0.818  |  |  |
|  | 40   | 19.4                              | 6.57                              | 0.962  |  |  |
|  |  |                                   |                                   |  |  |  |
|  | ·  | <sup>a</sup> Calculated b         | y compiler                        |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   |                                   |  |  |  |
|  |  |                                   | AUXILIARY                         | INFORMATION  |  |  |
|  | D/APPARATUS/PR   |                                   |                                   | SOURCE AND PURITY OF MATERIALS:                            |  |  |
|  |  | oy shaking pow                    |                                   |  |  |  |
| ne with DMF for 24 h and transferred to a  |  |                                   |                                   | crystd from an EtOH-DMF mixt (3:1 by vol)                  |  |  |
| soly app which was of the percolation type |  |                                   | lation type                       | and dried over $P_2O_5$ . Its mp was $255^{\circ}C$ . Assa |  |  |
|  |  | n of that used                    | -                                 | by the Pharmacopeial method gave 100.0% pur                |  |  |
| and  | Griffiths (1).   | . The soln wa                     | s recycled                        | ty calcd with reference to the material dr:                |  |  |
|  |  | n a sintered-g                    |                                   | ed at 105°C.   |  |  |
| unti                                       | 1 satd (7-14 d   | lays). Sample                     | s were evapd                      | DMF (May and Baker Ltd) was distd under re-                |  |  |
| and  | the residues d   | lried to const                    | wt.                               | duced pressure and gave $n_D^{25} = 1.4283$ .              |  |  |
|  |  |                                   |                                   | ESTIMATED ERROR:   |  |  |
| 1  |  |                                   |                                   | Solv: mean values of duplicate runs are                    |  |  |

Soly: mean values of duplicate runs are given (authors).

Temp: ±0.05°C (authors).

**REFERENCES:** 

1. Davies, M.; Griffiths, D. M. L. Trans. Faraday Soc. <u>1953</u>, 49, 1405.

| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-                                       | Corby, T. C.; Elworthy, P. H.  |
| <pre>pyrimidinyl- (sulfadiazine);</pre>                                    | J. Pharm. Pharmac. <u>1971</u> , 23, Suppl.                                |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9] | 395-485.   |
| (2) n-Hexane; C <sub>6</sub> H <sub>14</sub> ; [110-54-3]                  |  |
|  |  |
|  |  |
| VARIABLES:<br>One temperature: 20 <sup>0</sup> C                           | PREPARED BY:<br>R. Piekos  |
| one cemperature. 20 c  | R. TIEROS  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Concentration of sulfadiazine in a same                                    | turated n-hexane solution at 20 <sup>0</sup> C                             |
| is 0 millimolal.   |  |
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| AUXILIARY  | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:  |
| The soly was detd in an app where n-hexane                                 | Sulfadiazine (MaCarthy's Ltd, Romford) was                                 |
| percolated through a plug of sulfadiazine                                  | a British Pharmacopeia product. It was re-                                 |
| supported on a 5/3 sintered glass disc. The                                | crystd twice from a DMF-EtOH mixt (1:3) and                                |
| Percolation was continued until the soln was                               | dried at $40^{\circ}$ C over P <sub>2</sub> 05. Its mp was $254^{\circ}$ C |
| satd (5-6 days). The concn of sulfadiazine                                 | (decompn). A spectroscopic grade n-hexane                                  |
| Was detd spectrophotometrically from a cali-                               |  |
|  | (2:2:4:) #40 4004 40 2002204   |
| bration curve using a Uvispek spectrophoto-                                |  |
| meter.   |  |
|  | ESTIMATED ERROR:   |
|  | Soly: not specified.   |
|  | Temp: ±0.05 <sup>o</sup> C (authors).                                      |
|  |  |
|  | REFERENCES:  |
|  | 1. Elworthy, P. H.; Lipscomb, F. J.  |
|  | J. Pharm. Pharmac. <u>1968</u> , 20, 790                                   |
|  |  |
|  |  |
|  |  |

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|---|---|---|
|   |   |   |

| 201/DO1001000   |   |
|---|---|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-   | ORIGINAL MEASUREMENTS:                  |
| pyrimidinyl- (sulfadiazine);  | Riess, W.                               |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [68-35-9]  | Intern. Congr. Chemotherapy, Proc.      |
| <ul><li>(2) Methane, trichloro- (chloroform);</li></ul>   | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| CHCl <sub>3</sub> ; [67-66-3]   |   |
|   |   |
| VARIABLES:  | PREPARED BY:                            |
| One temperature: 20 <sup>0</sup> C  | R. Piekos                               |
|   |   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of sulfadiazine in chloroform at $20^{\circ}$ C is 15 mg% ( 6.0 x $10^{-4}$ mol dm <sup>-3</sup> solution, compiler ). |   |
|   |   |
|   | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:         |
| Nothing specified.  | Nothing specified.                      |
|   |   |
|   | ESTIMATED ERROR:                        |
|   | Nothing specified.                      |
|   | REFERENCES :                            |
|   |   |

| COMPONENTS:                                   | ORIGINAL MEASUREMENTS:                    |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-2-          | Yamazaki, M.; Aoki, M.; Kamada, A.;       |
| pyrimidinyl- (sulfadiazine);                  | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]              | 37-40.                                    |
| (2) Methane, trichloro- (chloroform);         |   |
| CHC1 <sub>3</sub> ; [67-66-3]                 |   |
| VARIABLES:                                    | PREPARED BY:                              |
| One temperature: 30 <sup>0</sup> C            | R. Piekos                                 |
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| EXPERIMENTAL VALUES:                          |   |
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| Solubility of sulfadiazine in chlorofo        | rm at 30°C is 0.49 mmol/L                 |
| $(0.12 \text{ g dm}^{-3}, \text{ compiler}).$ |   |
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| AUXILIARY                                     | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:                   | SOURCE AND PURITY OF MATERIALS:           |
| Sulfadiazine (0.5 g) was placed in an L-      | Nothing specified.                        |
| shaped tube together with 20 ml of chloro-    |   |
| form. The mixt was shaken in a thermostat     |   |
| until equilibrium was attained. The sulfa-    |   |
| - · · · · · · · · · · · · · · · · · · ·       |   |
| diazine was assayed in the supernatant        |   |
| spectrophotometrically at 545 nm on a Beck-   |   |
| mann DU spectrophotometer. The results were   |   |
| taken from a calibration graph.               |   |
|   | ESTIMATED ERROR:                          |
|   | Soly: not specified.                      |
|   | Temp: ±1 <sup>0</sup> C (authors).        |
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|   | REFERENCES:                               |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-4-  | Roblin, R. O., Jr.; Williams, J. H.;  |
| pyrimidinyl- (4- sulfapyrimidine);  | Winnek, P. S.; English, J. P.   |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; [599-82-6] | J. Am. Chem. Soc. 1940, 62, 2002-5.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    | -   |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
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| EXPERIMENTAL VALUES:  |   |
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| Solubility of 4-sulfapyrimidine in wa                                       | $37^{\circ}$ c is 35% mg/100 cm <sup>3</sup>  |
|   |   |
| solution ( $1.41 \times 10^{-2} \text{ mol dm}^{-3}$ . com                  | piler ).  |
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| AUXILIARY   | INFORMATION   |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 231-2 <sup>0</sup> C (dec, cor), |
| Excess sulfonamide in water was heated and                                  |   |
| stirred on a steam bath for 30 min. The sus-                                | ,   |
| pension was then agitated for 24 h in a ther-                               |   |
| mostat at 37°C. A sample of the satd soln                                   | (19.9). Purity of the water was not spe-  |
| was withdrawn through a glass filter, dild,                                 | cified.   |
| and analyzed by the Marshall method (1)                                     |   |
| using a General Electric recording spectro-                                 |   |
| photometer for comparing the colors develop-                                |   |
| ed with those of the standards.   | ESTIMATED ERROR:  |
|   | Nothing specified.  |
|   |   |
|   |   |
|   | REFERENCES:   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|   | J. Pharmacol. <u>1939</u> , 66, 4.  |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-5-                            | ORIGINAL MEASUREMENTS:                              |
|  | Roblin, R. O., Jr.; Winnek, P. S.;                  |
| pyrimidiny1-; C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; | English, J. P.                                      |
| [17103-48-9]   | J. Am. Chem. Soc. <u>1942</u> , 64, 567-70.         |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                       |   |
| 2. 2.  |   |
| VARIABLES:   | PREPARED BY:  |
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| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
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| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-5-pyrimidinyl  | penzenesulfonamide in water at 37°C                 |
|  |   |
| is 9.8 mg/100 cm <sup>3</sup> solution ( $3.9 \times 10^{-3}$                  | ) <sup>-4</sup> mol dm <sup>-3</sup> , compiler ).  |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                     |
| Excess sulfonamide in water was heated and                                     | The sulfonamide, mp 260-1 <sup>0</sup> C (cor), was |
| stirred on a steam bath for 30 min. The  | prepd by the authors. Anal: %C 48.1 (calcd          |
| suspension was then agitated for 24 h in a                                     | 48.0); ZH 4.2 (4.0); ZN 22.5 (22.4).                |
| thermostat at 37°C. A sample of the satd                                       |   |
| -  | Purity of the water was not specified.              |
| soln was withdrawn through a glass filter,                                     |   |
| dild, and analyzed by the Marshall method                                      |   |
| (1) using a General Electric recording spec-                                   |   |
| trophotometer for comparing the colors de-                                     |   |
| veloped with those of the standards.   |   |
|  | ESTIMATED ERROR:                                    |
|  | Nothing specified.                                  |
|  |   |
|  |   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.             |
|  | J. Pharmacol. <u>1939</u> , 66, 4.                  |
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| <pre>COMPONENTS:<br/>(1) Aluminum, tris(4-amino-<u>N</u>-2-pyrimidinyl-<br/>benzenesulfonamidato-<u>N</u><sup>N</sup>, <u>0</u>)- (Al sulfa-<br/>diazine); C<sub>30</sub>H<sub>27</sub>AlN<sub>12</sub>O<sub>6</sub>S<sub>3</sub>; [71280-76-7]<br/>(2) Water; H<sub>2</sub>0; [7732-18-5]<br/>VARIABLES:<br/>One temperature: 28-30°C</pre> | ORIGINAL MEASUREMENTS:<br>Fox, Ch. L., Jr.; Modak, S.<br>Stanford, J. W.; Fox, P. L.<br>Scand. J. Plast. Reconstr. Surg.<br><u>1979</u> , 13(1), 89-94.<br>PREPARED BY:<br>R. Piekos |
| EXPERIMENTAL VALUES:<br>Solubility of Al(III) sulfadiazine in wa<br>is 6.6 mg% ( 8.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> solutio<br><sup>a</sup> Value given by one of the authors ( S.  | on, compiler ).  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Satd soln of Al sulfadiazine was prepared in<br>water and after 24 h aliquots from the clear<br>supernatant were assayed for sulfadiazine<br>content using the colorimetric method of<br>Bratton and Marshall (1). The soly value was<br>then calculated from the molecular formula.                          | Purity of the materials was not specified.   |
|  | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. 1939, 120, 537.   |

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| <pre>COMPONENTS:<br/>(1) Cerium, tris(4-amino-<u>N</u>-2-pyrimidinyl-<br/>benzenesulfonamidato-<u>N</u><sup>N</sup>,0)- (Ce sulfa-<br/>diazine); C<sub>30</sub>H<sub>27</sub>CeN<sub>12</sub>O<sub>6</sub>S<sub>3</sub>;<br/>[66269-03-2]<br/>(2) Water; H<sub>2</sub>0; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Fox, Ch. L., Jr.; Modak, S.;<br>Stanford, J. W.; Fox, P. L.;<br>Scand. J. Plast. Reconstr. Surg.<br><u>1979,</u> 13(1), 89-94. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 28-30 <sup>0</sup> C  | R. Piekos  |
| Solubility of Ce sulfadiazine in water<br>83.0 mg% (9.35 x 10 <sup>-4</sup> mol dm <sup>-3</sup> solution<br><sup>a</sup> Value given by one of the authors ( S  | on, compiler).   |
|  | INFORMATION  |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:  |
| Satd soln of Ce sulfadiazine was prepd in  | Neither source nor purity of the materials   |
| water and after 24 h aliquots from the   | was specified.   |
| clear supernatant were assayed for sulfa-  | The identity of the Ce sulfadiazine was ques-  |
| diazine content using the colorimetric me-   | tioned by Bult and associates (2) ( com-   |
| thod of Bratton and Marshall (1). The soly   | piler ).   |
| value was then calculated from the molecular   |  |
| · ······ was even catentared fiom rue motecular  |  |
| formula.   | ESTIMATED ERROR:   |

| <pre>COMPONENTS: (1) Chromium, bis(4-amino-<u>N</u>-2-pyrimidinyl-<br/>benzenesulfonamidato-<u>N</u><sup>N</sup>,<u>0</u>)- ( Cr(II)<br/>sulfadiazine); C<sub>20</sub>H<sub>18</sub>CrN<sub>8</sub>O<sub>4</sub>S<sub>2</sub>;<br/>[71261-84-2] (2) Water; H<sub>2</sub>O; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Fox, Ch. L, Jr.; Modak, S.;<br>Stanford, J. W.; Fox, P. L.<br>Scand. J. Plast. Reconstr. Surg.<br><u>1979,</u> 13(1), 89-94. |
|--|--|
| VARIABLES:   | PREPARED BY:   |
| One temperature: 28-30°C   | R. Piekos  |

EXPERIMENTAL VALUES:

Solubility of Cr(II) sulfadiazine in water at room temperature  $(28-30^{\circ}C)^{a}$  is 15.5 mg% ( 2.81 x  $10^{-4}$  mol dm<sup>-3</sup> solution, compiler ).

 $^{a}$ Value given by one of the authors ( S. M. ) in personal communication.

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:              |
|--|--|
| Satd soln of Cr(II) sulfadiazine was prepd   | The Cr(II) sulfadiazine was prepd by the     |
| in water and after 24 h aliquots from the    | authors as follows: an inorg. salt of CR(II) |
| clear supernatant were assayed for sulfa-    | was reacted with Na salt of sulfadiazine and |
| diazine content using the colorimetric me-   | the ppt was analyzed and characterized. No   |
| thod of Bratton and Marshall (1). The soly   | details were given, however.                 |
| value was then calculated from the molecular | Purity of the materials was not specified.   |
| formula.                                     |  |
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|  | ESTIMATED ERROR:                             |
|  | Nothing specified.                           |
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|  | REFERENCES:                                  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.      |
|  | J. Biol. Chem. <u>1939</u> , 120, 537.       |
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| COMPONENTS:<br>(1) Copper, (4-amino- <u>N</u> -2-pyrimidiny1-                              | ORIGINAL MEASUREMENTS:  |
|--|---|
| (i) copper, $(4-amino-N-2-pyimidinyi-benzenesulfonamidato-NN,0)- (Cu(I)$                   | Fox, Ch. L., Jr.; Modak, S.;  |
| sulfadiazine ); C <sub>10</sub> H <sub>9</sub> CuN <sub>4</sub> 0 <sub>2</sub> S;          | Stanford, J. W.; Fox, P. L.   |
| [71261-85-3]   | Scand. J. Plast. Reconstr. Surg.  |
|  | <u>1979</u> , <i>13(1)</i> , 89-94.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:<br>One temperature: 28-30 <sup>0</sup> C  | PREPARED BY:<br>R. Piekos   |
| one competituter 20 50 c   |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of Cu(I) sulfadiazine in wa   | ter at room temperature (28-30 <sup>0</sup> C) <sup>a</sup>                         |
| is 5.8 mg% (1.8 x $10^{-4}$ mol dm <sup>-3</sup> solut                                     |   |
| 15 5.6 mg/ (1.8 x 10 m01 dm 501dt  | ion, comparer /.  |
|  |   |
| <sup>a</sup> Value given by one of the authors ( S   | .M. ) in personal communication.  |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| Satd soln of Cu(I) sulfadiazine was prepd  | The Cu(I) sulfadiazine was prepd by the   |
| in water and after 24 h aliquots from the  | authors as follows: an inorg Cu(I) salt<br>was reacted with Na salt of sulfadiazine |
| clear supernatant were assayed for sulfa-  | and the ppt was analyzed and characterized.   |
| diazine content using the colorimetric me-   | No details were given, however.   |
| thod of Bratton and Marshall (1). The soly<br>value was then calculated from the molecular |   |
| formula.   | fully of the materials was not optimized  |
| lormuta.   |   |
|  | ESTIMATED ERROR:  |
|  | Nothing specified.  |
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|  | DEFEDENCUS.   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K, Jr.  |
|  | J. Biol. Chem. <u>1939</u> , 120, 537.  |
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| COMPONENTS:<br>(1) Copper, bis(4-amino- <u>N</u> -2-pyrimidiny1-                                 | ORIGINAL MEASUREMENTS:   |  |
|--|--|--|
| benzenesulfonamidato- $\underline{N}^{N}$ ,0)- (Cu(II)   | Fox, Ch. L., Jr.; Modak, S.;   |  |
| _  | Stanford, J. W.; Fox, P.L.   |  |
| <pre>sulfadiazine); C<sub>20</sub>H<sub>18</sub>CuN<sub>8</sub>O<sub>4</sub>S<sub>2</sub>;</pre> | Scand. J. Plast. Reconstr. Surg.   |  |
| [12171-53-8]   | <u>1979</u> , <i>13(1)</i> , 89–94.  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   | <u> </u>   |  |
| VARIABLES:   | PREPARED BY:   |  |
| One temperature: 28-30 <sup>0</sup> C  | R. Piekos  |  |
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| EXPERIMENTAL VALUES:   |  |  |
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| Solubility of Cu(II) sulfadiazine in v   | water at room temperature $(28-30^{\circ}C)^{a}$   |  |
| is 3.7 mg% ( 6.6 x 10 <sup>-5</sup> mol dm <sup>-3</sup> solu                                    | ition, compiler).  |  |
| <b>U</b>   |  |  |
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| <sup>a</sup> Value given by one of the authors ( S   | 5. M. ) in personal communication.   |  |
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| AUXILIARY INFORMATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |  |
| Satd soln of Cu(II) sulfadiazine was prepd   | Cu(II) sulfadiazine was prepd by the   |  |
| in water and after 24 h aliquots from the  | authors as follows: an inorg Cu(II) salt   |  |
| clear supernatant were assayed for sulfa-  | was reacted with Na salt of sulfadiazine   |  |
| diazine content using the colorimetric me-   | and the ppt was analyzed and characterized.  |  |
| -  |  |  |
| thod of Bratton and Marshall (1). The soly   | No details were given, however.  |  |
| value was then calculated from the molecular   | Purity of the materials was not specified.   |  |
| formula.   |  |  |
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|  | ESTIMATED ERROR:   |  |
|  | Nothing specified.   |  |
|  | the state of the s |  |
|  | REFERENCES :   |  |
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|  | 1. Bratton, A. C.; Marshall, E. K., Jr.  |  |
|  | J. Biol. Chem. <u>1939</u> , 120, 537.   |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                     |  |
|---|--|--|
| (1) Cobalt, bis(4-amino- <u>N</u> -2-pyrimidinyl-   | Fox, Ch. L., Jr.; Modak, S;                |  |
| benzenesulfonamidato- <u>N</u> N, <u>0</u> )-   | Stanford, J.W.; Fox, P.L.                  |  |
| ( Co sulfadiazine ); C <sub>20</sub> H <sub>18</sub> CoN <sub>8</sub> O <sub>4</sub> S <sub>2</sub> ; |  |  |
| [71280-79-0]  | Scand. J. Plast. Reconstr. Surg.           |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  | <u>1979</u> , <i>13(1)</i> , 89-94.        |  |
| VARIABLES:  | PREPARED BY:                               |  |
| One temperature: 28-30 <sup>0</sup> C   | R. Piekos                                  |  |
| EXPERIMENTAL VALUES:  |  |  |
| Solubility of Co(II) sulfadiazine in wa<br>is 86.9 mg% ( 1.56 x $10^{-3}$ mol dm <sup>-3</sup> sol    |  |  |
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| <sup>a</sup> Value given by one of the authors ( S. M. ) in personal communication.                   |  |  |
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| AUXILIARY   | INFORMATION                                |  |
| ME THOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:            |  |
|   |  |  |
| Satd soln of Co sulfadiazine was prepd in   | The Co(II) sulfadiazine was prepd by the   |  |
| water and after 24 h aliquots from the clear  | -  |  |
| supernatant were assayed for sulfadiazine   | reacted with Na salt of sulfadiazine and   |  |
| content using the colorimetric method of  | the ppt was analyzed and characterized. No |  |
| Bratton and Marshall (1). The soly value  | details were given, however.               |  |
| was then calculated from the molecular  | Purity of the materials was not specified. |  |
| formula.  |  |  |
|   |  |  |
|   | ESTIMATED ERROR:                           |  |
|   | Nothing specified.                         |  |
|   | REFERENCES :                               |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |  |
|   | J. Biol. Chem. <u>1939</u> , 120, 537.     |  |
|   | 5. 2000, onem. <u>1939</u> , 1203 337.     |  |
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| <pre>COMPONENTS:<br/>(1) Iron, tris(4-amino-<u>N</u>-2-pyrimidinyl-<br/>benzenesulfonamidato-<u>N</u><sup>N</sup>,0)- (Fe(III)<br/>sulfadiazine); C<sub>30</sub>H<sub>27</sub>FeN<sub>12</sub>O<sub>6</sub>S<sub>3</sub>;<br/>[71261-86-4]<br/>(2) Water; H<sub>2</sub>0; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Fox, Ch. L; Modak, S.;<br>Stanford, J. W.; Fox, P. L.<br>Scand. J. Plast. Reconstr. Surg.<br><u>1979</u> , 13(1), 89-94. |  |
|---|--|--|
| VARIABLES:  | PREPARED BY:   |  |
| One temperature: 28-30°C  | R. Piekos  |  |

EXPERIMENTAL VALUES:

Solubility of Fe(III) sulfadiazine in water at room temperature  $(28-30^{\circ}C)^{a}$  is 6.0 mg% (7.5 x  $10^{-5}$  mol dm<sup>-3</sup> solution, compiler ).

 $^{a}\ensuremath{\text{Value}}$  given by one of the authors ( S. M. ) in personal communication.

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                 | SOURCE AND PURITY OF MATERIALS:            |
|---|--|
| Satd soln of Fe(III) sulfadiazine was prepd | The Fe(III) sulfadiazine was prepd by      |
| in water and after 24 h aliquots from the   | the authors as follows: an inorg Fe(III)   |
| clear supernatant were assayed for sulfa-   | salt was reacted with Na salt of sulfa-    |
| diazine content using the colorimetric      | diazine and the ppt was analyzed and char- |
| method of Bratton and Marshall (1). The     | acterized. No details were given, however. |
| soly value was then calculated from the     | Purity of the materials was not specified. |
| molecular formula.                          |  |
|   |  |
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|   | ESTIMATED ERROR:                           |
|   | Nothing specified.                         |
|   |  |
|   | REFERENCES :                               |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
|   | J. Biol. Chem. 1939, 120, 537.             |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-                                    | ORIGINAL MEASUREMENTS:  |
|--|---|
|  | Modak, S. M.; Fox, Ch. L. Jr.                                     |
| <pre>pyrimidinyl-, monosilver (+) salt;</pre>  | Biochem. Pharmacol. <u>1973,</u> 22, 2391-                        |
| (AgSD); C <sub>10</sub> H <sub>9</sub> AgN <sub>4</sub> 0 <sub>2</sub> S; [22199-08-2] | 404.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
|  |   |
| VARIABLES:   | PREPARED BY:  |
|  |   |
| One temperature: 28°C  | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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|  |   |
| Solubility of AgSD in water at room to   | emperature ( $28^{\circ}$ C) is 0.54 mole per                     |
|  | •   |
| 100 ml water ( $5 \times 10^{-6}$ mol dm <sup>-3</sup> water                           | r, compiler).   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                                   |
| According to personal communication of one   | <sup>110m</sup> AgNO <sub>3</sub> obtained from the International |
| of the authors (C.L.F.) the following pro-   | Chem and Nuclear Corp was reacted with Na                         |
| cefure was employed: A satd soln of <sup>110m</sup>                                    | sulfadiazine ( source and purity not spe-                         |
| Ag sulfadiazine of known sp activity was   | cified ) to give <sup>110m</sup> AgSD with a sp acti-             |
|  |   |
| made and left at room temp (28°C) overnight.   |   |
| The supernatant was then taken out and cen-  | Purity of the water was not specified.                            |
| trifuged at higher speed to remove small   |   |
| floating particles of the solid. Radioac-  |   |
| tive measurement was done on the aliquot of  | ESTIMATED ERROR:  |
| the clear supernatant and the soly was calco   |   |
| using the sp activity of $^{110m}$ AgSD.   | Moening specified.  |
|  |   |
|  | REFERENCES:   |
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COMPONENTS: ORIGINAL MEASUREMENTS: (1) Benzenesulfonamide, 4-amino-N-2-Fox, Ch. L., Jr. Modak, S.; pyrimidiny1-, monosilver (+) salt; Stanford, J. W.; Fox, P. L. ( Ag sulfadiazine ); C<sub>10</sub>H<sub>9</sub>AgN<sub>4</sub>O<sub>2</sub>S; Scand. J. Plast. Reconstr. Surg. [22199-08-2] <u>1979</u>, *13(1)*, 89-94. (2) Water; Н20; [7732-18-5] VARIABLES: PREPARED BY: One temperature: 28-30°C R. Piekos **EXPERIMENTAL VALUES:** Solubility of Ag sulfadiazine in water at room temperature (28-30°C)<sup>a</sup> is 0.2 mg% (6 x  $10^{-6}$  mol dm<sup>-3</sup> solution, compiler ). <sup>a</sup>Values given by one of the authors (S. M.) in personal communication. AUXILIARY INFORMATION METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: Satd soln of Ag sulfadiazine was prepd in Nothing specified. water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calcd from the molecular formula. ESTIMATED ERROR: Nothing specified. **REFERENCES:** 

> Bratton, A. C.; Marshall, E. K., Jr. J. Biol. Chem. <u>1939</u>, 120, 537.

|   | 21   |
|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                         |
| (1) Benzenesulfonamide, 4-amino-N-2-  | Bult, A.; Klassen, H. B.                       |
| pyrimidinyl-, monosilver salt   | Arch. Pharm. (Weinheim) <u>1980</u> , 313(12), |
| (Ag sulfadiazine); C <sub>10</sub> H <sub>9</sub> AgN <sub>4</sub> 0 <sub>2</sub> S;                  | 1016-20.                                       |
| [22199-08-2]  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                      |
| EXPERIMENTAL VALUES:  |  |
| Solubility of Ag sulfadiazine in water<br>( 9.5 x 10 <sup>-6</sup> mol dm <sup>-3</sup> , compiler ). |  |
| AUXILIARY   | INFORMATION                                    |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                |
| Ag sulfadiazine was equilibrated with water   | Ag sulfadiazine was prepd by the earlier       |
| at $25\pm0.1^{\circ}$ C for one week in a vial with a   | reported method (1). Its purity was not        |
| parafilm - sheet covered rubber closure and   | specified.                                     |
| wrapped with Al foil. The vial was rotated  | Doubly distd water was used.                   |
| during equilibration in a thermostated bath.  |  |
| The satd soln was filtered through 25 mm in   |  |
| diam and 1.2 $\mu\text{m}$ av pore size filters (Selec-   |  |
| tron-filter, type ST69), Schleicher and   |  |
| Schüll, Dassel, Germany). The filtrate was  | ESTIMATED ERROR:                               |
| analyzed for sulfadiazine by uv spectrophoto-   | Soly: not specifed.                            |
| metry (Perkin Elmer 124) and for Ag by atomic   | Temp: ±0.1 <sup>0</sup> C (authors).           |
| absorption spectrophotometry.   |  |
|   | REFERENCES :                                   |
|   | 1. Fox, Ch. L., Jr.; Modak, S. M.              |
|   | Antimicrob. Agents Chemother. <u>1974</u> ,    |

6, 562.

| <ul> <li>COMPONENTS:         <ol> <li>Benzenesulfonamide, 4-amino-N-2-pyri-<br/>midinyl-, monosilver salt (Ag sulfadi-<br/>azine); C<sub>10</sub>H<sub>9</sub>AgN<sub>4</sub>O<sub>2</sub>S; [22199-08-2]</li> <li>Nitric acid; HNO<sub>3</sub>; [7697-37-2]</li> <li>Potassium nitrate; KNO<sub>3</sub>; [7757-79-1]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> </li> </ul> | ORIGINAL MEASUREMENTS:<br>Nesbitt, R. U., Jr.; Sandmann, B. J.<br>J. Pharm. Sci. <u>1977</u> , 66(4), 519-22. |  |
|--|---|--|
| VARIABLES:   | PREPARED BY:<br>R. Piekos   |  |
| EXPERIMENTAL VALUES:   |   |  |
| Table I  |   |  |
| Total molar solubility, S, of Ag sulfadiazine determined by the method of<br>known subtraction and the molar concentration of the silver ion determined<br>by direct potentiometry on identical samples at 25±0.1 <sup>0</sup> C, ionic strength<br>0.1M, in nitric acid buffers   |   |  |

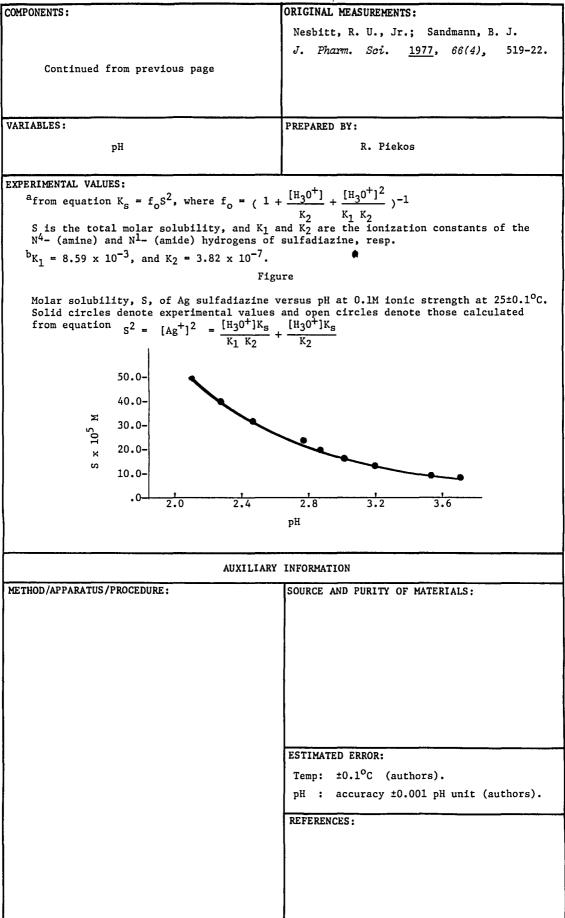
|      | pH 2.128            |                          | pH 3.851            |                                      |
|------|---------------------|--------------------------|---------------------|--------------------------------------|
| -    | S x 10 <sup>5</sup> | $[Ag^{+}] \times 10^{5}$ | S x 10 <sup>5</sup> | [Ag <sup>+</sup> ] x 10 <sup>5</sup> |
|      | 59.18               | 59.11                    | 6.690               | 6.455                                |
|      | 58.06               | 57.97                    | 6.690               | 6.517                                |
|      | 59.35               | 59.34                    | 6.434               | 6.517                                |
|      | 58.53               | 58.42                    | 6.768               | 6.475                                |
|      | 59.19               | 60.00                    | 6.586               | 6.375                                |
|      | 57.30               | 57.97                    | 6.612               | 6.455                                |
| Mean | 58.60               | 58,80                    | 6.466               | 6.629                                |
|      |                     |                          |                     |                                      |

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
|---|--|
| METHOD/APPARATUS/PROCEDURE:<br>Mixts of 100 mg of Ag sulfadiazine and 25 ml<br>of the HNO <sub>3</sub> -KNO <sub>3</sub> buffer with an ionic streng-<br>th adjusted to 0.1M with KNO <sub>3</sub> were placed in<br>paraffin-coated vials and rotated end-over-<br>end in a thermostated bath until equilibrium<br>soly was obtained. After filtration, the<br>solns were analyzed at $25\pm0.1^{\circ}$ C in paraffin-<br>coated beakers for the Ag-ion concn using a<br>Ag <sup>+</sup> -ion selective electrode (No.94-16, Orion<br>Res., Cambridge, Mass) standardized at 25±0.1<br>°C and an ionic strength of 0.1M. The elec-<br>trode displayed a Nernstian response through<br>out the concn range of 1 x $10^{-2}$ - 1.5 x $10^{-6}$ M<br>for the Ag <sup>+</sup> ion. The pH was measured with a<br>pH electrode (Corning Sci Instruments, Med-<br>field, Mass) standardized using standard buf-<br>fers meeting NBS requirements. The total Ag <sup>+</sup><br>concn was detd by the method of known sub-<br>traction (1,2) in the HNO <sub>3</sub> -buffered soln to<br>which a sufficient amt of a std soln of KI<br>was added to precipitate approx one-half of<br>the free Ag <sup>+</sup> ion. | All reagents were of anal grade. Ag sulfa-<br>diazine was prepd by the method of Braun and<br>Towle (3) and recrystd. Water had a sp cond<br>of (1-10) x $10^{-7}$ ohm <sup>-1</sup> cm <sup>-1</sup> .<br>The source of HNO <sub>3</sub> and KNO <sub>3</sub> was not speci-<br>fied.                                   |
|   | ESTIMATED ERROR: Soly: the means in Table I<br>are not statistically different at the 5%<br>level (authors). Std deviation of the mean<br>$K_s$ value in Table II is $\pm 0.12 \times 10^{-12}$<br>(authors). To be contd.   |
|   | REFERENCES: 1. Durst, R. A., in "Ion Selec-<br>tive Electrodes", R.A. Durst, Ed., NBS Spe-<br>cial Publ No 314, US Govt Printing Office,<br>Washington, DC, <u>1969</u> , p. 381.<br>2. Orion Research Inc Newsletter <u>1969</u> , 1, 25.<br>3. Braun, E. E.; Towle, J. L.<br>J. Am. Chem. Soc. <u>1941</u> , 63, 3523. |

| COMPONENTS:                   |  | ORIGINAL MEASUREMENTS:  |                   |
|-------------------------------|--|---|-------------------|
|                               |  | Nesbitt, R. U., Jr.; Sandmann, B.   |                   |
| Continued from                | previous page.                         | J. Pharm. Sci. <u>1977</u> , 66(4), 5   | 19-22.            |
|                               |  |   |                   |
| VARIABLES:                    | ······································ | PREPARED BY:  |                   |
| וק                            | ł                                      | R. Piekos   |                   |
| EXPERIMENTAL VALUES:          |  |   |                   |
|                               |  |   |                   |
|                               |  | able II   |                   |
| Calculation (<br>and ionic st |  | of Ag sulfadiazine <sup>a</sup> , K <sub>s</sub> , at 25±0.1 <sup>0</sup> C   |                   |
|                               | lengen of m.                           |   |                   |
| pH                            | f <sub>o</sub> b                       | [Ag <sup>+</sup> ] <sup>2</sup> K <sub>s</sub>  | —                 |
| 2.122                         | $2.688 \times 10^{-5}$                 | $2.980 \times 10^{-7}$ $8.04 \times 10^{-12}$   |                   |
| 2.373                         | $6.024 \times 10^{-5}$                 | $1.352 \times 10^{-7}$ 8.16 x $10^{-12}$  |                   |
| 2.630                         | $1.279 \times 10^{-4}$                 | $6.165 \times 10^{-8}$ 7.90 x $10^{-12}$  |                   |
| 2.891                         | $2.583 \times 10^{-4}$                 | $\begin{array}{ccc} 3.139 \times 10^{-8} & 8.14 \times 10^{-12} \\ \text{Mean} & 8.06 \times 10^{-12} \pm 0.12 \times 10^{-12} \end{array}$ | 10 <sup>-12</sup> |
|                               |  |   |                   |
| METHOD APPADATUS (PPC         |  | IARY INFORMATION  |                   |
| METHOD/APPARATUS/PRC          | CEDURE:                                | SOURCE AND PURITY OF MATERIALS:   |                   |
|                               |  |   |                   |
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|                               |  |   |                   |
|                               |  |   |                   |
|                               |  | ESTIMATED ERROR:  |                   |
|                               |  |   |                   |
|                               |  | REFERENCES:   | <u></u>           |
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NENTS :



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| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-<br/>pyrimidinyl-, monosilver salt (Ag sulfa-<br/>diazine); C<sub>10</sub>H<sub>9</sub>AgN<sub>4</sub>0<sub>2</sub>S; [22199-08-2]</li> </ol> | Nesbitt, R. U., Jr.; Sandmann, B. J.<br>J. Pharm. Sci. <u>19</u> 77, 66(4), 519-22.   |
| <pre>(2) 4-Morpholineethanesulfonic acid;<br/>C<sub>6</sub>H<sub>13</sub>NO<sub>4</sub>S; [4432-31-9]</pre>  | <u> </u>  |
| (3) 4-Morpholineethanesulfonic acid, sodium<br>salt; C <sub>6</sub> H <sub>12</sub> NNa0 <sub>4</sub> S; [71119-23-8]  |   |
| <ul> <li>(4) Potassium nitrate; KNO<sub>3</sub>; [7757-79-1]</li> <li>(5) Water; H<sub>2</sub>O; [7732-18-5]</li> </ul>  | PREPARED BY:  |
| VARIABLES: pH  | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
| -  | 5, in a 0.05M 4-morpholine-<br>buffer at 0.1M ionic<br>25±0.1 <sup>0</sup> C          |
| 6 5.40 x   | x 10 <sup>-6</sup>  |
| 7 3.19 >   | x 10 <sup>-6</sup>  |
|  |   |
| AUXILIARY  | INFORMATION   |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:   |
| Mixts of 100 mg of Ag sulfadiazine and 25 ml   | All reagents were of anal grade (source   |
| of 0.05M 4-morpholineethanesulfonic acid buf-  |   |
| fer were adjusted to an ionic strength of 0.1  | by the method of Braun and Towle(2) and<br>recrystd. The buffer soln was prepd by ti- |
| M with KNO3, placed in paraffin-coated vials<br>and rotated in a thermostated bath until equi-   |   |
| librium was obtained. After filtration the   | Water had a sp cond.of $(1-10) \times 10^{-7}$ ohm <sup>-1</sup>                      |
| solns were analyzed at 25±0.1°C and an ionic   | cm <sup>-1</sup> .  |
| stregnth of 0.1M in paraffin-coated beakers  |   |
| for the Ag <sup>+</sup> -ion concn using a Ag <sup>+</sup> -ion selec-   | ESTIMATED ERROR:  |
| tive electrode standardized using std buffers  |   |
| meeting NBS requirements. The total $Ag^+$ -ion  | Temp: ±0.1 <sup>0</sup> C (authors).  |
| concn was detd by the method of known addn   | pH : accuracy ±0.001 pH unit (authors).   |
| (1); the added reagent was a std soln of $A_{gNO_3}$ representing a 100-fold increase in the   | 10/0 1 07   |
| free $Ag^+$ ion present in the sample solns. The   |   |
| PH was measured with triple-purpose pH elec-<br>trode.   | 2. Braun, C. E.; Towle, J. L.<br>J. Am. Chem. Soc. <u>1941</u> , 63, 3523.            |
|  |   |

COMPONENTS: ORIGINAL MEASUREMENTS: Nesbitt, R. U., Jr.; Sandmann, B. J. J. Pharm. Sci. <u>1977,</u> 66(4) 519-22. Continued from previous page. VARIABLES: PREPARED BY: pН R. Piekos EXPERIMENTAL VALUES: Figure Equilibrium values of  $S^2$  versus  $[H_30^+]$  in 0.05M 4-morpholineethanesulfonic acid buffer at 0.1M ionic strength ( $KNO_3$ ) at  $25\pm0.1^{\circ}C$ 15.0-12.0-Σ 9.0s<sup>2</sup> x 10<sup>11</sup> 6.0-3.0-0.0-9.0 12.0 6.0 15.0 3.0 [H<sub>3</sub>0<sup>+</sup>] X 10<sup>7</sup> AUXILIARY INFORMATION METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: ESTIMATED ERROR: **REFERENCES:** 

| ORIGINAL MEASUREMENTS:   |
|--|
|  |
| Bult, A.; Klasen, H. B.<br>Arch. Fharm. (Weinheim, Ger.) <u>1980</u> ,           |
| <i>Aren. Fraim. (webneedin, ber.)</i> <u>1900</u> ,<br><i>313(12)</i> , 1016–20. |
|  |
|  |
| PREPARED BY:   |
| R. Piekos  |
|  |
|  |
| le in water at 25 <sup>0</sup> C is 3.4 mg/100 ml                                |
| Y INFORMATION  |
| SOURCE AND PURITY OF MATERIALS:  |
| The Ag sulfadiazine imidazole was synthe-  |
| sized by the authors. Analysis- Calcd: C   |
| 38.9, H 3.47, N 22.7, S 6.5, Ag 21.9%  |
| he Found: C 39.1, H 3.5, N 23.2, S 6.5, Ag 21.7%                                 |
| Sulfadiazine by amperometric titrn: 50.3   |
| er (lit 50.52).  |
| Doubly distilled water was used.   |
|  |
| ESTIMATED ERROR:   |
| y Soly: not specified.   |
| I Temp: ±0.1 <sup>o</sup> C (authors).   |
| REFERENCES :   |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |
|---|--|
| (1) Butanoic acid, 4-oxo-4-[[[4-(2-pyrimi-  | Bult, A.; Klasen, H. B.                      |
| dinylamino)sulfonyl]phenyl]amino]-, di-   | Arch. Pharm. (Weinheim, Ger.) 1980,          |
| silver(1+)salt (Ag succinylsulfadiazine)  | <i>313(12)</i> , 1016-20.                    |
| C <sub>14</sub> H <sub>12</sub> Ag <sub>2</sub> N <sub>4</sub> O <sub>5</sub> S; [76619-75-5] |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                    |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of Ag succinylsulfadiazine   | in water at $25^{\circ}$ C is 0.55 mg/100 ml |
| $(9.7 \times 10^{-6} \text{ mol dm}^{-3}, \text{ compiler }).$                                |  |
| (9.7 x 10 ° mol dm °, compiler ).   |  |
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| AUXILIARY   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| Ag succinylsulfadiazine was equilibrated with   |  |
| doubly distd water at 25±0.1 <sup>0</sup> C for one week                                      | by the authors. Analysis - Calcd: C 29.8,    |
| in a vial with a paraffin coated sheet rub-   | H 2.32, N 9.9, S 5.7, Ag 38.3%. Found: C     |
| ber closure and wrapped with Al foil. The vi-   | 29.0, H 2.1, N 9.7, S 5.5, Ag 37.0%          |
| al was rotated during equilibration in a ther   | Doubly distilled water was used.             |
| mostated bath. The satd soln was filtered   |  |
| through 25 mm in diam and $1.2\mum$ av pore size  |  |
| filters (Selectron filter type ST69, Sch-   |  |
| leicher and Schuell, Dassel, Ger.) The fil-   | ESTIMATED ERROR:                             |
| trate was analyzed for the sulfonamide by uv  | Soly: not specified.                         |
| spectrophotometry (Perkin Elmer 124) and for  | Temp: ±0.1 <sup>0</sup> C (authors).         |
| Ag by atomic absorption spectrophotometry.  |  |
|   | REFERENCES :                                 |
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| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-     pyrimidinyl, monosodium salt ( sodium     sulfadiazine); C<sub>10</sub>H<sub>9</sub>N<sub>4</sub>Na0<sub>2</sub>S;     [547-32-0] (2) Water; H<sub>2</sub>0; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Clark, W. G.; Strakosch, E. A.;<br>Levitan, N. I. J. Lab. Clin. Med.<br><u>1942,</u> 28, 188-9. |
|--|---|
| VARIABLES:   | PREPARED BY:  |
| Temperature  | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
| 6-1-1  |   |
| t/°C ————————————————————————————————————  |   |
| g/100 g water  | mol kg <sup>-1</sup> water <sup>a</sup>   |
| 25 50.0  | 1.84  |
| 37 65.0  | 2.39  |
| <sup>a</sup> Calculated by compil  | er  |
| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| A small tinted glass container contg excess  | Neither source nor purity of Na sulfadi-  |
| Na sulfadiazine in water was shaken in a wa-   |   |
| ter bath thermostat for 24 h. The satd soln<br>was then filtered by aspiration through a   | CO <sub>2</sub> -free distd water was used.   |
| washed and dried asbestos filter stick into  |   |
| a weighed weighing bottle. The entire app  |   |
| was kept at the temp at which the compd was  |   |
| dissolved. The amt dissolved was then detd   |   |
| by the method of Bratton and Marshall (1),   | ESTIMATED ERROR:<br>Soly: not specified.  |
| using a photoelectric colorimeter.   | Soly: not specified.<br>Temp: ±0.1 <sup>0</sup> C (authors).  |
| 1  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|  |   |
|  |   |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-   | Burlage, H. M.                           |
| pyrimidinyl-, monosodium salt ( sodium   | J. Am. Pharm. Assoc., Sci. Ed.           |
| sulfadiazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S·Na;                       | <u>1948</u> , <i>37</i> , 345.           |
| [547-32-0]   |  |
| (2) 2-Propanol; C <sub>3</sub> H <sub>8</sub> 0; [67-63-0]   |  |
| VARIABLES:   | PREPARED BY:                             |
| One temperature: 25 <sup>0</sup> C   | R. Piekos                                |
| EXPERIMENTAL VALUES:   |  |
| Solubility of sodium sulfadiazine in 2<br>solution ( 6.832 x 10 <sup>-3</sup> mol dm <sup>-3</sup> , com |  |
| AUXILIARY  | INFORMATION                              |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:          |
| Satd soln of sodium sulfadiazine in 2-propa-   |  |
| nol were prepd at 25 <sup>°</sup> C and definite vols of   | purity, manufd by Squibb. The source and |
| the solns were measured into tared dishes by   | purity of 2-propanol was not specified.  |
| means of standard pipets. The alcohol was  |  |
| allowed to evap at room temp and the residue   |  |
| was dried at 105 <sup>0</sup> C. In the case of losses   |  |
| due to apparent decompn, the residue was   |  |
| dried in a desiccator (1).   |  |
|  | ESTIMATED ERROR:                         |
|  | Nothing specified.                       |
|  |  |
|  |  |
|  | REFERENCES:                              |
|  | 1. Burlage, H. M.                        |
|  | J. Am. Pharm. Assoc., Sci. Ed.           |
|  | <u>1947</u> , 36(1), 16.                 |
|  |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-  | ORIGINAL MEASUREMENTS:  |
|--|---|
|  | Fox, Ch. L., Jr.; Modak, S.;  |
| pyrimidinyl-, zinc(2+) salt (zinc sulfa-   | Stanford, J. W.; Fox, P. L.   |
| diazine); C <sub>20</sub> H <sub>18</sub> N <sub>8</sub> 0 <sub>4</sub> S <sub>2</sub> Zn; | Scand. J. Plast. Reconstr. Surg.                                      |
| [66219-86-1]   | <u>1979</u> , <i>13(1)</i> , 89–94.                                   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 28-30°C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of Zn sulfadiazine in water a   | at room temperature ( 28-30 <sup>0</sup> C) <sup>a</sup>              |
| is 56.0 mg% ( $9.93 \times 10^{-4}$ mol dm <sup>-3</sup> solution                          | tion, compiler ).   |
|  | •   |
|  |   |
| <sup>a</sup> Value given by one of the authors (S.M.                                       | .) in personal communication.   |
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|  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                                       |
| Satd soln of Zn sulfadiazine was prepd in  | Neither source nor purity of the materials                            |
| water and after 24 h aliquots from the clear   | was specified.  |
| supernatant were assayed for sulfadiazine  | The identity of the Zn sulfadiazine was                               |
| content using the colorimetric method of   | questioned by Bult and associates (2)                                 |
| Bratton and Marshall (1). The soly value   | (compiler).   |
| was then calculated from the molecular formu-  | -   |
| 1a.  |   |
|  |   |
|  | ESTIMATED ERROR:  |
|  | Nothing specified.  |
|  |   |
|  |   |
| ]  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                               |
|  | J. Biol. Chem. <u>1939</u> , 120, 537.                                |
|  | 2. Bult, A.; Hulsing, N.; Weyland, J. W.<br>Pharm. Weekblad, Sci. Ed. |
|  | Pharm. Weekblad, Sci. Ed.<br><u>1980,</u> 2, 190; J. Pharm. Pharmacol |
|  | <u>1981,</u> 33, 171.   |

| Anthony N. Paruta<br>Department of Pharmaceutics<br>Jniversity of Rhode Island<br>Kingston, Rhode Island, USA |
|---|
| Jniversity of Rhode Island  |
| •   |
| Cingston, Rhode Island USA  |
| and   |
| Ryszard Piekos  |
| Faculty of Pharmacy, University of Gdansk   |
| Gdansk, Poland 1986   |
| 1   |

CRITICAL EVALUATION:

The solubility of the acetyl derivative of sulfadiazine in water at 310K has been reported by Roblin et al. (1) and Kikuth (2). The values given were  $5.13 \times 10^{-4}$  mol dm<sup>-3</sup> and 5.75 x  $10^{-3}$ , respectively. Only the former (1) supplied sufficient experimental details. Because of the uncertainty in Kikuth's value only a tentative average value of the solubility in water of  $5.44 \times 10^{-4}$  mol dm<sup>-3</sup> at 310K can be recommended. It should be noted that in this case the acetyl group causes about a ten fold decrease in the equilibrium solubility with respect to the parent compound.

The data reported for buffer solutions are compiled in Table I.

Table I: Solubility of Acetyl sulfapyrimidine at various pH levels in buffer solution, 293K and 310K

|           |     | $10^4 \text{ mol } \text{dm}^{-3}$ |      |
|-----------|-----|------------------------------------|------|
| Reference | pH  | 293K                               | 310K |
| 3         | 5.9 | 4,52                               | 7.2  |
| 4         | 6.0 | 7.9                                | -    |
| 3         | 7.0 | 28.7                               | 56.8 |
| 4         | 7.0 | 24.6                               | -    |
| 3         | 8.0 | 86.5                               | -    |
| 4         | 8.0 | 71.2                               | -    |

There is a considerable discrepancy in the values. At pH = 7 an approximate value can be suggested, though that of Pulver and Suter (4) is about 86% of Krüger-Thiemer's (3). The simple average of about 26 x  $10^{-4}$  mol dm<sup>-3</sup> must be contrasted to the value of the parent compound. Sulfadiazine possesses an aqueous solubility at 293K of about 2 x  $10^{-4}$  mol dm<sup>-3</sup>. Since the acetyl derivative usually decreases solubility, it is unexpected to evidence a 13-fold enhancement of solubility.

### **REFERENCES:**

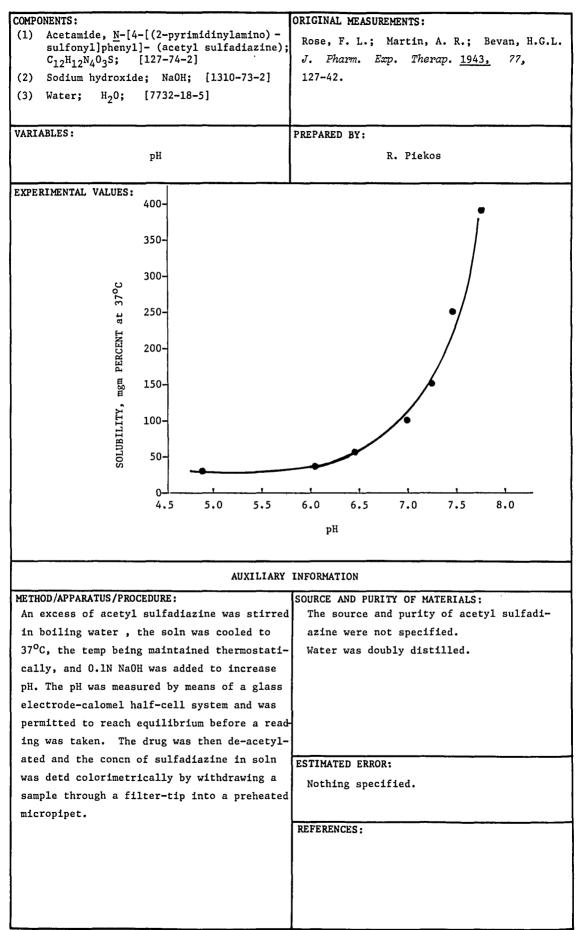
- Roblin, R. O., Jr.; Williams, J. H.; Winnek, P. S.; English, J. P. J. Am. Chem. Soc. <u>1940</u>, 62, 2002-5.
   Kikuth, W. Med. Welt <u>1943</u>, 17(26/27), 483-6.
   Kikuth, E. Anakaratza, Sandalan 1972, 2011(2011)
- (2) Krüger-Thiemer, E. Arch. Dermatol. Syphilis 1942, 183
  (4) Pulver, R.; Suter, R. Schweiz. Med. Wochenschr. 1943, 90-116. 183
- 73(13). 403-8.

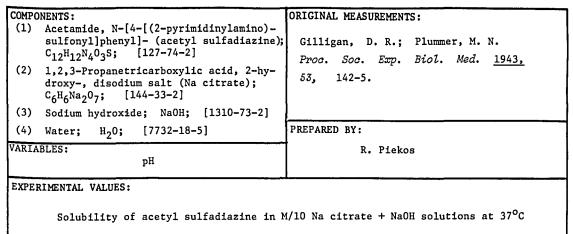
|   | 2   |
|---|---|
| <pre>COMPONENTS: (1) Acetamide, N-[4-[(2-pyrimidinylamino)     sulfonyl]phenyl]- (acetyl sulfapyri-     midine); C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>0<sub>3</sub>S; [127-74-2] (2) Water; H<sub>2</sub>0; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Roblin, R. O., Jr.; Williams, J. H.;<br>Winnek, P. S.; English, J. P.<br>J. Am. Chem. Soc. <u>1940</u> , 62,<br>2002-5. |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37°C   | R. Piekos   |
| Solubility fo acetyl sulfapyrimidine  |   |
| solution ( 5.13 x $10^{-4}$ mol dm <sup>-3</sup> , comp   | piler ).  |
|   |   |
| AUXILIAR  | RY INFORMATION  |
| METHOD /APPAPATUS / PROCEDURE .   | COURCE AND DURITY OF WATERIALS.   |

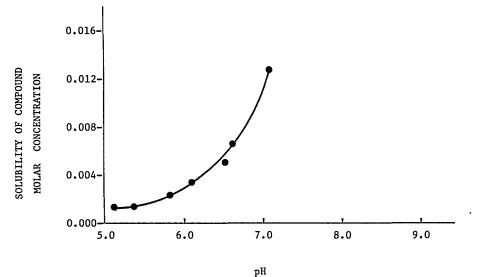
| 1 |   |  |
|---|---|--|
|   | METHOD/APPARATUS/PROCEDURE:                   | SOURCE AND PURITY OF MATERIALS;            |
|   | Excess sulfonamide in water was heated and    | The acetyl sulfapyrimidine, mp 258-9°C,    |
|   | stirred on a steam bath for 30 min. The sus-  | (cor), was prepd by the authors. Anal: %C  |
|   | pension was then agitated for 24 h in a ther- | 49.2 (calcd 49.4); %H 4.1 (4.1); %N 19.2   |
|   | mostat at 37°C. A sample of the satd soln     | (19.2). Purity of the water was not speci- |
|   | was withdrawn through a glass filter, dild,   | fied.                                      |
|   | and analyzed by the Marshall method (1) us-   |  |
|   | ing a General Electric recording spectropho-  |  |
|   | tometer for comparing the colors developed    |  |
| 1 | with those of the standards.                  | ESTIMATED ERROR:                           |
|   |   | Nothing specified.                         |
| Ì |   |  |
|   |   |  |
|   |   | REFERENCES :                               |
| l |   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
|   |   | J. Pharmacol. <u>1939</u> , 66, 4.         |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Acetamide, N-[4-[(2-pyrimidinylamino)  | Kikuth, W.   |
| sulfonyl]phenyl]- (acetyl sulfapyrimi-   | Med. Welt <u>1943</u> , 17(26/27), 483-6.  |
| dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2] | $\frac{1000}{1000} = \frac{1000}{1000} = \frac{1000}{1000$ |
| (2) Water; H <sub>2</sub> O; [7732-18-5]   |  |
| (2) water; H <sub>2</sub> 0; [//32-16-5]   |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of acetyl sulfapyrimidine in  | n water at 37°C is 168 mg/100 cm <sup>3</sup>  |
| solution ( $5.75 \times 10^{-3} \text{ mol dm}^{-3}$ , compil                      | ar )   |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
|  |  |
| Nothing specified.   | Acetyl sulfapyrimidine: not specified.   |
|  | The pH of the water was 7.0.   |
|  |  |
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|  | ESTIMATED ERROR:   |
|  |  |
|  | Nothing specified.   |
|  |  |
|  | REFERENCES :   |
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| COMPONENTS:   |                   |              | ORIGINAL MEASUREMENTS:  |
|---|-------------------|--------------|---|
| <pre>COMPONENTS: (1) Acetamide, N-[4-[(2-pyrimidinylamino) sulfonyl]phenyl]- (acetyl sulfadiazine); C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>0<sub>3</sub>S; [127-74-2]</pre> |                   | -            | Langecker, H.<br>Arch. Exptl. Path. Pharmakol. <u>1948</u> ,<br>205, 291-301.     |
| (2) Water; H <sub>2</sub> 0; [7732  | -18-5]            |              |   |
| VARIABLES:  |                   |              | PREPARED BY:<br>R. Piekos   |
| EXPERIMENTAL VALUES:  |                   |              |   |
|   |                   |              |   |
|   |                   |              |   |
|   | рН                |              | 11ity at 37°C<br>   |
|   |                   | mg%          |   |
|   | 5.7               | 23           | 7.9   |
|   | 6.3               | 24           | 8.2   |
|   | <sup>a</sup> Calo | culated by c | compiler  |
|   |                   |              |   |
|   |                   |              |   |
|   |                   |              |   |
|   | <u> </u>          | AUXILIARY    | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE  | diazine           | was hoiled   | SOURCE AND PURITY OF MATERIALS:<br>Source and purity of the materials were        |
| An excess of acetyl sulfadiazine was boiled<br>with water for 1 h in a sealed ampul follow-   |                   |              | not specified.  |
| ed by keeping the ampul a assaying, the solute was  |                   |              |   |
| NaOH soln (1) to cleave the acetyl group and<br>sulfadiazine was detd colorimetrically by   |                   |              |   |
| the method of Bratton and Marshall (2) using  |                   | 11 (2) using | 5   |
| a Havemann colorimeter (3), as well as by microanal detn of the solid residue.  |                   |              | ESTIMATED ERROR:  |
|   |                   |              | Nothing specified.  |
|   |                   |              | REFERENCES:   |
|   |                   |              | LI Scudi, J. V. J. Lab. Clin. Med.<br><u>1940</u> , 25, 404.                      |
|   |                   |              | 2. Bratton, A. G.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537. |
|   |                   |              | 3. Havemann, R. Klin. Wochenschr.<br><u>1940</u> , p. 503.                        |



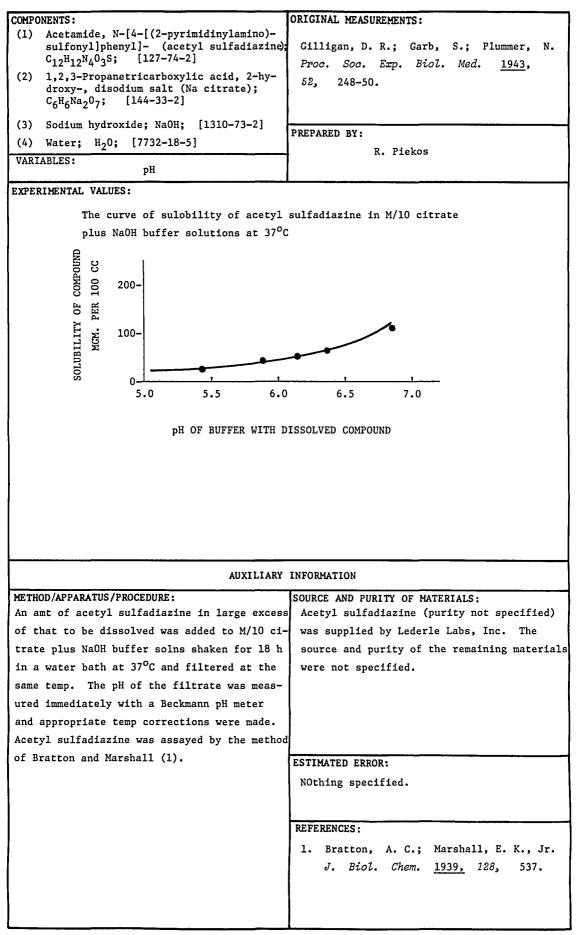




### AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                             | SOURCE AND PURITY OF MATERIALS:             |
|---|---|
| An excess of acetyl sulfadiazine was shaken             | Acetyl sulfadiazine was supplied by Lederle |
| in M/10 Na citrate + NaOH solns of various              | Labs, Inc. The source and purity of the     |
| $PH$ values for 18 h in a water bath at $37^{\circ}C$ , | remaining materials were not specified.     |
| and filtered in an incubator room at this               |   |
| temp. The pH of the filtrate was measured               |   |
| immediately at room temp with a Beckmann                |   |
| glass electrode pH meter and appropriate cor-           |   |
| rections for the differences between room               |   |
| temp and 37°C were applied. The amt of dis-             | ESTIMATED ERROR:                            |
| solved compd was measured by the method of              | Nothing specified.                          |
| Bratton and Marshall (1).                               |   |
|   |   |
|   | REFERENCES:                                 |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.     |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.      |
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|---|---|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |
| <ol> <li>Acetamide, N-[4-[(2-pyrimidinylamino)-<br/>sulfonyl]phenyl]- (acetylsulfapyrimi-</li> </ol>                          | Krüger-Thiemer, E.                          |
| dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]  | Arch. Dermatol. Syphilis <u>1942,</u> 183,  |
| (2) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                                     | 90-116.                                     |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:                                |
| One temperature: ca 20 <sup>0</sup> C; one pH: 4.37   | R. Piekos                                   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of acetyl sulfapyrimidine d<br>of pH 4.37 at room temperature (about<br>mol dm <sup>-3</sup> solution, compiler ). | <b>-</b> 7                                  |
| AUXILIARY   | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| Acetyl sulfapyrimidine (0.5 g) was dissolved  | Acetyl sulfapyrimidine (source not speci-   |
| in 10 cm <sup>3</sup> of the 0.735M (10%) KH <sub>2</sub> PO <sub>4</sub> soln of   | fied) gave no coloration upon diazotization |
| pH 4.37, shaken for 2 h at room temp (about   | of its satd soln, thus showing absence of   |
| $20^{\circ}$ C), and filtered. The filtrate was treated   |   |
| with equal vol of 2N HCl, and refluxed for 15   | the remaining materials were not specified. |
| min. After proper diln, a 1-cm <sup>3</sup> aliquot was   |   |
| withdrawn, acidified, cooled, and the sulfon-   |   |
| amide content was detd colorimetrically ( as  | 1   |
| sulfapyrimidine) by the Marshall method modi-   | ESTIMATED ERROR:                            |
| fied by Kimmig (1) using an Authenrieth colo-   | Soly: precision ±5% (author).               |
| rimeter. The pH was detd on an ultraiono-   | Temp: not specified.                        |
| graph usisng a glass electrode.   | pH : ±0.05 pH unit (author).                |
|   | REFERENCES :                                |
|   | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> , |
|   | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.  |
|   |   |

| COMPONENTS :   | ORIGINAL MEASUREMENTS:                       |
|--|--|
| (1) Acetamide, N-[4-[(2-pyrimidinylamino)-   | Krüger-Thiemer, E.                           |
| sulfonyl]phenyl]- (acetyl sulfapyri-<br>midine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2] | Arch. Dermatol. Syphilis 1942, 183,          |
| (2) Phosphoric acid, disodium salt;  | 90-116.                                      |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:                                 |
| One temperature: ca 20 <sup>0</sup> C; one pH: 8.74  | R. Piekos                                    |
| EXPERIMENTAL VALUES:   |  |
|  |  |
| Solubility of acetyl sulfapyrimidine ir  | a 0.705M (10%) Na <sub>2</sub> HPO, solution |
| of pH 8.74 at room temperature (about 2  |  |
|  | 10°C) 18 0.348 g% (1.873 X 10 - mol          |
| $dm^{-3}$ solution, compiler ).  |  |
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| AUXILIARY  | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:              |
| Acetyl sulfapyrimidine (0.5 g) was dissolved   | Acetyl sulfapyrimidine (source not speci-    |
| in 10 $\text{cm}^3$ of the 0.705M (10%) $\text{Na}_2\text{HPO}_4$ soln,  | fied) gave no coloration upon diazotization  |
| shaken for 2 h at room temp (about 20 <sup>0</sup> C),   | of its satd soln, thus showing absence       |
| and filtered. The filtrate was treated with  | of sulfapyrimidine. The source and purity    |
| equal vol of 2N HCl and refluxed for 15 min.   | of the remaining materials were not speci-   |
| After proper diln, a 1-cm <sup>3</sup> aliquot was with-   | fied.  |
| drawn, acidified, cooled, and the sulfonamide  |  |
| content was detd colorimetrically (as sulfa-   |  |
| pyrimidine) by the Marshall method modified  | ESTIMATED ERROR:                             |
| by Kimmig (1) using an Authenrieth colorime-   | Soly: precision ±5% (author).                |
| ter. The pH was detd on an ultraionograph  | Temp: not specified.                         |
| using a glass electrode.   | pH : ±0.05 pH unit (author).                 |
|  | REFERENCES :                                 |
|  | 1. Kimmig, J. Arch. Dermatol.                |
|  | 176, 722; Erg. Hyg. <u>1941</u> , 24, 398.   |
|  |  |
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|      | DNENTS:  | ORIGINAL MEASUREMENTS:                               |
|------|--|--|
| (1)  | Acetamide, N-[4-[(2-pyrimidinylamino)-<br>sulfonyl]phenyl]- (acetyl sulfapyrimi-<br>dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2] | Krüger-Thiemer, E.<br>Arch. Dermatol. Syphilis 1942, |
| (2)  | Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | 183, 90-116.   |
| (3)  | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |  |
| (4)  | Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:   |
| VARI | ABLES:<br>Temperature, pH  | R. Piekos  |

EXPERIMENTAL VALUES:

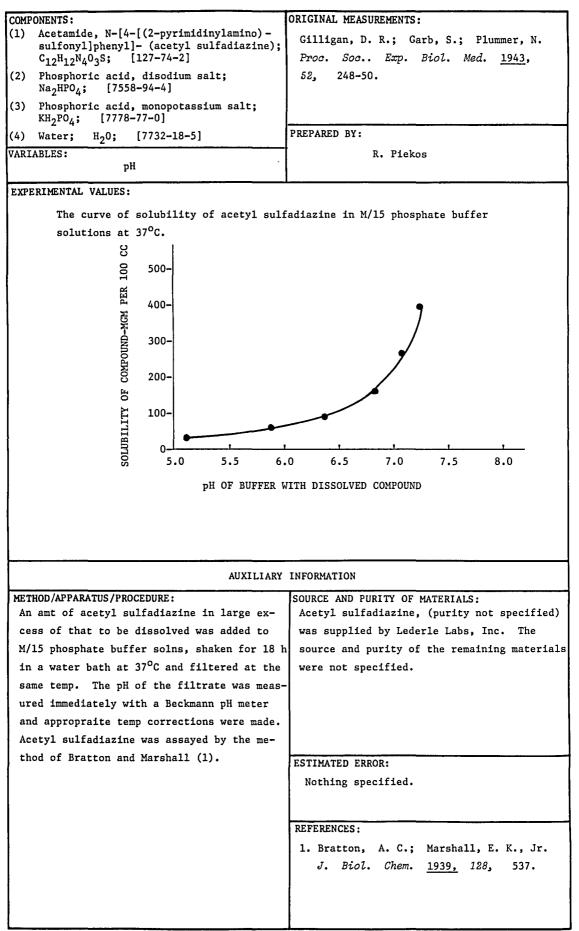
| Composition of 1/15M phosphate   |                                 |                    | Solubility |          |   |       |   |
|----------------------------------|---------------------------------|--------------------|------------|----------|---|-------|---|
| buffe                            | er solutions                    |                    | - рН       | Room tem | р (са 20 <sup>0</sup> С)                                      |       | 37 <sup>0</sup> C   |
| Na <sub>2</sub> HPO <sub>4</sub> | кн <sub>2</sub> ро <sub>4</sub> | %Content           |            | g%       | 10 <sup>3</sup> mol dm <sup>-3</sup><br>solution <sup>a</sup> | 3 g%  | 10 <sup>3</sup> mol dm <sup>-3</sup><br>solution <sup>a</sup> |
| 1.0                              | 99.0                            | 0.91               | 4.944      | 0.0082   | 0.28  | -     | -   |
| 10.0                             | 90.0                            | 0.91               | 5.906      | 0.0132   | 0.452   | 0.021 | 0.72  |
| 61.1                             | 38.9                            | 0.93               | 7.005      | 0.0840   | 2.87  | 0.166 | 5.68  |
| 9.5                              | 0.5                             | 0.733 <sup>b</sup> | 7.51       | 0.1810   | 6.19  | -     | -   |
| 94.7                             | 5.3                             | 0.95               | 8.018      | 0.2530   | 8.65  | -     | -   |
|                                  |                                 |                    |            |          |   |       |   |

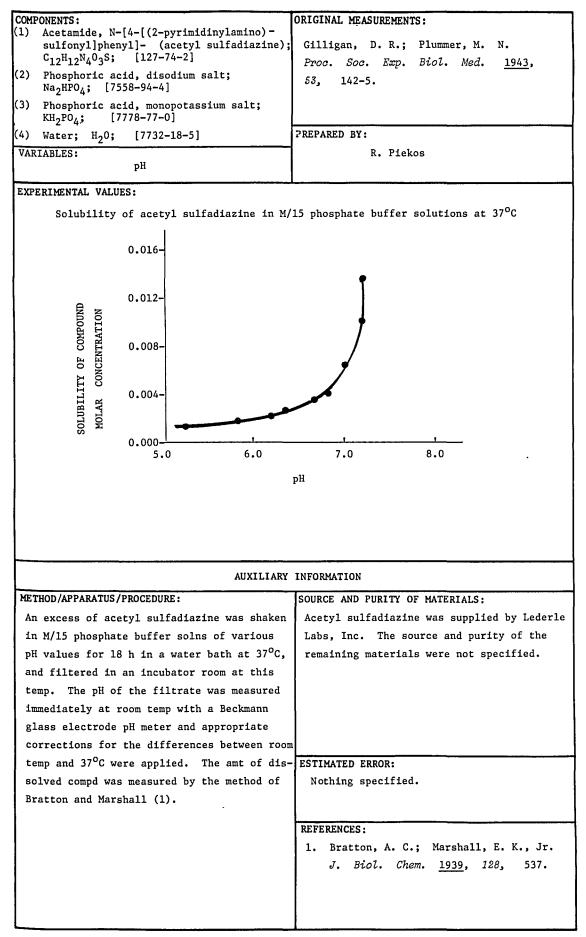
<sup>a</sup> Calculated by compiler.

b Molar content; 10% buffer solution.

### AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                                      | SOURCE AND PURITY OF MATERIALS:             |
|--|---|
| Acetyl sulfapyrimidine (0.5 g) was dissolved                     | Acetyl sulfapyrimidine (source not speci-   |
| in 10 cm <sup>3</sup> of a buffer soln, shaken for 2 h           | fied) gave no coloration upon diazotization |
| at $20^{\circ}$ C (or left for 48 h at $37^{\circ}$ C), and fil- | of its satd soln, thus showing absence of   |
| tered at respective temp. The filtrate was                       | sulfapyrimidine. the source and purity of   |
| treated with equal vol of 2N HCl and refluxed                    | the remaining materials were not specified. |
| for 15 min. After proper diln, a 1-cm <sup>3</sup> ali-          |   |
| quot was withdrawn, acidified cooled, and                        |   |
| the sulfonamide content was detd colorime-                       |   |
| trically (as sulfapyrimidine) by the Marshall                    | ESTIMATED ERROR:                            |
| method modified by Kimmig (1) using the                          | Soly: precision ±5% (author).               |
| Authenrieth colorimeter. The pH was detd on                      | Temp: not specified.                        |
| an ultraionograph using a glass electrode.                       | pH : ±0.05 pH unit (author).                |
|  | REFERENCES:                                 |
|  | 1. Kimmig, J. Arch. Dermatol. <u>1938</u> , |
|  | 176 722; Erg. Hyg. <u>1941</u> , 24, 398.   |
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|  |   |
|  |   |





| COMPONENTS:   |   |                                | ORIGINAL MEASUREMENTS:  |
|---|---|--------------------------------|---|
| <ol> <li>Acetamide, N-[4-[(2-pyrimidinylamino)-<br/>sulfonyl]phenyl]- (acetyl sulfadiazine);</li> </ol> |   |                                |   |
| C <sub>12</sub> H <sub>12</sub> N   | $[_{4}0_{3}S; [127-74]$                       | etyl sulfadiazine);<br>-2]     |   |
| (2) Phospho   | (2) Phosphoric acid, disodium salt;           |                                | Schweiz. Med. Wochenschr. <u>1943,</u><br>73(13), 403-8.                        |
| (3) Phospho   | [7558-94-4]<br>ric acid, monop<br>[7778-77-0] | otassium salt;                 |   |
| (4) Water;  |   | 18-51                          | PREPARED BY:  |
|   |   |                                | R. Piekos   |
|   |   |                                |   |
| EXPERIMENTAL  | . VALUES:                                     |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   | Colubility of oo               | $x_{\rm M}$ oulfodiaging in $V/15$ phosphate                                    |
|   | рН  |                                | etyl sulfadiazine in M/15 phosphate<br>ording to Sørensen) at 20 <sup>0</sup> C |
|   | P11   |                                |   |
|   |   | mg%                            | $10^3 \text{ mol } dm^{-3} \text{ a}$   |
|   | 6.0   | 23                             | 0.79  |
|   | 7.0   | 72                             | 2.46  |
|   | 8.0   | 208                            | 7.12  |
|   | <u> </u>                                      |                                |   |
|   |   |                                |   |
|   | •   | <sup>a</sup> Calculated by con | npiler.   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                | INFORMATION   |
| METHOD ABBAT  | RATUS/PROCEDURE:                              |                                | SOURCE AND PURITY OF MATERIALS:   |
| 1   |   |                                |   |
| Nothing s   | pecified.                                     |                                | Nothing specified.  |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                | ESTIMATED ERROR:  |
|   |   |                                | Nothing specified.  |
|   |   |                                |   |
|   |   |                                | REFERENCES :  |
|   |   |                                |   |
|   |   |                                |   |
|   |   |                                |   |
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|   | 24   |
|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
| <ol> <li>Acetamide, N-[4-[(2-pyrimidinylamino)-<br/>sulfonyl]phenyl]- (acetyl sulfapyrimi-</li> </ol> | Frisk, A. R.; Hagerman, G.;  |
| dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]                    | Helander, S.; Sjögren, B.  |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                 | Hygiea <u>1946,</u> 108(12), 639 <b>-</b> 51.  |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]             |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:   |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C; one pH: 6.1   | R. Piekos  |
| EXPERIMENTAL VALUES:  | ••••••••••••••••••••••••••••••••••••••   |
| Solubility of acetyl sulfapyrimidine in<br>at 37 <sup>0</sup> C is 35 mg/100 ml solvent (1.2 x        |  |
| AUXILIARY   | INFORMATION  |
|   |  |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of acetyl sulfapyrimidine in the                             | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials                      |
| phosphate buffer was shaken at $37^{\circ}$ C for 24  | was specified.   |
| h. The concn of acetyl sulfapyrimidine was  |  |
| detd by the Bratton and Marshall method (1)   |  |
| using a photoelec colorimeter.  |  |
| 9 a busecter cotottmeret.   |  |
|   |  |
|   |  |
|   |  |
|   | ESTIMATED ERROR:<br>Soly: precision ±4 mg/100 ml (authors).  |
|   | Temp and pH: not specified.  |
|   |  |
|   | REFERENCES :   |
|   | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.<br/>J. Biol. Chem. <u>1939</u>, 128, 537.</li> </ol> |
|   | · · · · · · · · · · · · · · · · · · ·  |
|   |  |

| 242   |  |   |                          |   |  |
|---|--|---|--------------------------|---|--|
| (1)<br>(2)<br>(3)<br>(4)<br>VARI  | DNENTS:<br>Acetamide, N-[4-[(2-p)<br>sulfonyl]phenyl]- (N'<br>azine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S;<br>Phosphoric acid, disoc<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]<br>Phosphoric acid, monop<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]<br>Water; H <sub>2</sub> O; [7732-<br>ABLES:<br>pH<br>RIMENTAL VALUES: | 4-acetylsu<br>[127-74-<br>dium salt;<br> <br> <br>potassium = | lfadi <del>-</del><br>2] | ORIGINAL MEASUREME<br>Hekster, Y. A.;<br>Damsma, J. E.;<br>J. Antimicrob.<br>133-44.<br>PREPARED BY:<br>R. P1 | Vree, T. B.;<br>Friesen; W. T.<br><i>Chemother</i> . <u>1981</u> , 8,        |
|   |  | рН  | Solu                     | bility at 25 <sup>0</sup> C   |  |
|   |  | •   | mg/l                     | $10^3 \text{ mol } \text{dm}^{-3}$  | a  |
|   |  | 5.5   | 411                      | 1.41  |  |
|   |  | 7.5   | 1620                     | 5.54  |  |
| a Calculated H  |  |   | culated b                | y compiler  |  |
|   |  |   |                          |   |  |
| <b></b>   |  |   |                          | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns of N <sup>4</sup> -acetylsulfadiazine were  |  |   |                          | SOURCE AND PURITY   | OF MATERIALS:<br>purity of the materials                                     |
| prepd in phosphate buffers of pH 5.5 and 7.5  |  |   |                          | were not specif   | •  |
| at room temp (25°C). The conc of the solute   |  |   |                          |   |  |
| was measured by means of a Spectra Physics  |  |   |                          |   |  |
| 3500B high-performance liquid chromatograph   |  |   | tograph                  |   |  |
| equipped with a column oven (Model 748) and a   |  |   | 48)and a                 | 1   |  |
| Pye-Unicam LC-UV spectrophotometric detector.   |  |   |                          |   |  |
|   | detector was connected   |   |                          |   |  |
| A stainless steel column (10 cm x 4.6 mm i.d.) was packed with Lichrosorb RPS, 5 $\mu$ m, obtained from Chrompack. An injection loop of 100 |  |   | n, obtain-<br>p of 100   | The detection 1<br>was 0.5 mg/l (at   | imit of the solute by HPLC<br>uthors). The error in<br>pH was not specified. |
| 1   | $\mu 1$ was used. The oven temp was $40^{\circ}\text{C}$ . Detection of the solute was performed at 260 nm.  |   |                          | REFERENCES:   |  |

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|-------|--|---|
| COMP  | ONENTS:                                  | EVALUATOR:                                |
| (1)   | Benzenesulfonamide, 4-amino-N-(4-methyl- |   |
|       | 2-pyrimidinyl)- (sulfamerazine)          | Department of Pharmaceutics               |
| 1     | $C_{11}H_{12}N_4O_2S;$ [127-79-7]        | University of Rhode Island                |
| 1     | 11 12 4 2 4                              | Kingston, Rhode Island, USA               |
| (2)   | Water                                    | and                                       |
| 1     |  | Ryszard Piekos                            |
| 1     |  | Faculty of Pharmacy, University of Gdansk |
|       |  | Gdansk, Poland 1986                       |

CRITICAL EVALUATION:

Six reports (1-6\_) on the solubility of sulfamerazine in water at 303K and 310K are in Table I.

Table I: Solubility of Sulfamerazine in water, 303K and 310K

|           | 10 <sup>3</sup> mo | 1 dm <sup>-3</sup> (*indicates mol kg <sup>-1</sup> ) |
|-----------|--------------------|---|
| Reference | <u>303</u> K       | 310K  |
| 1         | -                  | 1.20  |
| 2         | -                  | 2.50  |
| 3         | -                  | 0.965*  |
| 4         | -                  | 1.4   |
| 5         | 0.89               | -   |
| 6         | 0.91               | -   |

The two values given for 303K are very close and self consistant with the data at 310K (1-4), thus the recommended value is given as 9 x  $10^{-4}$  mol dm<sup>-3</sup>. At 310K, the values of Kikuth (2) and Sapoznikova et al. (3) were not considered further, because the equilibration time was insufficient or unreported. The results given by Roblin et al. (1) and Langecker (4) were derived for 24 hour equilibrium periods. The recommended value at 310K for sulfamerazine is  $1.3 \times 10^{-3} \text{ mol dm}^{-3}$ .

### **REFERENCES:**

- (1) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P.

- (1) Kobili, K.G., Gr., alliand, J.M., and J. Harden, J. A. M. Chem. Soc. <u>1940</u>, 62, 2002-5
  (2) Kikuth, W. Med. Welt <u>1943</u>, 17(26/27), 483-6.
  (3) Sapoznikova, N.V.; Postovakii, I. Ya. Zh. Prikl. Khim. <u>1944</u>, 17,
  (4) Langecker, H. Arch. Exptl. Path. Pharmakol. <u>1948</u>, 205, 291-301. 427-34.
- (5) Yamasaki, M.; Aoki, M.; Kamada, A.; Yata, N. Yakusaigaku <u>1967</u>, 27(1), 37-40. 77-8,86.
- (6) Bhattacharyya, R.; Basu, U.P. Indian Pharmacist 1950, 6(3)

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                | Roblin, R. O., Jr.; Williams, J. H.;                                       |
| 2-pyrimidinyl)- (sulfamerazine);  | Winnek, P. S.; English, J. P.  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | J. Am. Chem. Soc. <u>1940</u> , 62, 2002–5.                                |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamerazine in water at                                     | 37 <sup>o</sup> C is 31.8 mg/100 cm <sup>3</sup> solution                  |
| $(1.20 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler}).$              |  |
| (1.20 x 10 mol dm , compiler).  |  |
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| ΔΗΥΤΙΤΑΡΥ   | INFORMATION  |
|   |  |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 235-6°C (dec, cor), |
| stirred on a steam bath for 30 min. The sus                                 |  |
| 1   | (calcd 50.0); %H 4.4 (4.6); %N 21.1 (21.2).                                |
| mostat at 37°C. A sample of the satd soln                                   | Purity of the water was not specified.                                     |
| was withdrawn through a glass filter, dild,                                 | fully of the water was not specified.                                      |
|   |  |
| and analyzed by the Marshall method (1) us-                                 |  |
| ing a General Electric recording spectropho-                                |  |
| tometer for comparing the colors developed                                  |  |
| with those of the standards.  | ESTIMATED ERROR:   |
|   | Nothing specified.   |
|   | 1  |
| 1   |  |
|   | PFFFPFNCVS.  |
|   | REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.                     |
|   |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                                    |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                                    |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                |   |
| 2-pyrimidinyl)- (sulfamerazine);  | Kikuth, W.  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Med. Welt. <u>1943,</u> 17(26/27), 483-6.             |
|   |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |   |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
|   | Nº I LONGO  |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamerazine in water a                                      | t $37^{\circ}$ C is 66.0 mg/100 <sup>3</sup> solution |
|   |   |
| $(2.50 \times 10^{-3} \text{ mol } \text{dm}^{-3}).$                        |   |
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| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                       |
| 12 INOD/APPAKAIUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                       |
| Nothing specified.  | Sulfamerazine: not specified.                         |
|   | The pH of the water was 7.0.                          |
|   |   |
|   |   |
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|   |   |
|   | ESTIMATED ERROR:                                      |
|   |   |
|   | Nothing specified.                                    |
| •   |   |
|   | REFERENCES:   |
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| 60)/D/  |  |                       |  | ODICINAL NEACUDENERS                                      |  |
|---|--|-----------------------|--|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4-methyl- |  | ORIGINAL MEASUREMENTS |  |   |  |
|   | 2-pyrimidinyl)- (sulfamerazine);                                 |                       | Sapoznnikova, N. V;  | Postovskil, I. Ya.<br><u>1944,</u> 17, 427-34.            |  |
|   | C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; | [127-79-7]            |  | DA. FF66.6. KADA.   | <u>1944,</u> 17, 427-34.   |
| (2)   | Water; H <sub>2</sub> O;   | [7732-18-             | 5]   |   |  |
| VARI  | ABLES:   | <u></u>               |  | PREPARED BY:  |  |
|   | Temperat   | ure                   |  | R. Pieko  | s  |
|   | _  |                       |  |   |  |
| EXPE  | RIMENTAL VALUES:   |                       |  | _   |  |
|   |  |                       |  |   |  |
|   |  |                       |  |   |  |
|   |  |                       |  |   |  |
|   |  |                       | Solu   | bility  |  |
|   |  | t/ <sup>0</sup> C     |  |   |  |
|   |  |                       | Weight%  | 10 <sup>3</sup> mol kg <sup>-1</sup> water <sup>a</sup>   |  |
|   |  | 37                    | 0.0255 <sup>b</sup>  | 0.965   |  |
|   |  | 50                    | 0.050  | 1.89  |  |
|   |  | 75                    | 0.172  | 6.52  |  |
|   |  | 99                    | 0.319  | 12.1  |  |
|   |  | <sup>b</sup> Cal      | culated by comp<br>culated from th<br>,300 cal mol <sup>-1</sup> ) | iler<br>e heat of dissolution                             |  |
|   |  |                       |  | INFORMATION   |  |
| METH  | IOD/APPARATUS/PRO  | CEDUDE .              |  |   |  |
|   | famerazine was d   |                       | n water to form  | SOURCE AND PURITY OF<br>Pure, recrystd sulfa              |  |
| a satd soln which was occasionally agitated                 |  | Its mp conformed to   | that reported in the   |   |  |
| in a glass vessel immersed in a thermostat.                 |  | literature.           |  |   |  |
| The equilibrium was usually attained after                  |  | Purity of the water   | was not specified.   |   |  |
| 1 h. Five-to 100-cm <sup>3</sup> samples of the satd        |  |                       |  |   |  |
| soln were placed in Pt crucibles or dishes                  |  |                       |  |   |  |
|   | evapd to drynes  | •                     |  |   |  |
| 110-115 <sup>0</sup> C. The residue was dried to const      |  |                       |  |   |  |
| wt  | at 105-110 <sup>0</sup> C and                                    | l weighed.            |  | at 37, 50, and 75 <sup>0</sup> C.<br>was poor due to evap | results were obtained<br>At 99 <sup>0</sup> C the accuracy<br>n of water during sam-<br>p: ±0.05 <sup>0</sup> C (authors). |
|   |  |                       |  | REFERENCES:   | -  |
|   |  |                       |  |   |  |
|   |  |                       |  |   |  |
|   |  |                       |  |   |  |
|   |  |                       |  |   |  |
|   |  |                       |  | 1   |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]<br>(2) Water; H <sub>2</sub> O; [7732-18-5]<br>VARIABLES:<br>Temperature<br>EXPERIMENTAL VALUES:  |                   | razine);  | ORIGINAL MEASUREMENTS:<br>Langecker, H.<br>Arch. Exptl. Path. Pharmakol. <u>1948</u> ,<br>205, 291-301.<br>PREPARED BY:<br>R. Piekos   |
|--|-------------------|---|--|
|  | 10                | S   | blubility  |
|  | t/ <sup>0</sup> C | mg%   | $10^4 \text{ mol } dm^{-3} \text{ a}$  |
|  | 25                | 21  | 7.9  |
|  | 37                | 37  | 14   |
|  |                   |   |  |
|  |                   | AUXILIAR  | Y INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of sulfamerazine was boiled with<br>water and left for 24 h in a vessel protect-<br>ed from access of $CO_2$ . The sulfamerazine<br>concn was detd colorimetrically by the me-<br>thod of Bratton and Marshall (1) using a<br>Havemann colorimeter (2), as well as by<br>microanal detn of the solid residue. |                   | vessel protect<br>ulfamerazine<br>y by the me-<br>(1) using a<br>vell as by |  |
|  |                   |   | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. G.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.<br>2. Havemann, R. Klin. Wochenschr.<br><u>1940</u> , p. 503. |

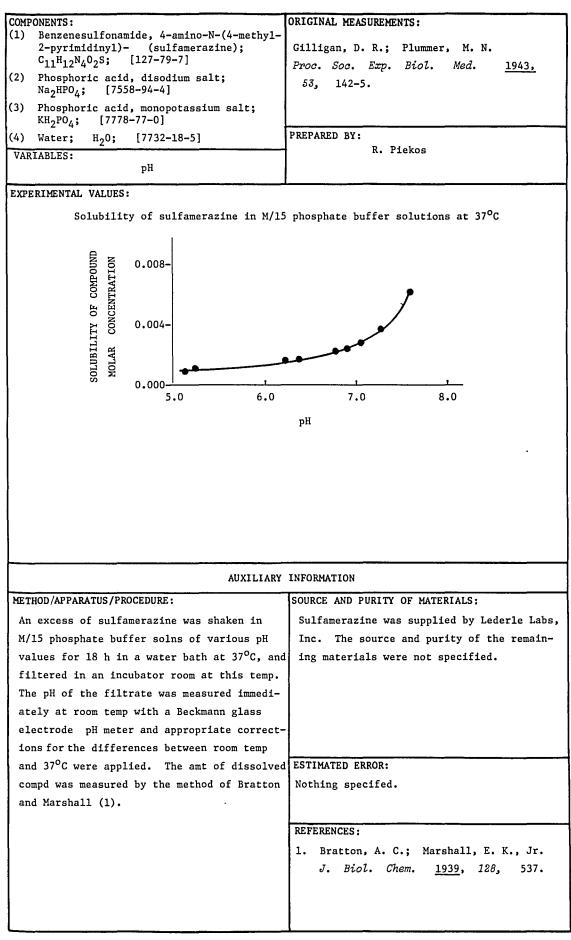
L

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                | Bhattacharyya, R.; Basu, U. P.                  |
| 2-pyrimidinyl)- (sulfamerazine);  | Indian Pharmacist <u>1950</u> , 6(3), 77-8, 86. |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Inatan Inatimacist 1950, 0(07, 77-8, 80.        |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |   |
| VARIABLES:  | PREPARED BY:                                    |
| One temperature: 30 <sup>0</sup> C  | R. Piekos                                       |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamerazine in water a                                      | t 30 <sup>0</sup> C is 24 mg per 100 ml         |
| $(9.1 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler }).$              |   |
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| AUXILIARY   | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                 |
| A weighed sample of sulfamerazine was placed                                | Neither source nor purity of the sulfa-         |
| in a clean reagent bottle and a known vol of                                | merazine was specified.                         |
| water was added. The mixt was shaken in a                                   | Doubly distd water was used.                    |
| mech shaker at 80-100 strokes/min. After                                    |   |
| at least 24 h the mixt was filtered through                                 |   |
| a clean, dried and weighed sintered-glass                                   |   |
| crucible. At the end of the filtration                                      |   |
| the crucible was washed with about 1 ml of                                  |   |
| water, dried at 105°C for 2-3 h, cooled, and                                |   |
| weighed to const wt.  | Soly: not specified.                            |
|   | Temp: ±0.2 <sup>0</sup> C (authors).            |
|   | REFERENCES:                                     |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                           |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                |  |
| 2-pyrimidinyl)- (sulfamerazine);  | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), 37-40. |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |  |
| -   |  |
| VARIABLES:  | PREPARED BY:                                     |
| One temperature: 30°C   | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamerazine in water  | at 30°C is 0.89 mmol/L                           |
| _   |  |
| $(0.24 \text{ g dm}^{-3}, \text{ compiler}).$                               |  |
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| AUXILIARY   | INFORMATION                                      |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                  |
| Sulfamerazine (0.5 g ) was placed in an L-                                  | Nothing specified.                               |
| shaped tube together with 20 ml of water.                                   |  |
| The mixt was shaken in a thermostat until                                   |  |
| equilibrium was attained. The sulfamerazine                                 |  |
| was assayed in the supernatant spectrophoto-                                | 1  |
| metrically at 545 nm on a Beckmann DU spec-                                 |  |
| trophotometer. The results were taken from                                  |  |
| a calibration graph.  |  |
|   | ESTIMATED ERROR:                                 |
|   | Soly: not specified.                             |
|   | Temp: $\pm 1^{\circ}C$ (authors).                |
| · · · · · · · · · · · · · · · · · · ·                                       | temp, at o (additions).                          |
|   | REFERENCES:                                      |
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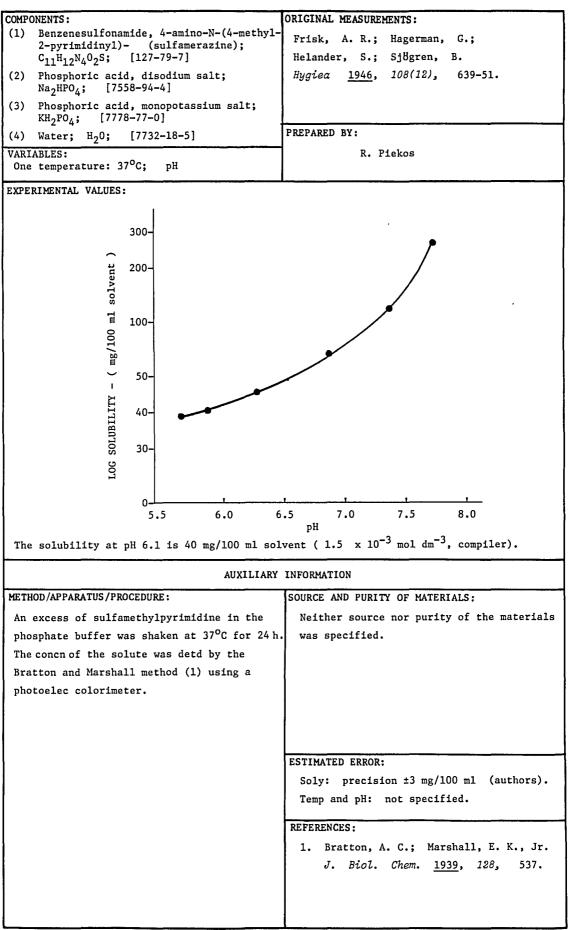
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-  |   |
| 2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Holz, E.; Garcia Onandia, T.; Holz, S.<br>Acta Cient. Venezolana <u>1955,</u> 6(2), |
| (2) Sodium hydroxide; NaOH; [1310-73-2]   | 68-73.  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  | 00-73.  |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| Concentration of NaOH   | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
| Concentration Volume of the NaOH soln requ<br>of NaOH soln to dissolve 1 g of sulfamera<br>at 26 <sup>0</sup> C | ired Solubility of sulfamerazine<br>zine at 26 <sup>0</sup> C                       |
| N cm <sup>3</sup>   | mol dm <sup>-3</sup> NaOH soln <sup>a</sup>   |
| 1/10 40.9   | 0.0925  |
| 1/4 15.8  | 0.239   |
| 1/2 8.0   | 0.473   |
| 1.00 4.0  | 0.946   |
| 1.25 3.2  | 1.18  |
| 1.30 3.3  | 1.15  |
| 1.40 8.6  | 0.440   |
| 1.50 13.2   | 0.287   |
| 2.00 36.4   | 0.104   |
| 2.50 156  | 0.0242  |
| <sup>a</sup> Calculated by compile  | r   |
| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |
| Nothing specified.  | Nothing specified. Distd water was used.  |
|   |   |
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|   |   |
|   |   |
|   | ESTIMATED ERROR:  |
|   | Nothing specified.  |
|   |   |
|   | REFERENCES :  |
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| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(4-methyl-<br/>2-pyrimidinyl)- (sulfamerazine);<br/>C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S; [127-79-7]<br/>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]<br/>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]<br/>(4) Water; H<sub>2</sub>O; [7732-18-5]<br/>VARIABLES:<br/>pH<br/>EXPERIMENTAL VALUES:</pre> | ORIGINAL MEASUREMENTS:<br>Langecker, H.<br>Arch. Exptl. Path. Pharmakol. <u>1948</u> ,<br>205, 291-301.<br>PREPARED BY:<br>R. Piekos |
|--|--|
| pu of the 1/15M Solubility   | y at 37°C  |
| pH of the 1/15MSOLUBIII.<br>phosphate buffermg%  | $10^3$ mol dm <sup>-3</sup> a  |
| 4.9 34   | 1.2  |
| 5.9 35   | 1.3  |
| 6.9 86   | 3.2  |
| 7.5 144  | 5.4  |
|  | `  |
|  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| An excess of sulfamerazine was added to a<br>buffer soln and boiled for 1 h in a sealed<br>ampul followed by keeping the ampul at 37°C.<br>The concn of sulfamerazine was detd colori-<br>metrically by the method of Bratton and<br>Marshall (1) using a Havemann colorimeter<br>(2), as well as by microanal detn of the<br>solid residue.   | Source and purity of the materials were<br>not specified.  |
| ·  | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.                                     |

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| 204  |   |
|--|---|
| COMPONENTS:  | ORIGINAL MEASUREMENTS:                  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4-methyl-<br/>2-pyrimidinyl)- (sulfamerazine)-</li> </ol>  | Riess, W.                               |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]  | Intern. Congr. Chemotherapy, Proc.,     |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                            |
| VARIABLES:<br>One temperature: 20 <sup>0</sup> C; one pH: 7.4  | R. Piekos                               |
| Solubility of sulfamerazine in M/15 S<br>at 20 <sup>0</sup> C is 70 mg% ( 2.7 x 10 <sup>-3</sup> mol   |   |
|  | INFORMATION                             |
|  | ·····                                   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |
| Sörensen buffer solns of varying pH $(7-8)$<br>were prepd, satd with sulfamerazine at $20^{\circ}$ C,<br>their pH was measured at equilibrium, and<br>the sulfamerazine was assayed colorimetri-<br>cally. The measured pH values were then<br>plotted against concn, and the soly at pH<br>7.4 was detd by interpolation (personal<br>communication). | Nothing specified.                      |
|  | ESTIMATED ERROR:                        |
|  | Nothing specified.                      |
|  | REFERENCES :                            |
|  |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |
|---|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(4-methyl-<br/>2-pyrimidinyl)- (sulfamerazine);</pre>                    | Yamazaki, M.; Aoki, M.; Kamada, A.;             |
| 2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Yata, N. Yakuzaigaku <u>1967</u> , 27(1),       |
| <ul><li>(2) Phosphoric acid, disodium salt;</li></ul>   | 37-40.  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  |   |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                       |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:                                    |
| VARIABLES:  | R. Piekos                                       |
| One temperature: 30 <sup>o</sup> C; one pH: 7.4   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfamerazine in a phosp  | nate buffer solution of pH 7.4 ( $\mu$ = 0.17 ) |
|   |   |
| at $30^{\circ}$ C is 2.45 mmol/L ( 0.647 g dm <sup>-3</sup>   | , compiler ).                                   |
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| AUXILIARY   | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                 |
| Sulfamerazine (0,5 g) was placed in an L-   | Nothing specified.                              |
| shaped tube together with 20 ml of the buf-   |   |
| fer soln. The mixt was shaken in a thermo-  |   |
| stat until equilibrium was attained. The  |   |
| sulfamerazine was assayed in the supernatant  |   |
| spectrophotometrically at 545 nm on a Beck-   |   |
| mann DU spectrophotometer. The results were   |   |
| taken from a calibration graph.   |   |
|   | POTIMATED EDDOD.                                |
|   | ESTIMATED ERROR:                                |
|   | Soly and pH: not specified.                     |
|   | Temp: ±1°C (authors).                           |
|   | REFERENCES ;                                    |
| ]   |   |
|   |   |
|   |   |

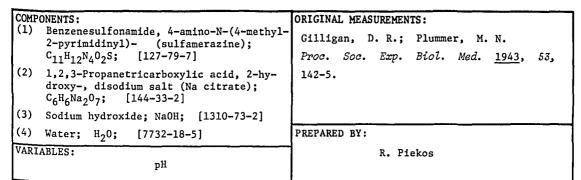
| 256  |   |   |
|------|---|---|
| (1)  | ONENTS:<br>Benzenesulfonamide, 4-amino- <u>N</u> -(4-methyl-<br>2-pyrimidinyl)- (sulfamerazine);<br>$C_{11}H_{12}N_4O_2S$ ; [127-79-7]<br>Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] | ORIGINAL MEASUREMENTS:<br>Hekster, Ch. A.; Vree, T. B.<br>Antibiotics Chemother. <u>1982</u> , 31,<br>22-118. |
| (3)  | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   |   |
| (4)  | Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:  |
| VARI | ABLES: pH   | R. Piekos   |
| EXPE | ERIMENTAL VALUES:   | L   |
|      | Solul   | bility at 25 <sup>0</sup> C   |

| рН               |      |                               |
|------------------|------|-------------------------------|
|                  | mg/1 | $10^4$ mol dm <sup>-3</sup> a |
| 5.5              | 238  | 9.00                          |
| 7.5 <sup>b</sup> | 840  | 31.8                          |

<sup>a</sup>Calculated by compiler.

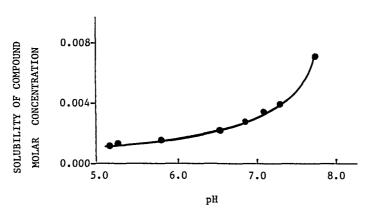
<sup>b</sup>Erroneous pH value of 7.0 is given in the article.

| AUXILIARY  | INFORMATION   |
|--|---|
| METHOD/APPARATUS/PROCEDURE:<br>The earlier developed method (1) was used<br>(personal communication). Satd solns of<br>sulfamerazine were prepd in phosphate buf-<br>fers of pH 5.5 and 7.5 at 25°C. The concn<br>of the solute was measured by means of a<br>Spectra Physics 3500B high-performance<br>liquid chromatograph equipped with a Model<br>748 column oven and a Pye-Unicam LC-UV | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor the purity of the<br>materials was specified.   |
| spectrophotometric detector.   | ESTIMATED ERROR:<br>Soly: the detection limit of the solute by<br>HPLC was 0.5 mg/l (authors).<br>The errors in temp and pH were not specified.<br>REFERENCES:<br>1. Hekster, Y. A.; Vree, T. B.;<br>Damsma, J. E.; Friesen, W. T.<br>J. Antimicrob. Chemother <u>1981</u> , 8,<br>133. |





Solubility of sulfamerazine in M/10 Na citrate + NaOH solution at 37°C



### AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: An excess of sulfamerazine was shaken in M/10 Na citrate + NaOH solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS: Sulfamerazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR: Nothing specified.

**REFERENCES:** 

 Bratton, A. C.; Marshall, E. K., Jr. J. Biol. Chem. <u>1939</u>, 128, 537.

| COMPONENTS:   |                                      | ORIGINAL MEASUREMENTS:  |  |  |  |  |  |
|---|--------------------------------------|---|--|--|--|--|--|
| l) Benzenesulfonamide, 4-a  |                                      |   |  |  |  |  |  |
| 2-pyrimidinyl)- (sulf   |                                      | Sonnenberg, H.; Oelert, H.; Baumann, K.                       |  |  |  |  |  |
| $C_{11}H_{12}N_4O_2S;$ [127-79-   |                                      | Pflügers Arch. Ges. Physiol. <u>1965</u> ,                    |  |  |  |  |  |
| (2) Benzene, methy1- (tolue<br>[108-88-3]                                     | , .                                  | 286, 171-80.  |  |  |  |  |  |
| (3) Mannitol; C <sub>6</sub> H <sub>14</sub> O <sub>6</sub> ; [8              |                                      |   |  |  |  |  |  |
| (4) Phosphoric acid, disodi<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] | um salt;                             |   |  |  |  |  |  |
| (5) Phosphoric acid, monopo   | tassium salt;                        | PREPARED BY:  |  |  |  |  |  |
| кн <sub>2</sub> ро <sub>4</sub> ; [7778-77-0]                                 |                                      | R. Piekos   |  |  |  |  |  |
| (6) Sodium chloride; NaCl;<br>(7) Water; H <sub>2</sub> O; [7732-1            |                                      |   |  |  |  |  |  |
| VARIABLES: pH   |                                      |   |  |  |  |  |  |
| EXPERIMENTAL VALUES:  |                                      | <b></b>   |  |  |  |  |  |
| Relative lipoid solubili  | ty determined on                     | the basis of concentration measurements of                    |  |  |  |  |  |
|   |                                      | $_1$ ) and after (c <sub>e</sub> ) equilibration with toluene |  |  |  |  |  |
|   | рН                                   | $(100 - \frac{100}{c_4}^{c_e})$                               |  |  |  |  |  |
|   | P**                                  |   |  |  |  |  |  |
|   |                                      | <sup>c</sup> i  |  |  |  |  |  |
|   | 5 <sup>a</sup>                       | 8   |  |  |  |  |  |
|   |                                      | 1   |  |  |  |  |  |
|   | 5 <sup>a</sup>                       | 8   |  |  |  |  |  |
| <sup>a</sup> Composition of perfusat  | 5 <sup>a</sup><br>8 <sup>b</sup>     | 8   |  |  |  |  |  |
| • •   | 5 <sup>a</sup><br>8 <sup>b</sup><br> | 8<br>2  |  |  |  |  |  |

| consisting of | 5.5 | ml | of | 0.022M | кн <sub>2</sub> ро <sub>4</sub> | and | 94.5 | ml | of | 0.022M | Na2HPO4. |  |
|---------------|-----|----|----|--------|---------------------------------|-----|------|----|----|--------|----------|--|
|               |     |    |    |        |                                 |     |      |    |    |        |          |  |

| AUXILIARY                                   | INFORMATION                             |
|---|---|
| METHOD/APPARATUS/PROCEDURE:                 | SOURCE AND PURITY OF MATERIALS:         |
| Lipoid solubilities were detd by shaking    | None given.                             |
| equal volumes of the perfusate and toluene  |   |
| for 20 min and measuring the concn of sul-  |   |
| famerazine by the spectrophotometric method |   |
| of Bratton and Marshall (1) in an aq phase  |   |
| before and after this procedure.            |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                        |
|   | None given.                             |
|   | None Broom                              |
|   |   |
|   | REFERENCES:                             |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr. |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|   |   |
|   |   |
|   |   |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4-methyl-   | ORIGINAL MEASUREMENTS:  |
|---|---|
| 2-pyrimidinyl)- (sulfamerazine);  | Sonnenberg, H.; Oelert, H.; Baumann, K.   |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]   | Pflügers Arch. Ges. Physiol. <u>1965</u> ,  |
| (2) Mannitol; C <sub>6</sub> H <sub>14</sub> O <sub>6</sub> ; [87-78-5]   | 286, 171-80.  |
| (3) Methane, trichloro- (chloroform);<br>CHCl <sub>3</sub> ; [67-66-3]  |   |
| <ul> <li>(4) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>  |   |
| (5) Phosphoric acid, monopotassium salt;  | PREPARED BY:  |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   | R. Piekos   |
| (6) Sođium chloride; NaCl; [7647-14-5]<br>(7) Water: H <sub>2</sub> O: [7732-18-5]  |   |
| (7) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES: pH   |   |
| EXPERIMENTAL VALUES:<br>Relative lipoid solubility determined on  | ]   |
| of sulfamerazine in perfusates <sup>a,b</sup> before  |   |
| chloroform  | (c1) and arter (ce) equilibration with  |
| Chioroform  |   |
|   | 100 c   |
| pH (  | $100 - \frac{100 c}{c_4} e$ )   |
|   | -1  |
| 5 <sup>a</sup>  | 72  |
| 8 <sup>b</sup>  | <i></i>   |
| 85  | 34  |
|   | , <u>, , , , , , , , , , , , , , , ,</u>  |
|   |   |
| <sup>a</sup> Composition of perfusate: 110 mmol/1 NaC   | 1, 35 mmol/l mannitol in a phosphate  |
|   | $H_2PO_4$ and 1.2 ml of 0.022M $Na_2HPO_4$ .  |
| buffer consisting of 98.8 ml of 0.022M K  |   |
|   |   |
| buffer consisting of 98.8 ml of 0.022M K<br><sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   | , 100 mmol/l mannitol in a phosphate  |
|   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH   |   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH   | <sub>2</sub> PO <sub>4</sub> and 94.5 ml of 0.022M Na <sub>2</sub> HPO <sub>4</sub> .   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaC1<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:   | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaC1<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking   | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for   | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaC1<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking   | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for   | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method  | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method  | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.   |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:  |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |
| <sup>b</sup> Composition of perfusate: 68 mmol/l NaCl<br>buffer consisting of 5.5 ml of 0.022M KH<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Lipoid solubilities were detd by shaking<br>equal volumes of the perfusate and CHCl <sub>3</sub> for<br>20 min and measuring the concn of sulfa-<br>merazine by the spectrophotometric method<br>of Bratton and Marshall (1) in the aq phase | 2PO4 and 94.5 ml of 0.022M Na2HPO4.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>None given.<br>ESTIMATED ERROR:<br>None given.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |

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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                                     |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-  | Dolique, R.; Foucault, J.                                  |
| 2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Trav. soc. pharm. Montpellier 1952,                        |
| (2) Ethanol; $C_2H_60$ ; [64-17-5]  |  |
| (3) 1,2,3-Propanetriol; C <sub>3</sub> H <sub>8</sub> O <sub>3</sub> ; [56-81-5]                                | 12, 145-53.  |
| (4) Water; H <sub>2</sub> O; [7732-18-5]  |  |
| ••  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 26-28°C  | R. Piekos  |
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| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamerazine in a mixtur   | e of 1,2,3-propanetriol and 95° ethanol                    |
| ( 2:1 by wt ) at 26-28 <sup>0</sup> C is 0.45% ( 1.7  | $\times 10^{-2}$ mol kg <sup>-1</sup> solvent, compiler ). |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                            |
| The sulfamerazine content was detd by diazo-  | Nothing specified.   |
| tization of the amine group in a cold acidi-  | -  |
| fied 0.1N KNO2 soln. An excess of KNO2 was  |  |
| detected by using iodinated starch.   |  |
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|   | ESTIMATED ERROR:   |
|   | Nothing specified.   |
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|   | REFERENCES :   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                 |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                     |  |
| 2-pyrimidinyl)- (sulfamerazine);   | Dolique, R.; Foucault, J.                              |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]  | Trav. soc. pharm. Montpellier <u>1952</u> ,            |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [64-17-5]                          | <i>12</i> , 145–53.                                    |
| (3) 1,2,3-Propanetriol; C <sub>3</sub> H <sub>8</sub> O <sub>3</sub> ; [56-81-5] | •  |
| (4) Urea; $CH_4N_20$ ; [57-13-6]   |  |
|  |  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:   |
| VARIABLES:   | R. Piekos  |
| One temperature: 26-28°C   | A. I IEKOB   |
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| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfamerazine at 26-28°C   | in a saturated solution of urea                        |
| in a mixture of 1,2,3-propanetriol and   | 95 <sup>0</sup> ethanol (2:1 by wt), containing        |
|  | •  |
| 54.5 g of urea per 100 g of the mixture  | e, is 0.465% ( 1.76 x $10^{-2}$ mol kg <sup>-1</sup> , |
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| compiler ).  |  |
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| AUXILIARY  | INFORMATION  |
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| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                        |
| The sulfamerazine content was detd by diazo-                                     | Nothing specified.                                     |
| tization of the amine group in a cold acidi-                                     |  |
|  |  |
| fied 0.1N KNO2 soln. An excess of KNO2 was                                       |  |
| detected by using iodinated starch.  |  |
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|  | ESTIMATED ERROR:                                       |
|  | ESTIMATED ERROR:                                       |
|  | ESTIMATED ERROR:<br>Nothing specified.                 |
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|  | Nothing specified.                                     |

| COMPONENTS:   |                                       | ORIGINAL MEASUREMENTS:                                  |
|---|---------------------------------------|---|
| (1) Benzenesulfonamide, 4-ami   |                                       | Sekikawa, H.; Nakano, M.; Arita, T.                     |
| 2-pyrimidinyl)- (sulfam   | erazine);                             | Chem. Pharm. Bull. <u>1978,</u> 26(1), 118-26.          |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] |                                       |   |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [64-1                         | /->]                                  |   |
|   |                                       |   |
| VARIABLES:  |                                       | PREPARED BY:  |
| Temperature   |                                       | R. Piekos   |
|   |                                       |   |
| EXPERIMENTAL VALUES:  |                                       |   |
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|   |                                       |   |
|   | t/ <sup>0</sup> C Solut               | oility <sup>a</sup>                                     |
|   | 10 <sup>3</sup> mol                   | dm <sup>-3</sup> solution                               |
| -   |                                       |   |
|   | 10                                    | 3.57  |
|   | 20                                    | 4.46  |
|   | 30                                    | 6.32  |
|   | 40                                    | 8.99  |
|   |                                       | 2.8   |
|   | 50 5                                  |   |
| -   | • • • • • • • • • • • • • • • • • • • |   |
| <sup>a</sup> Original d   | ata are presente                      | ed graphically.   |
|   |                                       |   |
| Ine numeri  | cal values are §                      | given by the authors.                                   |
|   |                                       |   |
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|   | AUXILIARY                             | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   |                                       | SOURCE AND PURITY OF MATERIALS:                         |
| After attaining equilibrium,  | sample solns                          | Sulfamerazine, mp 235 <sup>0</sup> C, was obtained from |
| were removed by a syringe and   | filtered quick-                       | Na sulfamerazine (Tanabe Seiyaku Co.) by                |
| ly through a membrane filter  | (pore size 0.2                        | addn of HCl <sub>ac</sub> and recrystn from EtOH. Abs   |
| $\mu$ ) and sulfamerazine was ass   | ayed spectropho-                      |   |
| tometrically at 270 nm using  | a Hitachi Type                        | EtOH following the conventional procedures.             |
| 200-20 spectrophotometer.   |                                       |   |
|   |                                       |   |
|   |                                       |   |
|   |                                       | ESTIMATED ERROR:  |
|   |                                       | Nothing specified.                                      |
|   |                                       |   |
|   |                                       | REFERENCES :  |
|   |                                       | 121 LILINGS ;   |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                   |
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                |  |
| 2-pyrimidinyl)- (sulfamerazine);  | <i>Sci. Ed.</i> <u>1948</u> , <i>37</i> , 345.           |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] |  |
| (2) 2-Propanol; C <sub>3</sub> H <sub>8</sub> 0; [67-63-0]                  |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 25 <sup>0</sup> C  | R. Piekos  |
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| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamerazine in 2-propa                                      | nol at 25 <sup>°</sup> C is 0.1740 g/100 cm <sup>3</sup> |
|   | -  |
| solution ( $6.583 \times 10^{-3} \text{ mol dm}^{-3}$ , comp                | iler).   |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                          |
| Satd solns of sulfamerazine in 2-propanol                                   | The sulfamerazine was manufd by Sharp                    |
| were prepd at 25°C and definite vols of the                                 | and Dohme and was of the U.S.P. purity.                  |
| solns were measured into tared dishes by                                    | The source and purity of 2-propanol were                 |
| means of standard pipets. The alcohol was                                   | not specified.   |
| allowed to evap at room temp and the residue                                | -  |
|   |  |
| Was dried at 105 <sup>o</sup> C. In the case of losses                      |  |
| due to apparent decompn, the residue was                                    |  |
| dried in a desiccator (1).  | ECTIMATED EDDAD.   |
|   | ESTIMATED ERROR:   |
|   | Nothing specified.                                       |
|   |  |
|   | REFERENCES:  |
|   |  |
|   | 1. Burlage, H. M. J. Pharm. Assoc.,                      |
|   | Sci. Ed. <u>1947</u> , 36(1), 16.                        |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                         |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                |  |
| 2-pyrimidinyl)- (sulfamerazine);  | Sunwoo, C.; Eisen, H.                          |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | J. Pharm. Sci. <u>1971</u> , 60, 238-44.       |
|   |  |
| (2) Ethanol, 2-ethoxy-; C <sub>4</sub> H <sub>10</sub> 0 <sub>2</sub> ;     |  |
| [110-80-5]  |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                      |
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| EXPERIMENTAL VALUES:  |  |
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| The mole fraction solubility of sulfame                                     | cazine in 2-ethoxyethanol at 25 <sup>0</sup> C |
|   |  |
| is 0.0109 ( 3.29 g/100 g solution, comp:                                    | lier ),  |
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| AUXILIARY   | INFORMATION                                    |
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| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                |
| Soly was detd by the method reported by                                     | The USP sulfamerazine (American Cyanamid       |
| Restaino and Martin (1). Sulfamerazine was                                  | Co., Pearl River, N.Y.), recrystd from         |
| assayed on a Coleman-Hitachi 124 double-bear                                | warm alcohol and an industrial grade 2-        |
| spectrophotometer at 270 nm after diln of a                                 | ethoxyethanol (Cellosolve solvent, Union       |
| sample with 95% ethanol or water.   | Carbide, New York, N.Y.) were used.            |
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|   | ESTIMATED ERROR:                               |
|   | Temp: $\pm 1.0^{\circ}$ (authors).             |
|   | Soly: the mean of 3 runs was given             |
|   | (authors).                                     |
|   | REFERENCES:                                    |
|   |  |
|   | 1. Restaino, F. A.; Martin, A. N.              |
|   | J. Pharm. Sci. <u>1964</u> , 53, 636.          |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methy1-                                |  |
| 2-pyrimidinyl)- (sulfamerazine);  | Intern. Congr. Chemotherapy, Proc.,          |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | 3rd, Stuttgart <u>1963</u> , 1, 627-32.      |
| (2) Methane, trichloro- (chloroform);                                       |  |
| CHCl <sub>3</sub> ; [67-66-3]   |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature   | R. Piekos                                    |
| •                                     |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfamerazine in chlorof                                      | orm at 20°C is 37 mg% ( $1.4 \times 10^{-3}$ |
| mol $dm^{-3}$ solution, compiler ).   |  |
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| AUXILIARY   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| Nothing specified.  |  |
| Nothing specified.  | Nothing specified.                           |
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|   | ESTIMATED ERROR:                             |
|   | Nothing specified.                           |
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|   | REFERENCES:                                  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-                                | Yamazaki, M.; Aoki, M.; Kamada, A.;       |
| 2-pyrimidinyl)- (sulfamerazine);  | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | 37-40.                                    |
| <pre>(2) Methane, trichloro- (chloroform);</pre>                            |   |
| CHC1 <sub>3</sub> ; [67-66-3]   |   |
| VARIABLES:  | PREPARED BY:                              |
| One temperature: 30 <sup>0</sup> C  | R. Piekos                                 |
| one temperature. 50 G   | A. LICKOS                                 |
| EXPERIMENTAL VALUES:  |   |
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| Calubrithm of sulfarmonday in oblass  | form of 2000 to 2 00 mmol/I               |
| Solubility of sulfamerazine in chloro                                       | JIOLM AL 30 C 18 3.00 MMOT/L              |
| $(0.814 \text{ g dm}^{-3}, \text{ compiler}).$                              |   |
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| AUXILIARY   | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:           |
| Sulfamerazine (0.5 g) was placed in an L-                                   | Nothing specified.                        |
| shaped tube together with 20 ml of chloro-                                  |   |
| form. The mixt was shaken in a thermostat                                   |   |
| until equilibrium was attained. The sulfa-                                  |   |
| merazine was assayed in the supernatant                                     |   |
| spectrophotometrically at 545 nm on a Beck-                                 |   |
| mann DU spectrophotometer. The results                                      |   |
| were taken from a calibration graph.  |   |
|   | ESTIMATED ERROR:                          |
|   | Soly: not specified.                      |
|   | Temp: ±1 <sup>0</sup> C (authors).        |
|   | REFERENCES :                              |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-        |                            | ORIGINAL MEASUREMENTS:                            |
|--|----------------------------|---|
|  | •                          | Sekikawa, H.; Nakano, M.; Arita, T.               |
|  | famerazine);               | Chem. Pharm. Bull. 1978, 26(1),                   |
| $C_{11}H_{12}N_4O_2S;$ [127-79]                  | -7]                        | 118-26.   |
| (2) 2-Pyrrolidinone, 1-eth                       | ynyl-,polymers             | 110-20.   |
| (poly(vinyl pyrrolidon                           |                            |   |
| [9003-39-8] K-15                                 |                            |   |
|  | / 17 F]                    | PREPARED BY:                                      |
| (3) Ethanol; C <sub>2</sub> H <sub>6</sub> 0; [6 | 4-1/-5J                    | R. Piekos   |
| VARIABLES:<br>Temperature                        |                            |   |
|  | <del></del>                |   |
| EXPERIMENTAL VALUES:                             |                            |   |
| 1  |                            |   |
|  |                            |   |
|  |                            |   |
|  | •                          |   |
|  | $M \times 10^2$            | sulfamerazine                                     |
|  | t/ <sup>0</sup> C solubil: | ized by 1M vinyl                                  |
|  | pvrroli                    | done equivalent                                   |
| ·  |                            | •   |
|  | 10.0                       | 0. (01  |
|  | 10.0                       | 0.631   |
|  |                            |   |
|  | 20.0                       | 0.770   |
|  | 20.0                       | 0.050   |
|  | 30.0                       | 0.950   |
|  |                            |   |
| l.   | 40.0                       | 1.16  |
| }  |                            | 1 00  |
|  | 50.0                       | 1.39  |
|  |                            |   |
| · · ·  |                            |   |
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|  |                            |   |
|  |                            |   |
|  | AUXILIARY                  | INFORMATION                                       |
| METHOD/APPARATUS/PROCEDURE                       | •                          | SOURCE AND PURITY OF MATERIALS:                   |
|  |                            | Sulfamerazine, mp 235°C, was obtained from        |
| After attaining equilibring                      |                            |   |
| were removed by a syringe                        | and filtered quick         |   |
| ly through a membrane fil:                       | ter (pore size             | addn of HCl <sub>aq</sub> and recrystn from EtOH. |
| $0.2\mu$ ) and sulfamerazine v                   | was assayed spec-          | Poly(viny1 pyrrolidone) K-15 was from Dai-        |
| trophotometrically at 270                        |                            |   |
|  | -                          |   |
| Type 200-20 spectrophotom                        |                            | was obtained by drying and distn of EtOH          |
| cant absorbance was found                        | for poly(vinyl             | following the conventional procedure.             |
| Pyrrolidone).                                    |                            |   |
|  |                            | ESTIMATED ERROR:                                  |
|  |                            |   |
|  |                            | Nothing specified.                                |
|  |                            |   |
|  |                            |   |
| 1  |                            | REFERENCES:                                       |
|  |                            |   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                         |
|--|--|
| <ol> <li>Zinc, bis[4-amino-N-(4-methyl-2-pyri-</li> </ol>  | Fox, Ch. L., Jr.; Modak, S.;                   |
| midiny1)benzenesulfonamidato- <u>N</u> N,0]-   | Stanford, J. W.; Fox, P. L.                    |
| (Zn(II) sulfamerazine); C <sub>22</sub> H <sub>20</sub> N <sub>8</sub> 0 <sub>4</sub> S <sub>2</sub> Zn; | Scand. J. Plast. Reconstr. Surg. <u>1979</u> , |
| [71496-63-4]   | 13(1), 89-94.                                  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:                                   |
| One temperature: 28-30°C   | R. Piekos                                      |
| one cemperature. 20-50 C   | A. FIERDS                                      |
| EXPERIMENTAL VALUES:   |  |
| EXTERIAL VALUES.   |  |
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|  |  |
| Solubility of Zn(II) sulfamerazine in  |  |
| is 25.2 mg% ( $4.24 \times 10^{-4}$ mol dm <sup>-3</sup> sol   | ution, compiler ).                             |
|  |  |
|  |  |
| <sup>a</sup> Value given by one of the authors ( S   | 5. M. ) in personal communication.             |
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| AUXILIARY  | INFORMATION                                    |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                |
| Satd soln of Zn(II) sulfamerazine was prepd  | The Zn(II) sulfamerazine was prepd by the      |
| inwater and after 24 h aliquots from the   | authors as follows: an inorg Zn salt was       |
| clear supernatant were assayed for sulfa-  | reacted with Na salt of sulfamerazine and      |
| merazine content using the colorimetric  | the ppt was analyzed and characterized. No     |
| method of Bratton and Marshall (1). The soly   | details were given, however.                   |
| value was then calcd from the molecular  | Purity of the materials was not specified.     |
| formula.   | • •••••••••••••••••••••••••••••••••••••        |
|  |  |
|  |  |
|  | ESTIMATED ERROR:                               |
|  | Nothing specified.                             |
|  |  |
|  | REFERENCES:                                    |
|  | 1. Bratton, A. C.; Marshall, E. K, Jr.         |
|  | J. Biol. Chem. 1939, 120, 537.                 |
|  | <i>a. 2000. onem. <u>1757</u>, 120, 351.</i>   |
|  |  |
|  |  |

| COMPONENTS:               |   | EVALUATOR:  |
|---------------------------|---|---|
| (1) Acetamide             | e, N-[4-[[(4-methy1-2-pyri-             | Anthony N. Paruta   |
| midinyl)a                 | mino]sulfonyl]phenyl-                   | Department of Pharmaceutics   |
|                           | sulfamerazine)                          | University of Rhode Island  |
| $C_{13}H_{14}N_{4}C_{13}$ | ) <sub>3</sub> S; [127-73-1]            | Kingston, Rhode Island, USA   |
|                           | 5                                       | and   |
| (2) Water                 |   | Ryszard Piekos  |
|                           |   | Faculty of Pharmacy, University of Gdansk   |
|                           |   |   |
| CRITICAL EVALU            |   | Gdansk, Poland 1986   |
|                           | ATION:<br>.ubility of Acetyl sulfameraz | Gdansk, Poland 1986   |
|                           |   | Gdansk, Poland 1986   |
|                           | ubility of Acetyl sulfameraz.           | Gdansk, Poland 1986<br>gine in water, 310K<br>10 <sup>4</sup> mol dm <sup>-3</sup> (*indicates mol kg <sup>-1</sup> )         |
|                           | ubility of Acetyl sulfameraz.           | Gdansk, Poland 1986<br>Sine in water, 310K<br>10 <sup>4</sup> mol dm <sup>-3</sup> (*indicates mol kg <sup>-1</sup> )<br>310K |

There is a 15% difference in the two closer values (1,3). Roblin's (1) is based using a 24 hour equilibrium time, but that of Sapozhnikova and Postovskii (3) used only one hour, probably a presaturation condition, which is the probable reason for the lower value (1). The approximate solubility in water at 310K can be given as 8.5 x  $10^{-4}$  mol dm<sup>-3</sup>. This value is consistant with the parent compound, it being 14 times smaller.

#### **REFERENCES:**

- (1) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P.

- J. Am. Chem. Soc. <u>1940</u>, 62, 2002-5. (2) Kikuth, W. Med. Welt <u>1943</u>, 17(26/27), 483-6. (3) Sapozhnikova, N.V.; Postovskii, I. Ya. Zh. Prikl. Khim. <u>1944</u>, 17, 427-34.

| 270  |  |
|--|--|
| <pre>COMPONENTS: (1) Acetamide, N-[4-[[(4-methyl-2-pyrimidin-<br/>yl)amino]sulfonyl]phenyl]- (acetyl<br/>sulfamerazine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub>S;<br/>[127-73-1] (2) Water; H<sub>2</sub>O; [7732-18-5]</pre>  | ORIGINAL MEASUREMENTS:<br>Roblin, R. O., Jr.; Williams, J. H.;<br>Winnek, P. S.; English, J. P.<br>J. Am. Chem. Soc. <u>1940</u> , 62, 2002-5. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfamerazine in v<br>solution ( 9.14 x 10 <sup>-4</sup> mol dm <sup>-3</sup> , compi   |  |
| AUXILIARY  | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:  |
| Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The sus-<br>pension was then agitated for 24 h in a ther-<br>mostat at 37°C. A sample of the satd soln<br>was withdrawn through a glass filter, dild,<br>and analyzed by the Marshall method (1) using | Acetyl sulfamerazine, mp 248-9 <sup>0</sup> C (cor), was<br>prepd by the authors. Anal: %C 51.0 (calcd   |

ESTIMATED ERROR: Nothing specified.

**REFERENCES:** 

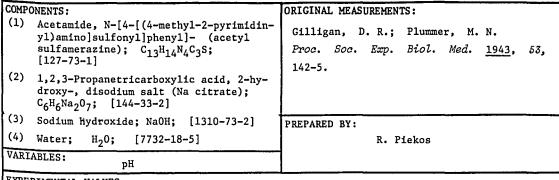
ter for comparing the colors developed with

those of the standards.

 Bratton, A. C.; Marshall, E. K., Jr. J. Pharmacol. <u>1939</u>, 66, 4.

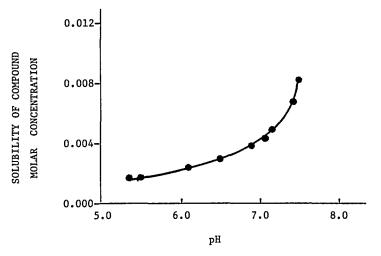
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                               |
|---|--|
| (1) Acetamide, N-[4-[[(4-methyl-2-pyrimidin-  | 17.11. sl. 17  |
| yl)amino]sulfonyl]phenyl]- (acetyl  | Kikuth, W.   |
| <pre>sulfamerazine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>0<sub>3</sub>S;</pre> | Med. Welt <u>1943</u> , 17(26/27), 483-6.            |
| [127-73-1]<br>(2) Nature V 0 (7700 10 5)  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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|   |  |
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|   |  |
|   |  |
| Solubility of acetyl sulfamerazine in v   | $rator at 37^{\circ}C$ is 115 mg/100 cm <sup>3</sup> |
|   |  |
| solution ( $3.75 \times 10^{-3} \text{ mol dm}^{-3}$ , comp                         | ller ).  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                      |
| Nothing specified.  | Acetyl sulfamerazine: not specified.                 |
| working specified.  |  |
|   | The pH of the water was 7.8                          |
|   |  |
|   |  |
|   |  |
|   |  |
|   |  |
|   |  |
|   | ESTIMATED ERROR:                                     |
|   | Nothing specified.                                   |
|   |  |
|   | DEPENDING  |
|   | REFERENCES:  |
|   |  |
|   |  |
|   |  |
|   |  |
|   |  |

| 272  |  |
|--|--|
| COMPONENTS:<br>(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidin<br>yl)amino]sulfonyl]phenyl]- (acetyl<br>sulfamerazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S;<br>[127-73-1]<br>(2) Water; H <sub>2</sub> O; [7732-18-5]<br>VARIABLES:<br>Temperature<br>EXPERIMENTAL VALUES:  | ORIGINAL MEASUREMENTS:<br>Sapozhnikova, N. V.; Postovskii, I. Ya.<br>Zh. Prikl. Khim. <u>1944</u> , 17, 427-34.<br>PREPARED BY:<br>R. Piekos   |
| t/°C   | ubility<br>mol kg <sup>-1</sup> water <sup>a</sup>   |
| 37       0.024         75       0.170  | 0.78<br>5.56   |
| <sup>2</sup> Calculated by compi   | ler  |
| AUXILIAR   | ( INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Acetyl sulfamerazine was dissolved in water<br>to form a satd soln which was occasionally<br>agitated in a glass vessel immersed in a<br>thermostat. The equilibrium was usually<br>attained after 1 h. Five - to 100-cm <sup>3</sup><br>samples of the satd soln were placed in Pt<br>crucibles or dishes and evapd to dryness at<br>temps lower than 110-115°C. The residue<br>was dried to const wt at 105-110°C and<br>weighed. | SOURCE AND PURITY OF MATERIALS:<br>Pure, recrystd acetyl sulfamerazine was used<br>Its mp conformed to that reported in the<br>literature.<br>Purity of the water was not specified. |
|  |  |



### EXPERIMENTAL VALUES:

Solubility of acetyl sulfamerazine in M/10 Na citrate + NaOH solutions at  $37^{\circ}C$ 



#### AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                             | SOURCE AND PURITY OF MATERIALS:            |
|---|--|
| An excess of acetyl sulfamerazine was shaken            | Acetyl sulfamerazine was supplied by       |
| in M/10 Na citrate + NaOH solns of various              | Lederle Labs, Inc. The source and purity   |
| $PH$ values for 18 h in a water bath at $37^{\circ}C$ , | of the remaining materials were not speci- |
| and filtered in an incubator room at this               | fied.                                      |
| temp. The pH of the filtrate was measured               |  |
| immediately with a Beckmann glass electrode             |  |
| pH meter and appropriate corrections for                |  |
| the differences between room temp and 37°C              |  |
| were applied. The amt of dissolved compd                | ESTIMATED ERROR:                           |
| was measured by the method of Bratton and               | Nothing specified.                         |
| Marshall (1).   |  |
|   |  |
|   | REFERENCES:                                |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
|   | J. Biol. Chem. 1939, 128, 537.             |
|   |  |
|   |  |
| 1   | 1  |

| 274   |   |
|---|---|
| <ul> <li>COMPONENTS:</li> <li>(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidin-yl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>C<sub>3</sub>S; [127-73-1]</li> <li>(2) Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> <li>(3) Phosphoric acid, monopotassium salt; KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> | ORIGINAL MEASUREMENTS:<br>Gilligan, D. R.; Plummer, M. N.<br>Proc. Soc. Exp. Biol. Med. <u>1943</u> , 53,<br>142-5. |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES:  | R. Piekos   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of acetyl sulfamerazine in M/:<br>0.012-   | 15 phosphate buffer solutions at 37 <sup>0</sup> C  |
| 0.002-<br>0.008-<br>0.004-<br>0.004-<br>0.000-<br>5.0<br>6.0<br>pH  | 7.0   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>An excess of acetyl sulfamerazine was sha-  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS;<br>Acetyl sulfamerazine was supplied by Leder-                       |
| ken in M/15 phosphate buffer solns of var-<br>ious pH values for 18 h in a water bath at<br>37°C, and filtered in an incubator room at<br>this temp. The pH of the filtrate was meas-<br>ured immediately at room temp with a Beck-<br>mann glass electrode pH meter and appropri-<br>ate corrections for the differences between   | le Labs, Inc. The source and purity of<br>the remaining materials were not specified.                               |
| room temp and 37 <sup>0</sup> C were applied. The amt<br>of dissolved compd was measured by the me-<br>thod of Bratton and Marshall (1).  | ESTIMATED ERROR:<br>Nothing specified.  |
|   | REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.                    |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |  |
|---|--|--|
| (1) Acetamide, N-[4-[[(4-methyl-2-pyrimi-   | Budah A D A Hanangara C A  |  |
| <pre>dinyl)amino]sulfonyl]phenyl]- (acetyl sulfamethylpyrimidine);</pre>  | Frisk, A. R.; Hagerman, G.;  |  |
| $C_{13}H_{14}N_{4}O_{3}S;$ [127-73-1]   | Helander, S.; Sjögren, B.  |  |
| <ul> <li>Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>  | Hygiea <u>1946</u> , 108(12), 639 <b>-</b> 51.   |  |
| <ul> <li>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul>  | PREPARED BY:   |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | R. Piekos  |  |
| VARTABLES:  |  |  |
| One temperature: 37°C; one pH: 6.1<br>EXPERIMENTAL VALUES:  | L  |  |
| Solubility of acetyl sulfamethylpyrimi<br>pH 6.1 at 37 <sup>0</sup> C is 53 mg/100 ml solvent   |  |  |
| AUXILIARY   | INFORMATION  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |  |
| An excess of acetyl sulfamethylpyrimidine in<br>the phosphate buffer was shaken at 37°C for<br>24 h. The concn of the solute was detd by<br>the Bratton and Marshall method (1) using a<br>photoelec colorimeter. |  |  |
|   | ESTIMATED ERROR:   |  |
|   | Soly: precision ±4 mg/100 ml (authors).  |  |
|   | Temp and pH: not specified.  |  |
|   | REFERENCES:  |  |
|   | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.<br/>J. Biol. Chem. <u>1939</u>, 128, 537.</li> </ol> |  |
| 1   | 1  |  |

| COMPONENTS: |  |   |                                |            | ORIGINAL MEASUREMENTS:   |      |
|-------------|--|---|--------------------------------|------------|--|------|
|             | dinyl)amino<br>(N <sup>4</sup> -acetyls<br>C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S | sulfony<br>ulfamera<br>; [127<br>acid, di | [127-73-1]<br>, disodium salt; |            | Hekster, Ch. A.; Vree,<br>Antibiotics Chemother.<br>22-118.              | 31,  |
| (3)         | Phosphoric<br>KH <sub>2</sub> PO <sub>4</sub> ; [  | acid, mc<br>7778-77-                      |                                | um salt;   | PREPARED BY:   | <br> |
| (4)         | Water; H <sub>2</sub>  | 0; [77                                    | 32-18-5]                       |            | R. Piekos  |      |
| VARI        | ABLES:   | pH  |                                |            |  |      |
| EXPE        | RIMENTAL VALU  | · · · ·                                   |                                |            |  | <br> |
| EXPE        | RIMENTAL VALU  | · · · ·                                   | рН                             | Sc         | plubility at 25 <sup>0</sup> C   |      |
| EXPE        | RIMENTAL VALU  | · · · ·                                   | рН                             | 50<br>mg/1 | olubility at 25 <sup>0</sup> C<br>10 <sup>3</sup> mol dm <sup>-3 a</sup> |      |
| EXPE        | RIMENTAL VALU  | · · · ·                                   | рН<br>5.5                      | <u></u>    |  |      |

<sup>a</sup>Calculated by compiler

<sup>b</sup>Erraneous pH value of 7.0 is given in the article.

| AUXILIARY  | INFORMATION   |
|--|---|
| METHOD/APPARATUS/PROCEDURE:<br>The earlier developed method (1) was used<br>(personal communication). Satd solns of<br>N <sup>4</sup> -acetylsulfamerazine were prepd in phos-<br>phate buffers of pH 5.5 and 7.5 at 25°C.<br>The concn of the solute was measured by<br>means of a Spectra Physics 3500B high-per-<br>formance liquid chromatograph equipped with<br>a Model 748 column oven and a Pye-Unicam | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor the purity of the<br>materials was specified.   |
| LC-UV spectrophotometric detector.   | <ul> <li>ESTIMATED ERROR:<br/>Soly: the detection limit of the solute by<br/>HPLC was 0.5 mg/l (authors).<br/>The errors in temp and pH were not specified.</li> <li>REFERENCES:</li> <li>1. Hekster, Y. A.; Vree, T. B.;<br/>Damsma, J. E.; Friesen, W. T.<br/>J. Antimicrob. Chemother. <u>1981</u>,<br/>8, 133.</li> </ul> |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                  |
|--|---|
| (1) Acetamide, N-[4-[[(4-methyl-2-pyrimi-  | Sonnenberg, H.; Oelert, H.; Baumann, K. |
| dinyl)amino]sulfonyl]phenyl]-<br>(acetylsulfamerazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S; | Pflügers Arch. Ges. Physiol. 1965,      |
| [127-73-1]   | 286, 171-80.                            |
| $C_7H_8$ ; [108-88-3]  |   |
| (3) Mannitol; C <sub>6</sub> H <sub>14</sub> O <sub>6</sub> ; [87-78-5]  |   |
| (4) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                                    |   |
| (5) Phosphoric acid, monopotassium salt;   | PREPARED BY:                            |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]<br>(6) Sodium chloride; NaCl; [7647-14-5]                                  | R. Piekos                               |
| (7) Water; H <sub>2</sub> O; [7732-18-5]   |   |
| VARIABLES: pH  |   |
| EXPERIMENTAL VALUES:   | -                                       |
| Relative lipoid solubility determined  |   |
| measurement of acetylsulfamerazine in  | -                                       |
| and after (c <sub>e</sub> ) equilibration with tolu  | ene                                     |
|  |   |
|  | $100 c_{0}$                             |
| рН (1  | $00 - \frac{100 c_{e}}{c_{i}} $         |
| -a   |   |
| 5 <sup>a</sup>   | 8                                       |
| 8 <sup>b</sup>   | 0                                       |
| buffer consisting of 5.5 ml of 0.022M KH   |   |
| AIIXILIARY   | INFORMATION                             |
|  |   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |
| Lipoid solubilities were detd by shaking   | None given.                             |
| equal volumes of the aperfusate and toluene  |   |
| with acetylsulfamerazine for 20 min and  |   |
| measuring the concn of acetylsulfamerazine   |   |
| by the spectrophotometric method of Bratton  |   |
| and Marshall (1) in an aq phase before and   |   |
| after this procedure.  |   |
|  |   |
|  | ESTIMATED ERROR:                        |
|  | None given.                             |
|  |   |
|  |   |
|  | REFERENCES:                             |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr. |
|  | J. Biol. Chem. 1939, 128, 537.          |
|  |   |
|  |   |
|  |   |

|      | ONENTS:   | ORIGINAL MEASUREMENTS:                    |
|------|---|---|
| (1)  | Acetamide, N-[4-[[(4-methy1-2-pyri-   | Sonnenberg, H.; Oelert, H.; Baumann, K.   |
|      | midinyl)amino]sulfonyl]phenyl]-   |   |
|      | (acetylsulfamerazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S;<br>[127-73-1] | Pflügers Arch. Ges. Physiol. <u>1965,</u> |
| (2)  | Mannitol; C <sub>6</sub> H <sub>14</sub> O <sub>6</sub> ; [87-78-5]                                   | 286, 171-80.                              |
| (3)  | Methane, trichloro- (chloroform);   |   |
|      | CHC1 <sub>3</sub> ; [67-66-3]   |   |
| (4)  | Phosphoric acid, disodium salt;   |   |
|      | Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | PREPARED BY:                              |
| (5)  | Phosphoric acid, monopotassium salt;  | PREPARED BY:                              |
|      | KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   | R. Piekos                                 |
| (6)  | Sodium chloride; NaCl; [7647-14-5]  |   |
| (7)  | Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARI | ABLES: pH   |   |

EXPERIMENTAL VALUES:

Relative lipoid solubility determined on the basis of concentration measurements of acetylsulfamerazine in perfusates<sup>a,b</sup> before  $(c_1)$  and after  $(c_e)$  equilibration with chloroform

| рH             | $(100 - \frac{100 c}{c_1}e$ | ) |
|----------------|-----------------------------|---|
| 5 <sup>a</sup> | 42                          |   |
| 8 <sup>b</sup> | 0                           |   |

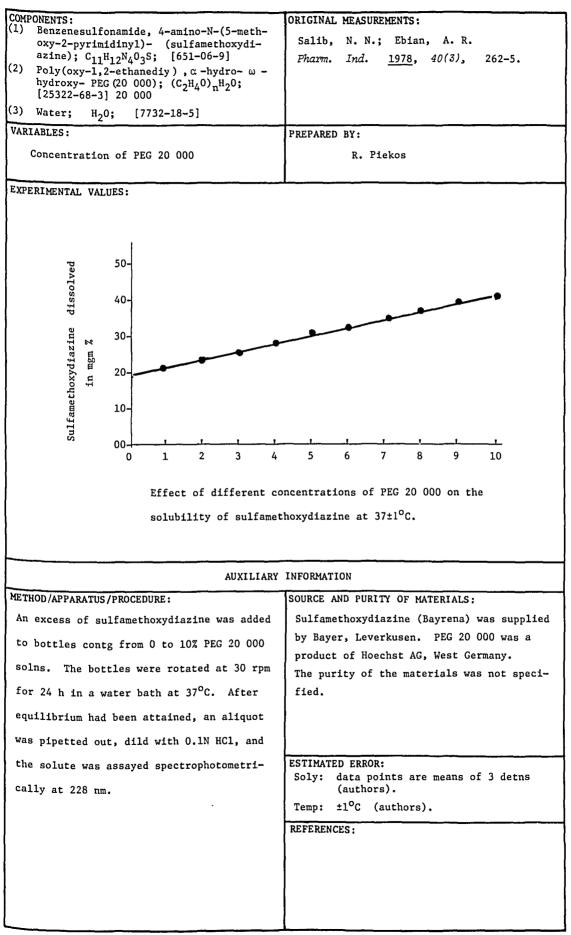
<sup>a</sup>Composition of perfusate: 110 mmol/1 NaCl, 35 mmol/1 mannitol in a phosphate

buffer conisting of 98.8 ml of 0.022M KH<sub>2</sub>PO<sub>4</sub> and 1.2 ml of 0.022M Na<sub>2</sub>HPO<sub>4</sub>. <sup>b</sup>Compositor of perfusate: 68 mmol/l NaCl, 100 mmpl/l mannitol in a phosphate buffer consisting of 5.5 ml of 0.022M KH<sub>2</sub>PO<sub>4</sub> and 94.5 ml of 0.022M Na<sub>2</sub>HPO<sub>4</sub>.

| AUXILIARY                                    | INFORMATION                             |
|--|---|
| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:         |
| Lipoid solubilities were detd by shaking     | None given.                             |
| equal volumes of the perfusate and chloro-   |   |
| form with acetylsulfamerazine for 20 min and |   |
| measuring the concn of acetylsulfamerazine   |   |
| by the spectrophotometric method of Bratton  |   |
| and Marshall (1) in an aq phase before and   |   |
| after this procedure.                        |   |
|  |   |
|  | ESTIMATED ERROR:                        |
|  | None given                              |
|  |   |
|  | REFERENCES:                             |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr. |
|  | J. Biol. Chem. <u>1939,</u> 128, 537.   |
|  |   |
|  |   |
|  |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                 |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-               | Roblin, R. O., Jr.; Winnek, P. S.;                     |
| <pre>methoxy-2-pyrimidiny1)-;</pre>                 | English, J. P. J. Am. Chem. Soc.                       |
| $C_{11}H_{12}N_4O_3S;$ [3213-22-7]                  |  |
|   | <u>1942,</u> 64, 567-70.                               |
| <sup>(2)</sup> Water; H <sub>2</sub> 0; [7732-18-5] |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 37°C                               | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:                                |  |
|   |  |
|   |  |
|   |  |
|   |  |
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|   |  |
| Solubility of 4-amino-N-(4-methoxy-2-               | pyrimidinyl)benzenesulfonamide in                      |
|   |  |
| water at 37°C is 18.2 mg/100 cm <sup>3</sup> solu   | tion (6.49 $10^{-4}$ mol dm <sup>-3</sup> , compiler). |
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|   | INFORMATION  |
|   | ······································                 |
| METHOD / APPARATUS / PROCEDURE :                    | SOURCE AND PURITY OF MATERIALS:                        |
| Excess sulfonamide in water was heated and          | The sulfonamide, mp 241-2°C, was prepd                 |
| stirred on a steam bath for 30 min. The             | by the authors. Anal: %C 47.2 (calcd                   |
| suspension was then agitated for 24 h in a          | 47.1); ZH 4.4 (4.3); ZN 19.9 (20.0).                   |
|   | Purity of the water was not specified.                 |
| thermostat at 37°C. A sample of the satd            | Purity of the water was not specified.                 |
| soln was withdrawn through a glass filter,          |  |
| dild, and analyzed by the Marshall method           |  |
| (1) using a General Electric recording              |  |
| spectrophotometer for comparing colors deve-        | 1  |
| loped with those of the standards.                  | ESTIMATED ERROR:                                       |
|   | Nothing specified.                                     |
| 1   |  |
| •   |  |
|   | REFERENCES :   |
|   |  |
|   | 1. Bratton, A.C.; Marshall, E. K., Jr.                 |
|   | J. Pharmacol. <u>1939</u> , 66, 4.                     |
| 1   |  |
|   |  |
|   | 1  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-(5-meth-oxy-2-pyrimidinyl)- (sulfamethoxydi-azine); C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>S; [651-06-9]</li> <li>(2) Poly(oxy-1,2,-ethanediyl), α-hydro-ω-hydroxy- (PEG 6000); (C<sub>2</sub>H<sub>4</sub>O)<sub>n</sub>H<sub>2</sub>O; [25322-68-3] 6000</li> </ul>          | Salib, N. N.; Ebian, A. R.<br><i>Pharm. Ind.</i> <u>1978</u> , 40(3), 262-5.  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| Concentration of PEG 6000  | R. Piekos   |
| EXPERIMENTAL VALUES:   |   |
| 50-<br>50-<br>90-<br>90-<br>90-<br>90-<br>90-<br>90-<br>90-<br>90-<br>90-<br>9   |   |
| 1  | ncentrations of PEG 6000 on the<br>hoxydiazine at 37±1 <sup>0</sup> C .   |
|  |   |
| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| An excess of sulfamethoxydiazine was added<br>to bottles contg from 0 to 10% PEG 6000<br>solns. The bottles were rotated at 30 rpm<br>for 24 h in a water bath at 37°C. After<br>equilibrium had been attained, an aliquot<br>was pipetted out, dild with 0.1N HCl, and<br>the solute was assayed spectrophotometri-<br>cally at 228 nm. | PEG 6000 was a product of Hoechst AG,<br>West Germany. Sulfamethoxydiazine (Bay-<br>rena) was supplied by Bayer, Leverkusen.<br>The purity of the materials was not<br>specified. |
|  | ESTIMATED ERROR:<br>Soly: data points are means of 3 detns<br>(authors).<br>Temp: ±1°C (authors).<br>REFERENCES:  |



| 282   |   |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(5-meth-oxy-2-pyrimidinyl)- (sulfameter);<br/>C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>S; [651-06-9]</li> <li>Ethanol, 2-Ethoxy-; C<sub>4</sub>H<sub>10</sub>O<sub>2</sub>;<br/>[110-80-5]</li> </ol> | DRIGINAL MEASUREMENTS:<br>Sunwoo, C.; Eisen, H.<br>J. Pharm. Sci. <u>1971</u> , 60, 238-44.<br>PREPARED BY:   |
| One temperature: 25°C   | R. Piekos   |
| The mole fraction solubility of sulfameter in 2-ethoxyethanol at 25 <sup>0</sup> C<br>is 0.0119 ( 3.61 g/100 g solution, compiler ).  |   |
| AUXILIARY INFORMATION   |   |
| METHOD/APPARATUS/PROCEDURE:<br>Soly was detd by the method reported by<br>Restaino and Martin (1). Sulfameter was<br>assayed on a Coleman-Hitachi 124 double-beam<br>spectrophotometer at 271 nm after diln of a<br>sample with 95% alcohol or water.     | SOURCE AND PURITY OF MATERIALS:<br>Sulfameter (A. H. Robins Co., Richmond, Va)<br>was recrystd from warm alcohol. 2-ethoxy-<br>ethanol (Cellosolve solvent, Union Carbide,<br>New York, N. Y.) was of industrial grade. |

| FSTIMAT | ED ERROR | •          |
|---------|----------|------------|
| DOTIUN  |          |            |
| Temp:   | ±1.0°C   | (authors). |

| Soly: | the mean of 3 runs was given |
|-------|------------------------------|
|       | (authors).                   |

**REFERENCES**:

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Restaino, F. A.; Martin, A. N.
 J. Pharm. Sci. <u>1964</u>, 53, 636.

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| COMPONENTS:   |                      | ORIGINAL MEASUREMENTS:  |          |
|---|----------------------|---|----------|
| <ol> <li>Benzenesulfonamide,<br/>methoxy-2-pyrimidin<br/>methoxine, SMM); C</li> </ol>                                      | yl)- (sulfamono-     | Takayama, K.; Nambu, B.; Nagai, T.<br><i>Chem. Pharm. Bull.</i> <u>1978</u> , 26(10), |          |
| [651-06-9]<br>(2) 1,4,7,10,13,16-Hexa<br>(18-C-6); C <sub>12</sub> H <sub>24</sub> 0 <sub>6</sub><br>(3) Hydrochloric acid; | ; [17455-13-9]       | 2965-70.  |          |
| (4) Water; H <sub>2</sub> 0; [77  |                      |   |          |
| VARIABLES:  |                      | PREPARED BY:  |          |
| Temperature   |                      | R. Piekos   |          |
| EXPERIMENTAL VALUES:  | <u> </u>             |   |          |
|   |                      |   |          |
|   |                      | urated concentration<br>sulfamonomethoxine after                                      |          |
|   | t/°C                 |   |          |
|   |                      | omplexation of its 1:1  |          |
|   | Com                  | plex with 18-C-6 in 0.2N HCl  |          |
|   |                      | 10 <sup>2</sup> M   |          |
|   | 30                   | 0.390   |          |
|   | 35                   | 0.473   |          |
|   |                      |   |          |
|   | 40                   | 0.571   |          |
|   |                      | , ,, <del>,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,</del>                                     |          |
|   |                      |   |          |
|   |                      |   |          |
|   | AUXILIARY            | INFORMATION   |          |
| METHOD/APPARATUS/PROCEDU<br>An excess of the comple   |                      | SOURCE AND PURITY OF MATERIALS:<br>SMM (Dai-ichi Pharmaceutical Co) was               | recry-   |
| 50 ml of 0.2N HC1. The  | sampling was done    | std from a 30% (V/V) $Me_2CO - H_2O$ syst   | em.      |
| by a 1-ml pipet fitted  | -                    | 18-C-6 was of the reagent grade.  |          |
| ter. The concentratrio  |                      | The complex was prepd by the authors.   |          |
| was detd by uv spectrop<br>with 0.2N HCl.   | hotometry after dilg | Purity of the HCl soln was not specif   | ied.     |
|   |                      |   |          |
|   |                      | ESTIMATED ERROR:  |          |
|   |                      |   |          |
|   |                      | Nothing specified.  |          |
|   |                      | REFERENCES:   | <u> </u> |
|   |                      |   |          |
|   |                      |   |          |
|   |                      |   |          |
| L   |                      |   |          |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2-  |   |
|---|---|
|   | ORIGINAL MEASUREMENTS:<br>Roblin, R. O., Jr.; Winnek, P. S.;  |
| <pre>methoxy-5-pyrimidiny1)-;</pre>   | English, J. P. J. Am. Chem. Soc.  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [71119-37-4]   | <u>1942.</u> 64, 567-70.  |
| (2) Water; H <sub>2</sub> O; [7732-18-5]  | <u>1942</u> , 0 <sup>2</sup> , 907-70.  |
| $(2)$ water; $n_20$ ; $[7/32-10-5]$   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
| one competatule. 57 5   |   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of 4-amino-N-(2-methoxy-5-pyrimidinyl)benzenesulfonamide in water at $37^{\circ}$ C is 9.2 mg/100 cm <sup>3</sup> solution ( 3.3 x $10^{-4}$ mol dm <sup>-3</sup> , compiler ).  |   |
|   |   |
|   |   |
|   | INFORMATION   |
|   | SOURCE AND PURITY OF MATERIALS:   |
|   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4 <sup>0</sup> C (cor), was  |
| ETHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4 <sup>o</sup> C (cor), was<br>prepd by the authors. Anal: %C 47.3   |
| ETHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4 <sup>0</sup> C (cor), was  |
| ÆTHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4 <sup>0</sup> C (cor), was<br>prepd by the authors. Anal: %C 47.3   |
| ETHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1   |
| <b>GETHOD/APPARATUS/PROCEDURE:</b><br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1<br>(20.0). Purity of the water was not  |
| <b>ÆTHOD/APPARATUS/PROCEDURE:</b><br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,  | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1<br>(20.0). Purity of the water was not<br>specified.  |
| <b>GETHOD/APPARATUS/PROCEDURE:</b><br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method  | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1<br>(20.0). Purity of the water was not<br>specified.  |
| <b>GETHOD/APPARATUS/PROCEDURE:</b><br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec   | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1<br>(20.0). Purity of the water was not<br>specified.  |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %C 47.3<br>(calcd 47.1); %H 4.0 (4.3); %N 20.1<br>(20.0). Purity of the water was not<br>specified.  |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: % 47.3<br>(calcd 47.1); % 4.0 (4.3); % 20.1<br>(20.0). Purity of the water was not<br>specified.<br>-<br>ESTIMATED ERROR:  |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: % 47.3<br>(calcd 47.1); % 4.0 (4.3); % 20.1<br>(20.0). Purity of the water was not<br>specified.<br>-<br>-<br>ESTIMATED ERROR:<br>Nothing specified.   |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%   |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: ZC 47.3<br>(calcd 47.1); ZH 4.0 (4.3); ZN 20.1<br>(20.0). Purity of the water was not<br>specified.<br>-<br>ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%   |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec<br>trophotometer for comparing the colors deve | SOURCE AND PURITY OF MATERIALS:<br>The sulfonamide, mp 232-4°C (cor), was<br>prepd by the authors. Anal: ZC 47.3<br>(calcd 47.1); ZH 4.0 (4.3); ZN 20.1<br>(20.0). Purity of the water was not<br>specified.<br>-<br>ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr. |

| OMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(6-   | Yamazaki, M.; Aoki, M.; Kamada, A.;                                  |
| methoxy-4-pyrimidinyl)- (sulfamono-   | Yata, N. Yakuzaigaku <u>1967</u> , 27(1),                            |
| methoxine); $C_{11}H_{12}N_4O_3S$ ;   | 37-40.   |
| [1220-83-3]   |  |
| 2) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| ARIABLES:   | PREPARED BY:   |
| One temperature: 30°C   | R. Piekos  |
| XPERIMENTAL VALUES:   |  |
| Solubility of culture theying in a  |  |
| ( 4.8 x $10^{-2}$ g dm <sup>-3</sup> , compiler ).  | water at 30 <sup>0</sup> C is 0.17 mmol/L                            |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).   | vater at 30°C is 0.17 mmol/L<br>INFORMATION                          |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY  |  |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>WETHOD/APPARATUS/PROCEDURE:   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:                       |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:                       |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:                       |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:                       |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until<br>equilibrium was attained. The sulfamono-<br>methoxine was assayed in the supernatant   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:                       |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until<br>equilibrium was attained. The sulfamono-<br>methoxine was assayed in the supernatant<br>spectrophotometrically at 545 nm on a Beck-  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until<br>equilibrium was attained. The sulfamono-<br>methoxine was assayed in the supernatant<br>spectrophotometrically at 545 nm on a Beck-<br>mann DU spectrophotometer. The results were | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until<br>equilibrium was attained. The sulfamono-<br>methoxine was assayed in the supernatant<br>spectrophotometrically at 545 nm on a Beck-<br>mann DU spectrophotometer. The results were | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |
| ( 4.8 x 10 <sup>-2</sup> g dm <sup>-3</sup> , compiler ).<br>AUXILIARY<br>ETHOD/APPARATUS/PROCEDURE:<br>Sulfamonomethoxine (0.5 g) was placed in an<br>L-shaped tube together with 20 ml of water.<br>The mixt was shaken in a thermostat until<br>equilibrium was attained. The sulfamono-<br>methoxine was assayed in the supernatant<br>spectrophotometrically at 545 nm on a Beck-<br>mann DU spectrophotometer. The results were | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Nothing specified. |

REFERENCES:

| COMPONENTS :  | ORIGINAL MEASUREMENTS:                          |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-   |   |
| methoxy-4-pyrimidinyl)- (sulfamono-   | Ezerskii, M. L.; Per'kova, N. N.                |
| <pre>methoxine); C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>0<sub>3</sub>S;</pre>   | KhimFarm. Zh. <u>1979</u> , 13(11), 87-91.      |
| [1220-83-3]   |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:                                    |
| Grinding regime   | R. Piekos                                       |
| EXPERIMENTAL VALUES:  | I   |
|   |   |
| Specimen of sulfamonomethoxine  | Solubility at room temperature                  |
|   | $g/cm^3$ 10 <sup>4</sup> mol dm <sup>-3</sup> a |
| Commercial  | 0.000044 1.6                                    |
| Commercial, ground in ball mill   | 0.000058 2.1                                    |
| Commercial, ground in a jet mill  | 0.000054 1.9                                    |
|   |   |
| <sup>a</sup> Calculated by compiler   |   |
| AUXILIARY   | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by prolonged agitation<br>of an excess of sulfamonomethoxine in water<br>at room temp. The solns were then allowed<br>to stand for 12 h and filtered. The concn<br>of sulfamonomethoxine in the filtrate was<br>detd nitritometrically by the method of the<br>State Pharmacopeia X. |   |
|   | ESTIMATED ERROR:                                |
|   | Nothing specified.                              |
|   | REFERENCES :                                    |
|   |   |
|   |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                     |
|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(6-<br/>methoxy-4-pyrimidinyl)- (sulfamonometh-</li> </ol> | Ogata, H.; Shibazaki, T.; Inoue, T.;       |
| oxine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [1220-83-3]              | Ejima, A. Chem. Pharm. Bull. 1979,         |
| (2) Hydrochloric acid; HCl; [7647-01-0]   | 27(6), 1281-6.                             |
| (3) Water; H <sub>2</sub> O; [7732-18-5]  |  |
|   |  |
| VARIABLES:  | PREPARED BY:                               |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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|   |  |
| Solubility of sulfamonomethoxine in O   | 1N HCl at 37 <sup>0</sup> C is 1.336 mg/ml |
|   |  |
| $(4.766 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler }).$                                  |  |
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| AUXILIARY   | INFORMATION                                |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:            |
| A centrifuge tube contg 30 ml of 0.1N HCl   | Comm available 500-mg uncoated tablets of  |
| and 0.5-3.0 g of the sulfamonomethoxine   | sulfamonomethoxine were used.              |
| powder was tightly sealed and shaken at 37°C  |  |
| The concn of the dissolved drug was detd  | , hydrochioric acid was of reagent grade.  |
|   |  |
| spectrophotometrically following filtration   |  |
| through a Millipore filter (type EH, pore   |  |
| size 0.5 $\mu$ m), and the procedure was repeated   |  |
| every 24 h until a const concn was obtained.  | ESTIMATED ERROR:                           |
|   |  |
|   | Nothing specified.                         |
| •   |  |
|   | REFERENCES :                               |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                    |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-  |   |
| methoxy-4-pyrimidinyl)- (sulfamonometh-  | Yamazaki, M.; Aoki, M.; Kamada, A.;       |
| oxine); $C_{11}H_{12}N_4O_3S$ ; [1220-83-3]  | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                      | 37-40.                                    |
| <ul> <li>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                              |
| VARIABLES:   |   |
| One temperature: 30 <sup>o</sup> C; one pH: 7.4  | R. Piekos                                 |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfamonomethoxine in a  | phosphate buffer solution of pH 7.4       |
| $(\mu = 0.17)$ at $30^{\circ}$ C is 2.79 mmol/L (  | $0.782 \text{ g dm}^{-3}$ , compiler ).   |
|  | or of g um ; complici ).                  |
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|  | INFORMATION                               |
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| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;           |
| Sulfamonomethoxine (0.5 g) was placed in an  | Nothing specified.                        |
| L-shaped tube together with 20 ml of the   |   |
| buffer soln. The mixt was shaken in a ther-  |   |
| mostat until equilibrium was attained. The   |   |
| sulfamonomethoxine was assayed in the super-   | f   |
|  |   |
| natant spectrophotometrically at 545 nm on   |   |
| a Beckmann DU spectrophotometer. The re-   |   |
| sults were taken from a calibration graph.   |   |
|  | ESTIMATED ERROR:                          |
|  | Soly and pH: not specified.               |
|  |   |
|  | Temp: ±1 <sup>0</sup> C (authors).        |
|  | PEPEPEVCNO                                |
|  | REFERENCES:                               |
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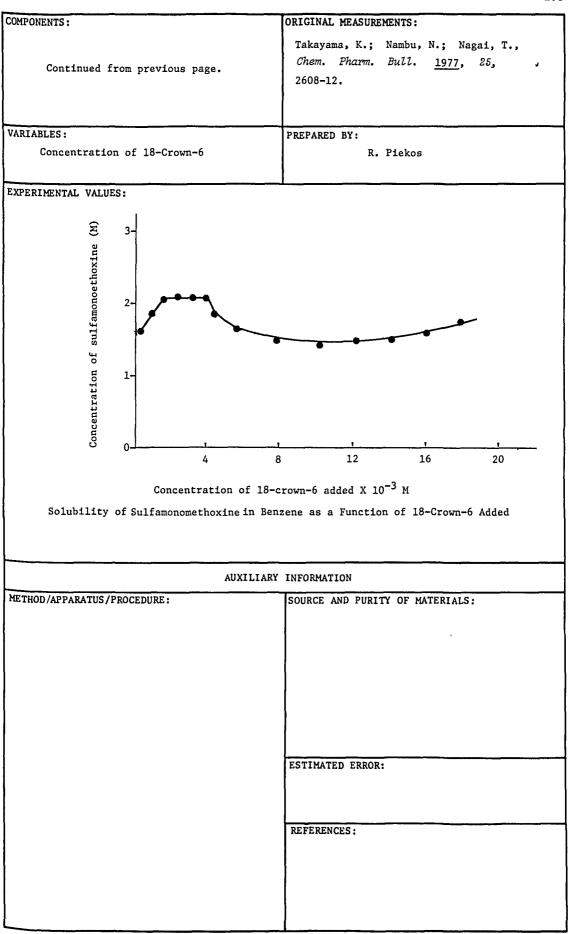
| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-<br>methoxy-4-pyrimidinyl)- (sulfamono-<br>methoxine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [1220-83-3]  | Takayama, K.; Hasegawa, S.; Sasagawa, S.;<br>Nambu, N.; Nagai, T. |
| <ul> <li>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>  | Chem. Pharm. Bull. <u>1978</u> , 26(1),                           |
| <ul> <li>Phosphoric acid, monopotassium salt;</li> <li>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul>   | 96-100.   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:  |
| VARIABLES:  | R. Piekos   |
| One temperature: 30°C; one pH: 7.0<br>EXPERIMENTAL VALUES:  | I   |
| Saturated concentration of sulfamonome<br>buffer of pH 7.0 at 30 <sup>0</sup> C is 3.47 x 10 <sup>-</sup>   | _   |
| AUXILIARY   | INFORMATION   |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                                   |
| The stationary disk method was employed (1).<br>At appropriate time intervals, 3-ml aliquots<br>of soln were withdrawn, the resultant amt<br>of volume was compensated by adding the<br>dissoln medium of the same temp. The concn<br>was detd by the UV spectrophotometry. | Sulfamonomethoxine (Dai-ichi Pharmaceutical                       |

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| COMPONENTS :   | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-  |   |
| methoxy-4-pyrimidinyl)- (sulfamono-  | Takayama, K.; Nambu, N.; Nagai, T.  |
| methoxine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>3</sub> S; [1220-83-3] | Chem. Pharm. Bull. <u>1977</u> , 25, 2608–12.                                 |
|  |   |
| (2) Benzene; C <sub>6</sub> H <sub>6</sub> ; [71-43-2]                                   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 10 <sup>0</sup> C   | R. Piekos   |
|  | N. TIEKUS   |
| EXPERIMENTAL VALUES:   |   |
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|  |   |
| Solubility of sulfamonomethoxine in b  | enzene at 10 <sup>0</sup> C is 1.45   |
| $\times 10^{-4} \text{ mol } dm^{-3} a$ .  |   |
|  |   |
|  |   |
| <sup>a</sup> Numerical value supplied by the aut   | hors.   |
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| AUXILIARY  | INFORMATION   |
|  |   |
| METHOD/APPARATUS/PROCEDURE:<br>The system was equilibrated in a sealed                   | SOURCE AND PURITY OF MATERIALS:<br>Sulfamonomethoxine, m.p. 205°C, was a very |
| vial for 72 h at $10^\circ$ . The satd soln was  | pure compd supplied by Dai-ichi Pharmaceu-                                    |
| rapidly filtered through a Toyo filter paper   | tical Co., Ltd.   |
| No. 5B, 1 $cm^3$ of the filtrate was evapd at  | 1   |
| $40^{\circ}$ C and the residue was dissolved in CHCl <sub>3</sub>                        | Purity of the benzene was not specified.                                      |
| to det the concn in the UV region using a  |   |
| Hitachi 124 spectrophotometer.   |   |
|  |   |
|  | ESTIMATED EDDOD.  |
|  | ESTIMATED ERROR:  |
|  | Nothing specified.  |
|  |   |
|  | REFERENCES:   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                    |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-  |   |
| methoxy-4-pyrimidinyl)- (sulfamono-  | Yamazaki, M.; Aoki, M.; Kamada, A.;       |
| methoxine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> 0 <sub>3</sub> S; [1220-83-3] | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
| (2) Methane, trichloro- (chloroform);  | 37-40.                                    |
| CHC1 <sub>3</sub> ; [67-66-3]  |   |
| VARIABLES:   |   |
|  | PREPARED BY:                              |
| One temperature: 30 <sup>0</sup> C   | R. Piekos                                 |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfamonomethoxine in chl  | oroform at 30°C is 2.63 mmol/L            |
|  |   |
| $(0.737 \text{ g dm}^{-3}, \text{ compiler }).$  |   |
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| AUXILIARY  | INFORMATION                               |
|  |   |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:           |
| Sulfamonomethoxine (0.5 g) was placed in an  | Nothing specified.                        |
| L-shaped tube together with 20 ml of chloro-   |   |
| form. The mixt was shaken in a thermostat  |   |
| until equilibrium was attained. The sulfa-   |   |
| monomethoxine was assayed in the supernatant   |   |
| spectrophotometrically at 545 nm on a Beck-  |   |
| mann DU spectrophotometer. The results were  |   |
| taken from a calibration graph.  |   |
| The a calibration graph.   | ECTIMATED EDDOD.                          |
|  | ESTIMATED ERROR:                          |
|  | Soly: not specified.                      |
|  | Temp: ±1°C (authors).                     |
|  | REFERENCES :                              |
| 1  | REFERENCED;                               |
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|---|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                |  |
| (1) Benzenesulfonamide, 4-amino-N-(6-meth-<br>oxy-4-pyrimidinyl)- (sulfamonometh-<br>oxine); C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [1220-83-3] | Takayama, K.; Nambu, N.; Nagai, T.                    |  |
| <ul> <li>(2) 1,4,7,10,13,16-Hexaoxacyclooctadecane<br/>(18-Crown-6); C<sub>12</sub>H<sub>24</sub>0<sub>6</sub>; [17455-13-9]</li> </ul>                                   | Chem. Pharm. Bull. <u>1977,</u> 25, 2608–12.          |  |
| (3) Benzene; $C_6H_6$ ; [71-43-2]   |   |  |
| VARIABLES:  | PREPARED BY:  |  |
| Concentration of 18-Crown-6   | R. Piekos   |  |
| EXPERIMENTAL VALUES:  | L   |  |
| Concentration of 18-Crown-6   |   |  |
| $10^3 \text{ mol } \text{dm}^{-3}$  | $10^4$ mol dm <sup>-3</sup>                           |  |
| 1.0   | 1.65  |  |
| 2.0   | 1.99  |  |
| 3.0   | 2.02  |  |
| 4.0   | 2.04  |  |
| 5.0   | 2.05  |  |
| 6.0   | 1.90  |  |
| 7.0   | 1.65  |  |
| 8.0   | 1.68  |  |
| 9.0   | 1.64  |  |
| 10.0  | 1.48  |  |
| 12.0  | 1.55  |  |
| 14.0  | 1.50  |  |
| 16.0  | 1.55  |  |
| 18.0  | 1.55  |  |
| 20.0  | 1.63  |  |
| <sup>a</sup> Numerical data supplied by the authors.  |   |  |
| AUXILIARY INFORMATION   |   |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                       |  |
| The system was equilibrated in a sealed via   | l Sulfamonomethoxine, m. p. 205 <sup>0</sup> C, was a |  |
| for 72 h at $10^{\circ}$ C. The satd soln was rapid-  | -   |  |
| ly filtered through a Toyo filter paper No.   |   |  |
| 5B, 1 cm <sup>3</sup> of the filtrate was evapd at $40^{\circ}$ C   |   |  |
| and the residue was dissolved in CHCl <sub>3</sub> to   | Purity of the benzene was not specified.              |  |
| det the concn in the UV region using a Hi-  | rarrey of the benzene was not specificat              |  |
| tachi 124 spectrophotometer.  |   |  |
| tachi 124 spectrophotometer.  | ·   |  |
|   | ESTIMATED ERROR:                                      |  |
|   | None specified.                                       |  |
|   | None opecified.                                       |  |
|   | REFERENCES :  |  |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                        |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(6-<br>methoxy-4-pyrimidinyl)1,4,7,10,13,16-                             | Takayama, K.; Hasegawa, S.;                   |
| Hexaoxacyclooctadecane complex 1:1 (SMM/   | Sasagawa, S.; Nambu, N.; Nagai, T.            |
| 18-Crown-6-complex); C <sub>23</sub> H <sub>36</sub> N <sub>4</sub> O <sub>9</sub> S;<br>[65177-18-6]      | Chem. Pharm. Bull. 1978, 26(1),               |
| <ul> <li>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>     | 96-100.                                       |
| (3) Phosphoric acid, monopotassium salt;   | ·····   |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]<br>(4) Water; H <sub>2</sub> O; [7732-18-5]                  | PREPARED BY:<br>R. Piekos                     |
| VARIABLES:   | R. Flekos                                     |
| One temperature: 30 <sup>o</sup> C; one pH: 7.0  |   |
| EXPERIMENTAL VALUES:<br>Saturated concentration of the 1:1 SMM/<br>phosphate buffer solution of 7.0 is 5.9 |   |
| AUXILIARY  | INFORMATION                                   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:               |
| The stationary disk method was employed (1).   | The complex was prepd by the authors and      |
| At appropraite time intervals, 3-ml aliquots   | contained a trace of the starting components. |
| of soln were withdrawn, the resultant amt  | Its identity was confirmed by X-ray diffrac-  |
| of vol was compensated by adding the dissoln   | tometry, IR spectrophotometry, differenctial  |
| medium at the same temp. The concn was   | scanning calorimetry and other methods (2).   |
| detd by the UV spectrophotometry.  | The source and purity of the remaining mate-  |
|  | rials were not specified.                     |
|  |   |
|  | ESTIMATED ERROR:                              |
|  | Nothing specified.                            |
|  |   |
|  | REFERENCES:                                   |
|  | l. Hamada, Y.; Nambu, N.; Nagai, T.           |
|  | Chem. Pharm. Bull. <u>1975</u> , 23, 1205.    |
|  | 2. Takayama, K.; Nambu, N.; Nagai, T.         |
|  | Chem. Pharm. Bull. <u>1977</u> , 25, 2608.    |
|  |   |

| COMPONENT   |   |  |
|---|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(5-methox          | ORIGINAL MEASUREMENTS:                      |  |
| 2-pyrimidiny1) 1,4,7,10,13,16-hexaox                                | y-<br>y- Takayama, K.; Nambu, N.; Nagai, T. |  |
| cyclooctadecane complex (1:1) (SMM/18-                              | Chem. Pharm. Bull. <u>1978</u> , 26(10),    |  |
| $(-6)); C_{11}H_{12}N_4O_3S \cdot C_{12}H_{24}O_6;$<br>[65177-18-6] | 2965-70.                                    |  |
| (2) Hydrochloric acid; HCl; [7647-01-0]                             |   |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]                            |   |  |
| VARIABLES:  | PREPARED BY:                                |  |
| Temperature   | R. Piekos                                   |  |
|   |   |  |
| EXPERIMENTAL VALUES:  |   |  |
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|   | Saturated concentration                     |  |
|   | of the complex in 0.2N HCl                  |  |
| t/°C  | 10 <sup>2</sup> M                           |  |
|   |   |  |
| 30  | 1.25  |  |
| 35  | 1.32  |  |
| 40  | 1.45  |  |
| 40  | 1.47  |  |
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| AUXILIAR  | Y INFORMATION                               |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |  |
| An excess of sample powder was dissolved t                          |   |  |
| 50 ml of 0.2N HCl. Sampling was done by a                           |   |  |
| 1-m1 pipet fitted with a G-4 glass filter.                          |   |  |
| The concn of SMM in the filtrate was detd                           | of benzene in a flask and stiring well for  |  |
| by uv spectrophotometry after dilg with                             | 10 days at 10°C. Purity of the HCl soln     |  |
| 0.2N HCL.   | was not specified.                          |  |
|   | was not specified.                          |  |
|   |   |  |
|   | ESTIMATED ERROR:                            |  |
|   |   |  |
|   | Nothing specified.                          |  |
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|   | REFERENCES:                                 |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                             |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-ethoxy-                                      |  |
| 2-pyrimidiny1)-; C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S; | English, J. P. J. Am. Chem. Soc.                   |
| [71138-72-2]  | <u>1942,</u> 64, 567-70.                           |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                       |
| One temperature: 37 <sup>o</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(4-ethoxy-2-py  | rimidinyl)benzonoculfonamide in                    |
|   |  |
| water at 37 <sup>0</sup> C is 5.3 mg/100 cm <sup>3</sup> soluti                   | on ( 1.8 x 10 <sup>-4</sup> mol dm <sup>-3</sup> , |
| compiler ).   |  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                    |
| Excess sulfonamide in water was heated and  | The sulfonamide, mp 255-6°C (cor), was             |
| stirred on a steam bath for 30 min. The   | prepd by the authors. Anal: %C 48.6                |
| suspension was then agitated for 24 h in a  | (calcd 49.0); %H 4.7 (4.8); %N 19.4                |
| thermostat at 37 <sup>0</sup> C. A sample of the satd                             | (19.0). Purity of the water was not                |
| soln was withdrawn through a glass filter, specified.                             |  |
| dild, and analyzed by the Marshall method   |  |
| (1) using a General Electric recording spec-                                      |  |
| trophotometer for comparing the colors deve-                                      |  |
| loped with those of the standards.  | ESTIMATED ERROR:                                   |
|   | Nothing specified.                                 |
|   |  |
|   | REFERENCES:  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.            |
|   | J. Pharmacol. <u>1939,</u> 66, 4.                  |
|   |  |
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| OMPONENTS:  | ORIGINAL MEASUREMENTS: |
|---|------------------------|
| <ol> <li>Benzenesulfonamide, 4-amino-(5-chloro-<br/>2-pyrimidinyl)-; C<sub>10</sub>H<sub>9</sub>ClN<sub>4</sub>O<sub>2</sub>S;<br/>[4482-46-6]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> |                        |
| VARIABLES:  | PREPARED BY:           |
| One temperature: 37°C   | R. Piekos              |
| XPERIMENTAL VALUES:   |                        |
| A ENTRENTAL VALUES:   |                        |
| A EXIMENTAL VALUES:   |                        |
|   |                        |
| Solubility of 4-amino-N-(5-chloro-2-<br>water at 37 <sup>o</sup> C is 1.8 mg/100 cm <sup>3</sup> solu   |                        |
| Solubility of 4-amino-N-(5-chloro-2-  |                        |

## AUXILIARY INFORMATION

Excess sulfonamide in water was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h in a thermostat at 37°C. A sample of the satd soln was withdrawn through a glass filter, dild, and analyzed by the Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors developed with those of the standards.

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS: The sulfonamide, mp 246-7°C (cor), was prepd by the authors. Anal: %C 42.2 (calcd 42.2). Purity of the water was not specified.

ESTIMATED ERROR: Nothing specified.

**REFERENCES:** 

1. Bratton, A. C.; Marshall, E. K., Jr. J. Pharmacol. <u>1939</u>, 66, 4.

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                 |  |
|--|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2-chloro-                   |  |  |
| 5-pyrimidiny1)-; $C_{10}H_9ClN_4O_2S;$                         | Roblin, R. O., Jr.; Winnek, P. S.;                     |  |
|  | English, J. P. J. Am. Chem. Soc.                       |  |
| [17103-49-0]   | <u>1942,</u> 64, 567-70.                               |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                       |  |  |
|  |  |  |
| VARIABLES:   | PREPARED BY:   |  |
| One temperature: 37 <sup>o</sup> C                             | R. Piekos  |  |
| One temperature: 37 <sup>o</sup> C                             | K. Flekos  |  |
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| EXPERIMENTAL VALUES:   |  |  |
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| Solubility of 4-amino-N-(2-chloro-5-pyri                       | midinvl)benzenesulfonamide in water                    |  |
|  |  |  |
| at $37^{\circ}$ C is 32.1 mg/100 cm <sup>3</sup> solution ( 1. | $13 \times 10^{-5}$ mol dm <sup>-5</sup> , compiler ). |  |
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| AUXILIARY  | INFORMATION  |  |
| METHOD/APPARATUS/PROCEDURE:                                    | SOURCE AND PURITY OF MATERIALS:                        |  |
|  |  |  |
| Excess sulfonamide in water was heated and                     | The sulfonamide, mp 206-7°C (cor), was                 |  |
| stirred on a steam bath for 30 min. The                        | prepd by the authors. Anal: %C 42.3                    |  |
| suspension was then agitated for 24 h in a                     | (calcd 42.2); %H 3.2 (3.2); %N 19.8 (19.7)             |  |
| thermostat at 37°C. A sample of the satd                       | Purity of the water was not specified.                 |  |
| soln was withdrawn through a glass filter,                     |  |  |
| dild, and analyzed by the Marshall method                      |  |  |
|  |  |  |
| (1) using a General Electric recording spec-                   |  |  |
| trophotometer for comparing the colors deve-                   |  |  |
| loped with those of the standards.                             | ESTIMATED ERROR:                                       |  |
|  | Nothing specified.                                     |  |
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|  | REFERENCES:  |  |
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|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                |  |
|  | J. Pharmacol. <u>1939</u> , 66, 4.                     |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4-amino-                                       | Anderson, G. W.; Faith, H. E.; Marson, H.W.   |
| 2-pyrimidiny1)-; C <sub>10</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub> S; | Winnek, P. S.; Roblin, R. O., Jr.   |
| [16806-00-1]  | J. Am. Chem. Soc. <u>1942</u> , 64,   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  | 2902-5.   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C  | R. Piekos   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| Solubility of 4-amino-N-(4-amino-2-pyri   | midinyl)benzenesulfonamide in   |
| water at $37^{\circ}$ C is 186 mg/100 cm <sup>-3</sup> solution                   |   |
|   | .on (7.01 x 10 mol dm ,   |
| compiler ).   |   |
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| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |
| Excess sulfonamide in water was heated and  | The sulfonamide, mp 271-2°C, was prepd by   |
| stirred on a steam bath for 30 min. The sus-                                      | 1   |
| pension was then agitated for 24 h in a ther-                                     |   |
| mostat. A sample of the satd soln was with-                                       | Purity of the water was not specified.  |
| drawn through a glass filter, dild, and ana-                                      |   |
| lyzed by the Marshall method (1) using a  |   |
| General Electric recording spectrophotometer                                      |   |
| for comparing the colors developed with those                                     |   |
| of the standards.   | ESTIMATED ERROR:  |
|   | Nothing specified.  |
|   | DEFEDENCIES.  |
|   | REFERENCES:   |
|   | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.</li> <li>J. Pharmacol. <u>1939</u>, 66, 4.</li> </ol> |
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NENTS:

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2-amino-<br/>5-pyrimidinyl)-; C<sub>10</sub>H<sub>11</sub>N<sub>5</sub>O<sub>2</sub>S;<br/>[71119-38-5]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol>   | Roblin, R. O., Jr.; Winnek, P. S.;<br>English, J. P. <i>J. Am. Chem. Soc.</i><br><u>1942</u> , 64, 567-70. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| Solubility of 4-amino-N-(2-amino-5-py<br>in water at 37 <sup>0</sup> C is 8.3 mg/100 cm <sup>3</sup> so<br>compiler ).   |  |
| AUXILIARY  | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:  |
| Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec-<br>trophotometer for comparing the colors deve-<br>loped with those of the standards. |  |
|  | DEPENDING  |
| •  | REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br><i>J. Pharmacol.</i> <u>1939</u> , 66, 4.        |

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |  |
|---|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-[4-<br/>(diethylamino)-2-pyrimidiny1]-;<br/>C<sub>14</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>S; [71119-24-9]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Anderson, G. W.; Faith, H. E.; Marson, H.W.<br>Winnek, P. S.; Roblin, R. O., Jr.<br><i>J. Am. Chem. Soc.</i> <u>1942</u> , <i>64</i> ,<br>2902-5. |  |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C  | PREPARED BY:<br>R. Piekos   |  |
| EXPERIMENTAL VALUES:  |   |  |

| Solubility of 4-amino-N-[4-(diethylamino)-2-pyrimidinyl]benzene-                      | -                  |
|---|--------------------|
| sulfonamide in water at $37^{\circ}$ C is 4.2 mg/100 cm <sup>3</sup> solution ( 1.3 x | × 10 <sup>-4</sup> |
| mol dm <sup>-3</sup> , compiler ).  |                    |

| AUXILIARY | INFORMATION |
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Excess sulfonamide in water was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h in a thermostat. A sample of the satd soln was withdrawn through a glass filter, dild, and analyzed by the Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors developed with those of the standards.

METHOD/APPARATUS/PROCEDURE:

| .S :         |
|--------------|
| C (cor), was |
| . %C 52.5    |
| ; %N 21.7    |
|              |
| specified.   |
|              |

ESTIMATED ERROR:

Nothing specified.

**REFERENCES:** 

 Bratton, A. C.; Marshall, E. K., Jr. J. Pharmacol. 1939, 66, 4.

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| J | V | 4 |

| COMPONENTS :  | ORIGINAL MEASUREMENTS:                                 |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4, 5-  | Caldwell, W. T.; Kornfeld, E. C.;                      |
| <pre>dimethy1-2-pyrimidiny1)-;</pre>  | Donnell, C. K. J. Am. Soc. Chem.                       |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [4462-43-5]                  | <u>1941,</u> 63, 2188-90.                              |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 29 <sup>0</sup> C  | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
| Solubility of 4-amino-N-(4,5-dimethyl-<br>in water at 29 <sup>0</sup> C is 20 mg/100 ml solut |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                        |
| Soly was detd by weighing the residue ob-   | The sulfonamide, mp 225-7-6.3 <sup>0</sup> C (cor, re- |
| tained by evapg to dryness a known volume   | crystd from aq dioxane), was prepd by con-             |
| of soln satd at 29 <sup>0</sup> C.  | densing 2-amino-4,5-dimethyl pyrimidine                |
|   | with acetylsulfanilyl chloride followed by             |
|   | hydrolysis with aq NaOH and pptn at pH 6.              |
|   | Anal: %N 20.09 (calcd 20.13). Purity of                |
|   | the water was not specified.                           |
|   |  |
|   | ESTIMATED ERROR:                                       |
|   | Nothing specified.                                     |
|   |  |
|   | REFERENCES :   |
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| COMPONENTS:  | EVALUATOR:  |
|--|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(4,6-di-<br/>methyl-2-pyrimidinyl)-<br/>(sulfadimezine) C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S<br/>[57-68-1]</pre> | Anthony N. Paruta<br>Department of Pharmaceutics<br>University of Rhode Island<br>Kingston, Rhode Island, USA |
| (2) Water  | and<br>Ryszard Piekos<br>Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986                     |

CRITICAL EVALUATION:

Four reports (1-4) gave solubility values at 293K in water are given in Table I.

Table I: Solubility of Sulfadimezine in water at 293K

|           | $10^3$ mol dm <sup>-3</sup> (*indicates mol kg <sup>-1</sup> ) |
|-----------|--|
| Reference | 293К   |
| 1         | 1.2*   |
| 2         | 1.2  |
| 3         | 3.3*   |
| 4         | 1.671*   |

The values given by Shkadova (3) and Gerencsér-Németh (4) are too high, the former (3) being 2.75 times higher and the latter (4) about 1.4 times higher. The recommended result is the value given by references (1,2) and can be stated as  $1.2 \times 10^{-3} \text{ mol dm}^{-3}$ at 293K in water.

**REFERENCES:** 

- (1) Gusyakov, V.P.; Likhol'ot, N.M. Farm. Zh. (kiev) 1960, 15(3), 21-4.

- (2) Likhol'ot, N.M. Farm. Zh. (Kiev) 1965, 20(5),  $\frac{1200}{44-6}$ . (3) Shkadova, A.I. Farm. Zh. (Kiev) 1969, 24(3), 39-41. (4) Gerencsér-Németh, M.; Harvath, M. Gyógyszerészet 1973, 17, 417-21.

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|---|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |  |
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   | Caldwell, W. T.; Kornfeld, E. C.;   |  |
| dimethy1-2-pyrimidiny1)- (sulfadi-  | Donnell, C. K. J. Am. Chem. Soc.  |  |
| mezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | <u>1941</u> , <i>63</i> , 2188-90.  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |
| -   |   |  |
| VARIABLES:  | PREPARED BY:  |  |
| One temperature: 29 <sup>0</sup> C  | R. Piekos   |  |
|   |   |  |
| EXPERIMENTAL VALUES:  |   |  |
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| Solubility of sulfadimezine in wate   | r at 29 <sup>0</sup> C is 150 mg/100 ml   |  |
| solution (5.39 x $10^{-3}$ mol dm <sup>-3</sup> , c                                 | -   |  |
| solution ( 5.39 x 10 - mol dm -, c  | ompiler ).  |  |
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|   | LARY. INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimezine, mp 178-80 <sup>0</sup> C (cor, recrystd |  |
| Soly was detd by weighing the residue ob  | from water) was sweed by condensing 2 and a   |  |
| tained by evapg to dryness a known volum  | e 4,6-dimethylpyrimidine with acetylsulfanilyl  |  |
| of soln satd at 29 <sup>0</sup> C.  | chloride followed by hydrolysis with aq NaOH  |  |
|   | and pptn at pH 6. Anal: %C 51.78 (calcd   |  |
|   | 51.78), %H 4.83 (5.07), %N 20.03, 20.17   |  |
|   | (20.13). Purity of the water was not  |  |
|   | specified.  |  |
|   | specificu.  |  |
|   | ESTIMATED ERROR:  |  |
|   | Nothing specified.  |  |
|   | would obecilien.  |  |
|   | REFERENCES :  |  |
|   | AUTERENCED;   |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-<br/>dimethyl-2-pyrimidinyl)- (sulfadi-<br/>mezine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol>  | Roblin, R. O., Jr.; Winnek, P. S.;<br>English, J. P. <i>J. Am. Chem. Soc.</i><br><u>1942</u> , 64, 567-70.  |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C  | PREPARED BY:<br>R. Piekos   |
| EXPERIMENTAL VALUES:  | L   |
|   |   |
| Solubility of sulfadimezine in water at ( 2.7 x $10^{-3}$ mol dm <sup>-3</sup> , compiler ).  | 37°C is 75 mg/100 cm <sup>3</sup> solution <sup>a</sup>   |
| <sup>a</sup> The compound tends to remain supersatur<br>of excess solid. The value represent<br>approached from low side (authors).   |   |
| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>stirred on a steam bath for 30 min. The<br>suspension was then agitated for 24 h in a<br>thermostat at 37°C. A sample of the satd<br>soln was withdrawn through a glass filter,<br>dild, and analyzed by the Marshall method<br>(1) using a General Electric recording spec-<br>trophotometer for comparing the colors deve-<br>loped with those of the standards. | SOURCE AND PURITY OF MATERIALS:<br>Sulfadiazine, mp 198-9°C (cor), was prepd<br>by the authors. Anal: % 52.0 (calcd<br>51.8); % 5.1 (5.0); % 20.0 (20.1).<br>Purity of the water was not specified.<br>ESTIMATED ERROR:<br>Nothing specified. |
|   | REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br><i>J. Pharmacol.</i> <u>1939</u> , 66, 4.   |

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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-<br/>dimethyl-2-pyrimidinyl)- (sulfadi-<br/>mezine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Gusyakov, V. P.; Likhol'ot, N. M.<br><i>Farm. Zh. (Kiev) <u>1960</u>, 15(3),</i> 21-4. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 20°C  | R. Piekos  |
| EXPERIMENTAL VALUES:   | <u> </u>   |
| Solubility of sulfadimezine in water a<br>( 1.2 x 10 <sup>-3</sup> mol kg <sup>-1</sup> , compiler ).  | t 20 <sup>0</sup> C is 0.033 g/100 g water   |
| AUXILIARY  | INFORMATION  |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:  |
| A small excess of sulfadimezine was equili-  | Sulfadimezine was carefully washed with  |
| brated for 8 h in a 50-ml test tube with 20  | water, alcohol, and dried. Its purity  |
| ml of water. Aliquots were taken with a  | conformed to the requirements of the State   |
| pipet fitted with a filter. Sulfadimezine  | Pharmacopeia VIII.   |
| was detd at 285 nm using a SF-4 spectropho-<br>tometer.  | Purity of the water was not specified.   |
|  | ESTIMATED ERROR:   |
|  | Soly: the accuracy corresponded to that of   |
|  | the colorimentric detns (authors:  |
|  | Temp: not specified.   |
|  | REFERENCES :   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-                             | ·   |
| dimethyl-2-pyrimidinyl)- (sulfadi-                                  | Likhol'ot, N. M.; Farm. Zh. (Kiev)        |
| mezine); $C_{12}H_{14}N_4O_2S$ ; [57-68-1]                          | <u>1965</u> , 20(5), 44-6.                |
|   |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                            |   |
| VARIABLES:  | PREPARED BY:                              |
|   |   |
| One temperature: 20°C   | R. Piekos                                 |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| Solubility of sulfadimezine in water                                | at 20 <sup>0</sup> C is 0.033 g/100 ml    |
| $(1.2 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler}).$       |   |
| $(1.2 \times 10^{\circ} \text{ mol dm}^{\circ}, \text{ compiler}).$ |   |
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| AUXILIARY   | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:           |
| An earlier described method was employed                            | Nothing specified.                        |
| (1) whereby a small excess of sulfadimezine                         |   |
| was equilibrated with 20 ml of water for 8                          |   |
| h in a 50-ml test tube. Aliquots were with                          |   |
| drawn through a filter and sulfadimezine                            |   |
| was assayed bromatometrically.                                      |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                          |
|   | Soly: not specified.                      |
|   | Temp: ±0.1 <sup>0</sup> C (authors).      |
|   |   |
|   | REFERENCES:                               |
|   | 1. Gusyakov, V. P.; Likhol'ot, N. M.      |
|   | Farm. Zh. (Kiev) <u>1960</u> , 15(8), 21. |
|   |   |
|   |   |
|   | 1   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   | Shkadova, A. I.  |
| dimethyl-2-pyrimidinyl)- (sulfadi-  | Farm. 2h. (Kiev) <u>1969</u> , 24(3), 39-41.   |
| mezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1]   | <u> </u>   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 20 <sup>0</sup> C  | R. Piekos  |
| EXPERIMENTAL VALUES:  | J  |
| Solubility of sulfadimezine in water a<br>(9.2 x 10 <sup>-2</sup> g/100 g, compiler). | t 20 <sup>0</sup> C is 0.33 x 10 <sup>-2</sup> mol/kg  |
| AUXILIARY   | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:  |
| A satd soln of sulfadimezine was equilibra-   | Purity of sulfadimezine conformed to the   |
| ted in a water thermostat at $20\pm0.1^{\circ}$ C. The                                | requirements of the State Pharmacopeia IX.   |
| concn of sulfadimezine was detd by alkali-  | Distd water was used.  |
| metric titrn.   |  |
|   | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1 <sup>O</sup> C (author).<br>REFERENCES: |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   | Gerencser-Németh, M.; Horváth, M.               |
| dimethyl-2-pyrimidinyl)- (sulfa-  | Gyogyszerészet <u>1973,</u> 17, 417–21.         |
| dimidine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] |   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| _   |   |
| VARIABLES:  | PREPARED BY:                                    |
| One temperature: 20 <sup>0</sup> C  | R. Piekos                                       |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| Solubility of sulfadimidine in water  | at 20 <sup>0</sup> C is 0.0465 g/100 g solution |
| $(1.67 \times 10^{-3} \text{ mol kg}^{-1} \text{ water, compil}$                      | er).  |
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|   | INFORMATION                                     |
|   |   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                 |
| A weighed excess of sulfadimidine was sha-  | Sulfadimidine (source and purity not spe-       |
| ken with water in a shaker at 120 rpm for   | cified) was dried at 100°C for 3 h or over      |
| 6 h. The soln was then filtered, the resi-  | concn $H_2SO_4$ for 72 h. Its mp was 196.5-8°C. |
| due was washed with the filtrate and finally  | Distd water was used.                           |
| with a small amt of distd water, dried and  |   |
| weighed.  |   |
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| 1   |   |
|   | ESTIMATED ERROR:                                |
|   | Soly: precision ±0.0003 g/100 g (2 detns)-      |
|   | compiler.                                       |
|   | Temp: not specified.                            |
|   | REFERENCES:                                     |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-</li> </ol>                    |  |
| dimethyl-2-pyrimidinyl)- (sulfa-   | Nasipuri, R. N.; Khalil, S. A. H.  |
| methazine; sulfadimidine);   | J. Pharm. Sci. <u>1973</u> , 62(3), 473-5.   |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] |  |
| (2) Water; $H_20$ ; [7732-18-5]  |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 24 <sup>°</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:   | 1  |
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| Equilibrium solubility of sulfamethazin                                    | he in water at 24°C is 1.424   |
| mmol/1 ( 0.3963 g dm <sup>-3</sup> , compiler ).                           |  |
|  |  |
| <sup>a</sup> The pH of the saturated aqueous solut:                        | lon was 5.6  |
| •                                    |  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| Sulfamethazine was assayed spectrophotome-                                 | Sulfamethazine was a BP grade sulfadimidine  |
| trically at 230 nm in a 0.05M HCl soln using                               |  |
| a Unicam SP 500 spectrophotometer.   | The purity of water was not specified.   |
|  | ine pulley of water was not specified.   |
|  |  |
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|  | ESTIMATED ERROR:   |
|  |  |
|  |  |
|  | Soly: ±1.9% (not stated accuracy or repro-   |
|  | Soly: ±1.9% (not stated accuracy or repro-<br>ducibility - authors).   |
|  | Soly: ±1.9% (not stated accuracy or repro-   |
|  | Soly: ±1.9% (not stated accuracy or repro-<br>ducibility - authors).<br>Temp: ±0.2 <sup>O</sup> C (authors). |
|  | Soly: ±1.9% (not stated accuracy or repro-<br>ducibility - authors).<br>Temp: ±0.2 <sup>O</sup> C (authors). |
|  | Soly: ±1.9% (not stated accuracy or repro-<br>ducibility - authors).<br>Temp: ±0.2 <sup>O</sup> C (authors). |
|  | Soly: ±1.9% (not stated accuracy or repro-<br>ducibility - authors).<br>Temp: ±0.2 <sup>O</sup> C (authors). |

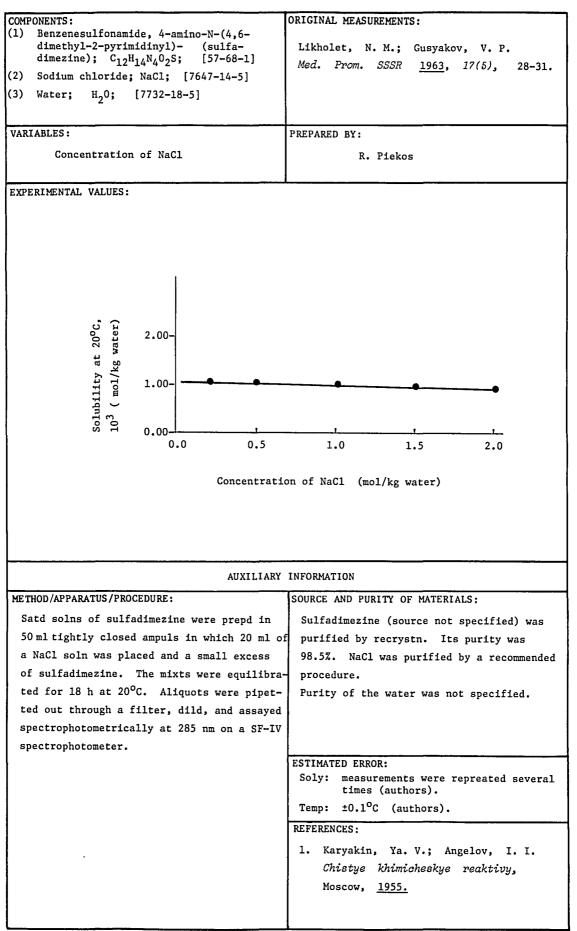
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                    |  |
|---|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   | Abdel Hadi, I.; Mezösi, J.;                               |  |
| dimethyl-2-pyrimidinyl)- (sulfa-  | Kedvessy, G.; Morvay, J.                                  |  |
| dimidine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | Pharmazie <u>1977</u> , 32, 791-3.                        |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |
|   |   |  |
| VARIABLES:  | PREPARED BY:  |  |
| One temperature: 22 <sup>0</sup> C  | R. Piekos   |  |
|   | l   |  |
| EXPERIMENTAL VALUES:  |   |  |
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| Solubility of cyrstalline forms I and   | IT of culfadimiding in veter                              |  |
|   |   |  |
| at 22 <sup>0</sup> C is equal and amounts to 0.35 mg                                  | g/ml water (1.3 x 10 <sup>-3</sup> mol dm <sup>-3</sup> , |  |
| compiler)   |   |  |
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| AUXILIARY   | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                           |  |
| Soly was detd as described by Martin (1).   | Sulfadimidine was a comm product (Reanal,                 |  |
| The system was equilibrated at 22 <sup>0</sup> C for 48 h                             |   |  |
|   | crystn from MeOH and EtOH resp, had both the              |  |
|   | mp of 197-8°C. Their identity was confirmed               |  |
|   | by IR spectroscopy, differential thermal                  |  |
|   | analysis and X-ray diffraction patterns.                  |  |
| 9   | Purity of the water was not specified.                    |  |
|   |   |  |
| 1   | ESTIMATED ERROR:  |  |
|   | Nothing specified.  |  |
|   |   |  |
|   | DEPERENCIA  |  |
|   | REFERENCES:   |  |
|   | 1. Martin, A. N. <i>Physical Pharmacy</i> ,               |  |
|   | Lea and Febiger, Philadelphia <u>1962</u> ,               |  |
|   | p. 340.   |  |
|   |   |  |
|   | 1   |  |

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|---|---|---|
| J | I | 2 |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6-<br>dimethyl-2-pyrimidinyl)- (sulfa-<br>dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1]<br>(2) Water; H <sub>2</sub> O; [7732-18-5] |   |  | EMENTS:<br>L.; Per'kova, N. M.<br><i>1979, 13(11)</i> , 87-91. |
|---|---|--|--|
| VARIABLES:  |   | PREPARED BY:   |  |
| Grinding regime<br>EXPERIMENTAL VALUES:   |   | R. Piekos  |  |
|   |   |  |  |
|   |   | Solubility at r  | oom temperature  |
|   | Specimen of sulfadiazine  |  | $10^3 \text{ mol } \text{dm}^{-3} \text{ a}$                   |
|   | Commercial  | 0.00036  | 1.3  |
|   | Commercial, ground in<br>a ball mill<br>Commercial, ground in   | 0.00036  | 1.3  |
|   | a jet mill  | 0.00038  | 1.4  |
|   | <sup>a</sup> Calculated by compiler.  |  |  |
| <u></u>   | AUXILIARY   | INFORMATION  | ······   |
| Satd solns w<br>of an excess<br>room temp.<br>stand for 12<br>sulfadimezing   | TUS/PROCEDURE:<br>ere prepd by prolonged agitation<br>of sulfadimezine in water at<br>The solns were then allowed to<br>h and filtered. The concn of<br>e in the filtrate was detd nitri-<br>by the method of the State<br>X. | Comm, pharmac<br>(source not s<br>a Pulverisett<br>C-1266-00 jet | water was not specified.                                       |

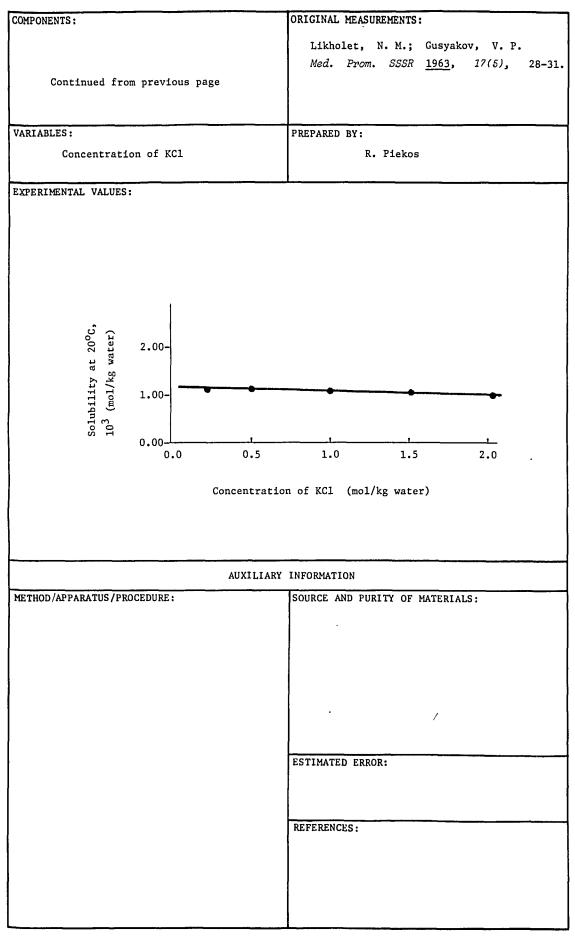
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6-                                | ORIGINAL MEASUREMENTS:   |  |
|---|--|--|
| dimethyl-2-pyrimidinyl)- (sulfa-  | Likholet, N. M.; Gusyakov, V. P.   |  |
| dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | Med. Prom. SSSR <u>1963</u> , 17(5), 28-31.                                |  |
| (2) Lithium chloride; LiCl; [7447-41-8]   |  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |  |
|   |  |  |
| VARIABLES:  | PREPARED BY:   |  |
| Concentration of LiCl   | R. Piekos  |  |
|   |  |  |
| EXPERIMENTAL VALUES:  |  |  |
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| ວິ ີສ 2.00-   |  |  |
| т 20<br>хат   |  |  |
| 03 (mol/kg water)   |  |  |
| 1 국 1.00-   |  |  |
|   |  |  |
|   |  |  |
|   | 1.0 1.5 2.0  |  |
|   | 1.0 1.0 2.0  |  |
| Concentrati   | on of LiCl (mol/kg water)  |  |
|   |  |  |
|   |  |  |
|   |  |  |
|   |  |  |
| AUXILIARY   | INFORMATION  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS.  |  |
| Satd solns of sulfadimezine were prepd in   | SOURCE AND PURITY OF MATERIALS;<br>Sulfadimezine was purified by recrystn. |  |
|   |  |  |
| 50-ml tightly closed ampuls in which 20 ml  | Its purity was 98.5%. LiCl was purified                                    |  |
| of a LiCl soln was placed and a small excess  | · · · ·  |  |
| of sulfadimezine. The mixts were equilibra-   | Purity of the water was not specified.                                     |  |
| ted for 18 h at 20°C. Aliquots were pipet-  |  |  |
| ted out through a filter, dild, and assayed   |  |  |
| spectrophotometrically at 285 nm on a SF-IV   |  |  |
| spectrophotometer.  |  |  |
|   | ESTIMATED ERROR:<br>Soly: measurements were repeated several               |  |
|   |  |  |
|   | times (authors).<br>Temp: ±0.1 <sup>0</sup> C (authors).                   |  |
|   |  |  |
|   | REFERENCES :   |  |
|   | l. Karyakin, Ya. V.; Angelov, I. I.  |  |
|   | Chistye khimicheskye reaktivy,   |  |
|   | Moscow, 1955.  |  |
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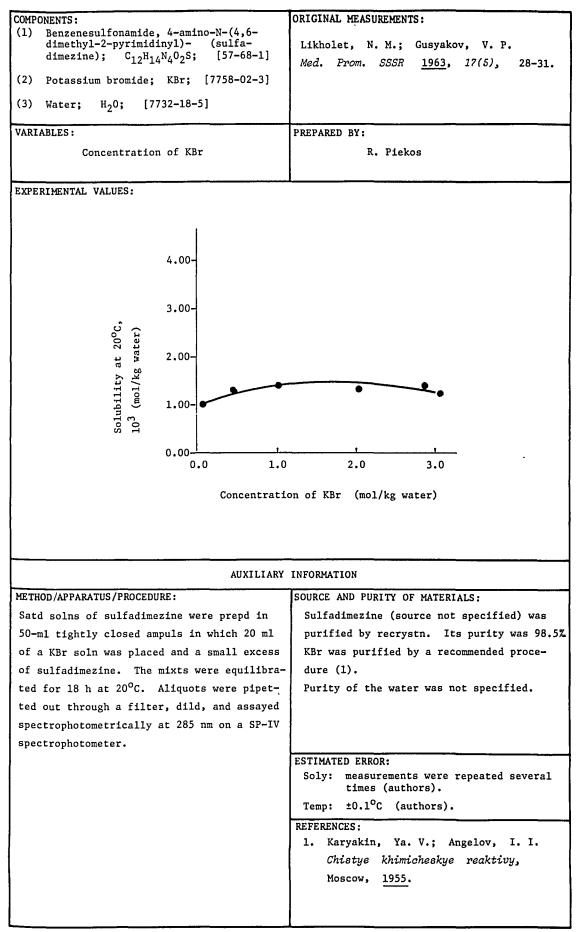


| COMPONENTS :   | ORIGINAL MEASUREMENTS:                         |                                   |
|--|--|-----------------------------------|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(4<br/>dimethyl-2-pyrimidinyl)- (sulfa-<br/>dimezine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</pre> | Gusyakov, V. P.; Liki                          |                                   |
| (2) Potassium chloride; KC1; [7447-40-7]   | Farm. Zh. (Kiev) <u>19</u>                     | <u>960</u> , <i>15(3)</i> , 21-4. |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |                                   |
| VARIABLES:   | PREPARED BY:                                   |                                   |
| Concentration of KCl   | R. Piekos                                      |                                   |
| EXPERIMENTAL VALUES:   |  |                                   |
| Concentration of KCl   | Solubility at 2                                | 20 <sup>0</sup> C                 |
| Weight %   |  | ol kg <sup>-1</sup> a             |
| 0.74   |  | <br>L.11                          |
| 1.82   | 0.030  | 1.01                              |
| 3.59   | 0.033  | L.19                              |
| 6.93   | 0.032  | 1.15                              |
| 12.97  | 0.025  | 0.90                              |
|  |  |                                   |
| AUXILIARY  | INFORMATION                                    |                                   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATE                      | ERIALS:                           |
| A small excess of sulfadimezine was equili-  | Sulfadimezine was carefu                       | -                                 |
| brated for 8 h in a 50-ml test tube with 20  | water, alcohol, and drie                       |                                   |
| ml of aqueous KCl soln. Aliquots were taken<br>with a pipet fitted with a filter. Sulfa-   | conformed to the require<br>Pharmacopeia VIII. | ements of the State               |
| dimezine was detd in the filtrate at 285 nm  | KCl was doubly crystd. Purity of the water     |                                   |
| using a SF-4 spectrophotometer.  | was not specified.                             | •                                 |
|  |  |                                   |
|  | ESTIMATED ERROR:                               |                                   |
|  | Soly: the accuracy corr<br>colorimetric detr   |                                   |
|  | Temp: not specified.                           |                                   |
|  | REFERENCES:                                    |                                   |
|  |  |                                   |
|  |  |                                   |
| L  |  | <u></u>                           |

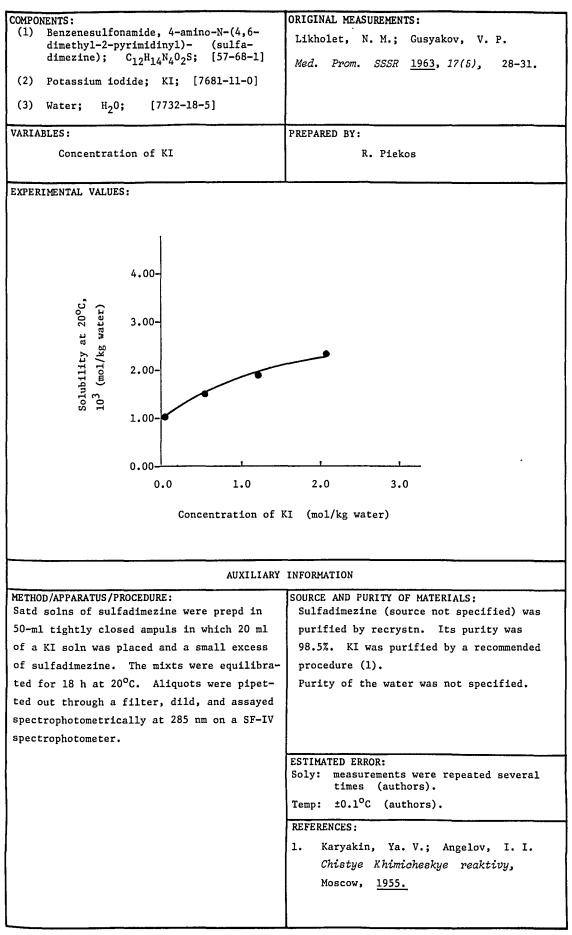
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6 -<br>dimethyl-2-pyrimidinyl)- (sulfa-<br>dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | ORIGINAL MEASUREMENTS:<br>Likholet, N. M.; Gusyakov, V. P.<br><i>Med. Prom. SSSR</i> <u>1963</u> , <i>17(5)</i> , 28-31. |  |  |
|--|--|--|--|
| (2) Potassium chloride: KCl; [7447-40-7]   |  |  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |  |  |
| VARIABLES:   | PREPARED BY:   |  |  |
| Concentration of KCl   | R. Piekos  |  |  |
|  |  |  |  |
| EXPERIMENTAL VALUES:   | <u>, , , , , , , , , , , , , , , , , , , </u>  |  |  |
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| <sup>2.00</sup>  |  |  |  |
| bility at 20°C (mol/kg water)  |  |  |  |
| Solubility at 20 <sup>0</sup> C,<br>10 <sup>3</sup> (mol/kg water)<br>-00.5  |  |  |  |
| 11 22  | · · · · · · · · · · · · · · · · · · ·  |  |  |
| 0.00-  |  |  |  |
| 1  | 2 3  |  |  |
| Concentration of KCl (mol/kg water)  |  |  |  |
|  |  |  |  |
| AUXILIARY  | INFORMATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimezine (source not specified) was  |  |  |
| Satd solns of sulfadimezine were prepd in<br>50-ml tightly closed ampuls in which 20 ml  | purified by recrystn. Its purity was 98.5%.  |  |  |
| of a KCl soln was placed and a small excess  | KCl was purified by a recommended procedure  |  |  |
| of sulfadimezine. The mixts were equilibra-  | (1). Purity of the water was not specified   |  |  |
| ted for 18 h at 20 <sup>0</sup> C. Aliquots were pipet-  |  |  |  |
| ted out through a filter, dild, and assayed  |  |  |  |
| spectrophotometrically at 285 nm on a SF-IV  |  |  |  |
| spectrophotometer.   |  |  |  |
|  | ESTIMATED ERROR:<br>Soly: measurements were repeated several<br>times (authors).   |  |  |
|  | Temp: ±0.1 <sup>0</sup> C (authors).   |  |  |
|  | REFERENCES:  |  |  |
|  | l. Karyakin, Ya. V.; Angelov, I. I.  |  |  |
|  | Chistye khimicheskye reaktivy <b>,</b>   |  |  |
|  | Moscow, <u>1955</u> .  |  |  |
|  |  |  |  |



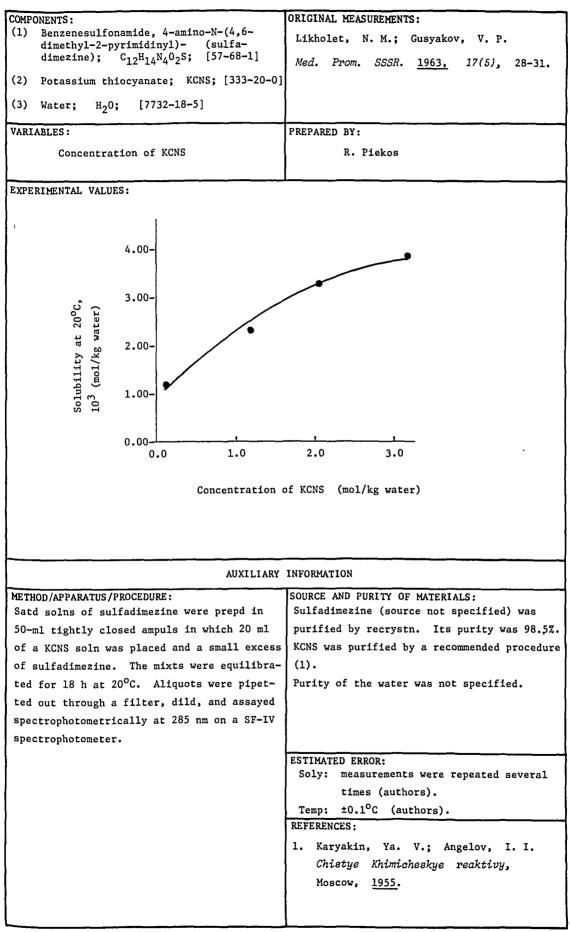
| COMPONENTS :  |                                   | ORIGINAL MEASUREMEN                       | TS:                                    |  |
|---|-----------------------------------|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   |                                   | Gusyakov, V. P.; Likhol'ot, N. M.         |  |  |
| dimethyl-2-pyrimidinyl)- (sulfa-<br>dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] |                                   | • •                                       |  |  |
|   | ium bromide; KBr; [7758-02-3]     | Farm. Zh. (Kiev                           | ) <u>1960</u> , <i>15(3)</i> , 21-4.   |  |
| <ul><li>(2) Potass</li><li>(3) Water;</li></ul>   |                                   |   |  |  |
|   |                                   | · · · · · · · · · · · · · · · · · · ·     |  |  |
| VARIABLES:  |                                   | PREPARED BY:                              |  |  |
| Co  | ncentration of KBr                | R. Piekos                                 |  |  |
| EXPERIMENTAL VALUES:  |                                   | <u> </u>                                  |  |  |
|   |                                   |   |  |  |
|   |                                   |   |  |  |
|   |                                   |   |  |  |
|   | Concentration of KBr              | Solubility                                | at 20°C                                |  |
|   | Weight %                          | g/100 g water                             | 10 <sup>3</sup> mol kg <sup>-1</sup> a |  |
|   | 1.17                              | 0.037                                     | 1.33                                   |  |
|   | 2.88                              | 0.041                                     | 1.47                                   |  |
|   | 5.61                              | 0.047                                     | 1.69                                   |  |
|   |                                   |   |  |  |
|   | 10.63                             | 0.046                                     | 1.65                                   |  |
|   | 19.22                             | 0.044                                     | 1.58                                   |  |
|   |                                   |   |  |  |
| <sup>a</sup> Calculated by compiler   |                                   |   |  |  |
|   |                                   |   |  |  |
|   |                                   | INFORMATION                               |  |  |
| METHOD/APPARATUS/PROCEDURE:<br>A small excess of sulfadimezine was equili-  |                                   | SOURCE AND PURITY O                       | F MATERIALS:<br>carefully washed with  |  |
| 1   | 8 h in a 50-ml test tube with 20  |   | d dried. Its purity con-               |  |
| ſ   | ous KBr soln. Aliquots were taken |   |  |  |
| with a pipet fitted with a filter. Sulfa-   |                                   | Pharmacopeia VIII. KBr was doubly crystd. |  |  |
| dimezine w  | as detd in the filtrate at 285 nm | Purity of the wate                        | r was not specified.                   |  |
| using a SF  | -4 spectrophotometer.             |   |  |  |
|   |                                   |   |  |  |
|   |                                   |   |  |  |
|   |                                   | ESTIMATED ERROR:<br>Soly: the accurac     | y corresponded to that of              |  |
|   |                                   |   | c detns (authors).                     |  |
|   |                                   | Temp: not specifi                         | .ed.                                   |  |
|   |                                   | REFERENCES:                               |  |  |
| ~   |                                   |   |  |  |
|   |                                   |   |  |  |
|   |                                   |   |  |  |
|   |                                   |   |  |  |
| L   |                                   | 1   |  |  |

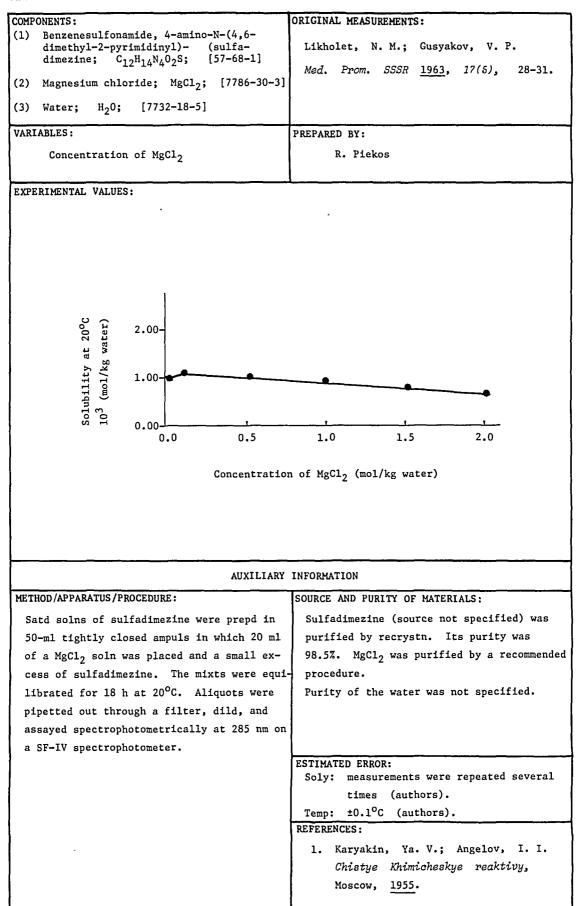


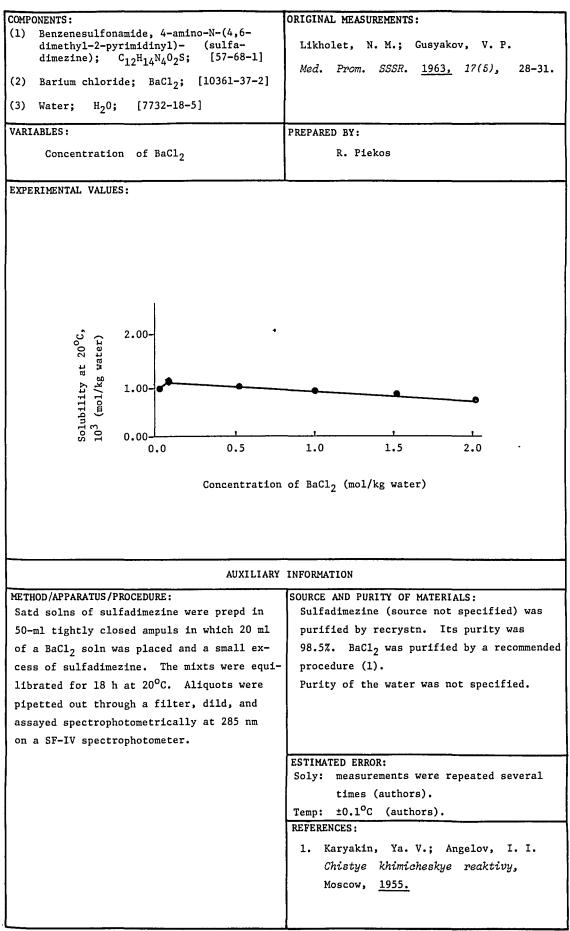
| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-   | ORIGINAL MERSOREMENTS:   |
| dimethyl-2-pyrimidinyl)- (sulfa-  | Gusyakov, V. P.; Likhol'ot, N. M                               |
| dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | Farm. Zh. (Kiev) <u>1960</u> , 15(3), 21-4.                    |
| (2) Potassium iodide; KI; [7681-11-0]   |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| Concentration of KI   | R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
|   |  |
|   | 2-1 1 / 1 / m - + - 20 <sup>9</sup> 0                          |
| Concentration of KI   | Solubility at 20°C   |
| Weight %  | g/100 g water 10 <sup>3</sup> mol kg <sup>-1 a</sup>           |
| 1.63  | 0.039 1.40   |
| 3.98  | 0.038 1.36   |
| 7.66  | 0.048 1.72   |
| 14.23   | 0.053 1.90   |
|   | ······   |
| <sup>a</sup> Calculated by comp   | biler  |
|   |  |
|   |  |
|   |  |
|   |  |
|   |  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                                |
| A small excess of sulfadimezine was equili-   |  |
| brated for 8 h in a 50-ml test tube with  | water, alcohol, and dried. Its purity con-                     |
| 20 ml aqueous KI soln. Aliquots were taker  | formed to the requirements of the State                        |
| with a pipet fitted with a filter. Sulfa-   | Pharmacopeia VIII. KI was doubly crystd.                       |
| dimezine was detd in the filtrate at 285 nm   | Purity of the water was not specified.                         |
| using a SF-4 spectrophotometer.   |  |
|   |  |
|   | ESTIMATED EDDOD.   |
|   | ESTIMATED ERROR:<br>Soly: the accuracy corresponded to that of |
|   | colorimetric detns (authors).<br>Temp: not specified.          |
|   | REFERENCES:  |
|   |  |
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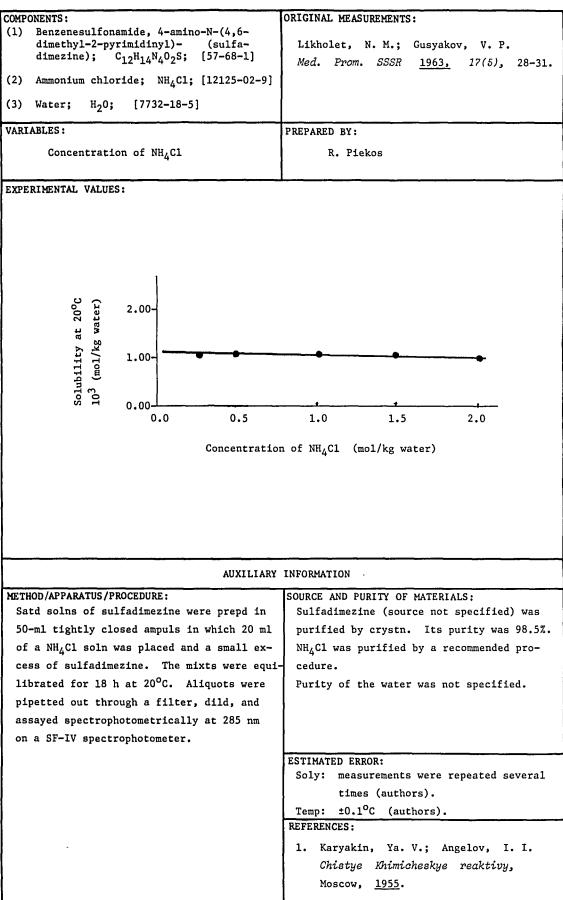


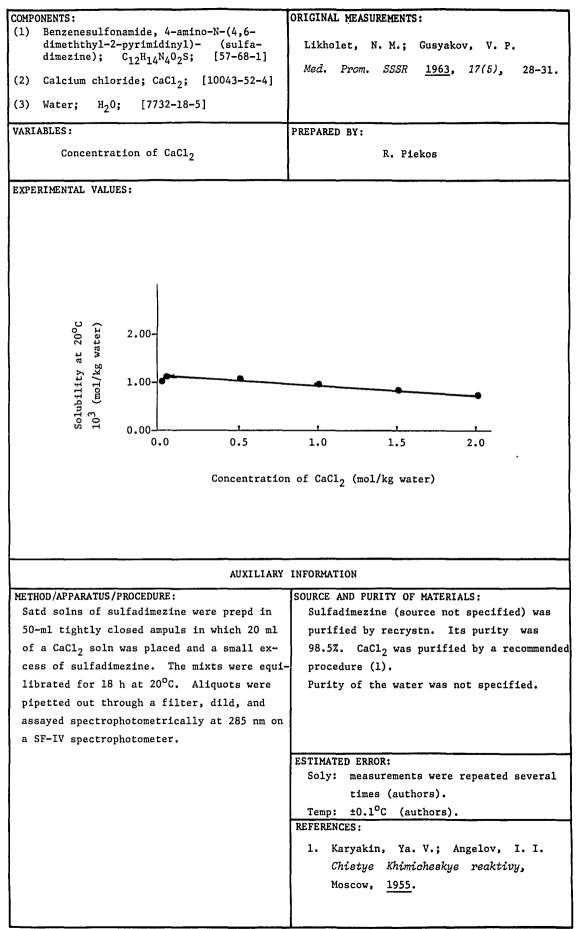
|   | ADTATIVIT AD LOUDE DUTC  |  |  |  |
|---|--|--|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6-                                | ORIGINAL MEASUREMENTS:   |  |  |  |
| dimethyl-2-pyrimidinyl)- (sulfa-  | Gusyakov, V. P.; Likhol'ot, N. M.  |  |  |  |
| dimezine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] | Farm. Zh. (Kiev) <u>1960</u> , 15(3), 21-4.                                |  |  |  |
| (2) Potassium thiocyanate; KSCN; [333-20-0]   |  |  |  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |  |  |  |
| VARIABLES:  | PREPARED BY:   |  |  |  |
| Concentration of KSCN   | R. Piekos  |  |  |  |
| EXPERIMENTAL VALUES:  |  |  |  |  |
|   |  |  |  |  |
|   |  |  |  |  |
|   |  |  |  |  |
| Concentration of KSCN   | Solubility at 20 <sup>0</sup> C  |  |  |  |
| Weight %  | g/100 g water $10^3$ mol kg <sup>-1 a</sup>                                |  |  |  |
| 0.96  | 0.036 1.2  |  |  |  |
| 2.37  | 0.039 1.4  |  |  |  |
| 4.63  | 0.047 1.6'   |  |  |  |
| 8.85  | 0.064 2.3  |  |  |  |
| 0.00  |  |  |  |  |
| <sup>a</sup> Calculated by compiler   |  |  |  |  |
| AIIXTLIARY  | INFORMATION  |  |  |  |
| METHOD /APPARATUS /PROCEDURE :  |  |  |  |  |
| A samll excess of sulfadimezine was equili-   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimezine was carefully washed with |  |  |  |
| brated for 8 h in a 50-ml test tube with 20   | water, alcohol, and dried. Its purity con-                                 |  |  |  |
| ml of aqueous KSCN soln. Aliquots were ta-  | formed to the requirements of the State                                    |  |  |  |
| ken with a pipet fitted with a filter. Sulfa-   | Pharmacopeia VIII. KSCN was doubly cyrstd.                                 |  |  |  |
| dimezine was detd in the filtrate at 285 nm   | Purity of the water was not specified.                                     |  |  |  |
| using a SF-4 spectrophotometer.   |  |  |  |  |
|   |  |  |  |  |
|   | FORTHUMER ERROR.   |  |  |  |
|   | ESTIMATED ERROR:<br>Soly: the accuracy corresponded to that of             |  |  |  |
|   | colorimetric detns (authors).  |  |  |  |
|   | Temp: not specified.   |  |  |  |
|   | REFERENCES:  |  |  |  |
|   |  |  |  |  |
|   |  |  |  |  |
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|   |  |  |  |  |



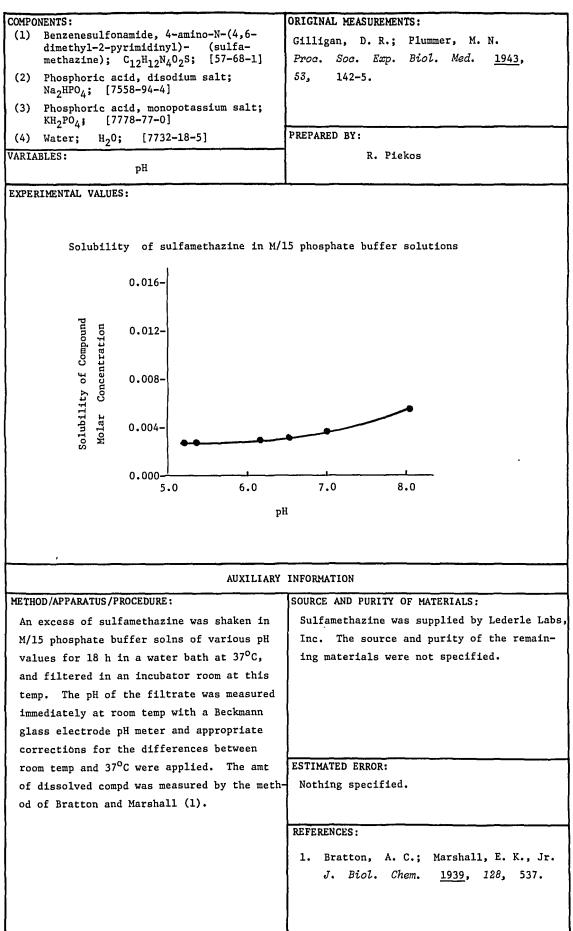








| 28   |                 |  |  |   |  |
|--|-----------------|--|--|---|--|
| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(4, 6-</pre>  |                 | ORIGINAL MEASUREMENTS:<br>Portnov, M. A.; Zasosov, V. A.;<br>Veselitskaya, T. A.; Mikhalev, V. A.<br><i>Med. Prom. SSSR</i> <u>1964</u> , <i>18(2)</i> , 36-9. |  |   |  |
| VARIABLES:   |                 |  | PREPARED BY:   |   |  |
| pH   |                 |  | R. Piekos  |   |  |
| EXPERIMENTAL VALUES:   |                 |  |  |   |  |
|  | рН              |  | Solubility a   | 1t 20 <sup>0</sup> C  |  |
|  |                 | g/100  | g solution   | 10 <sup>2</sup> mol kg <sup>-1</sup> a  |  |
|  | 1.1             | 0.6  | 5  | 2.33  |  |
| 1.5 0.3  |                 | .5   | 0.54   |   |  |
|  | <sup>a</sup> Ca | alculated  | l by compiler  |   |  |
|  | AU              | IXILIARY   | INFORMATION  |   |  |
| METHOD/APPARATUS/PROCEDURE   | :               |  | SOURCE AND PI  | JRITY OF MATERIALS:   |  |
| A test tube with an excess of sulfadimezine  |                 | Sulfadimezi  | ne (source not specified) con-                           |   |  |
| in a buffer soln was agitated for 6 h in a   |                 |  | formed to the requirements of the State                  |   |  |
| TS-15M thermostat and allo   |                 |  | -  | a IX. The buffer solns were   |  |
| 2 h. If, after 30 min of agitation, the pH<br>differed from the required value, it was<br>readjusted by the addn of a NaOH or HCl soln.<br>A sample was withdrawn through a tube fitted<br>with a filter and the sulfadimezine concn |                 | Purity of t  | chemically pure reagents.<br>he water was not specified. |   |  |
| was detd by diazotization<br>tric end point detection.   | with potent     | :1ome-   |  | ROR:<br>: not specified.<br><sup>o</sup> C (authors).                           |  |
|  |                 |  |  | r, M. A.; Veselitskaya, T. A.<br>v, V. A. <i>Med. Prom. SSSR</i><br>16(12), 27. |  |



| 20100 01001000 -  |               |                    |  |  |  |
|---|---------------|--------------------|--|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4  | -amino-N-(4,6 | 6-                 | ORIGINAL MEASUREMENTS:                     |  |  |
| dimethy1-2-pyrimidiny1)- (Elkosin);   |               |                    | Meier, R.; Allemann, O.; von Meyenburg, H. |  |  |
| $C_{12}H_{14}N_{4}O_{2}S;$ [57-68-1]  |               |                    | Schweiz. Med. Wochenschr. 1944,            |  |  |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4] |               |                    | 74(42), 1091-5.                            |  |  |
| (3) Phosphoric acid, mono<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]            |               | lt;                |  |  |  |
| (4) Water; H <sub>2</sub> 0; [7732  | 2-18-5]       |                    | PREPARED BY:                               |  |  |
| VARIABLES:  |               |                    | R. Piekos                                  |  |  |
| pH  |               |                    |  |  |  |
| EXPERIMENTAL VALUES:  |               |                    | • · · · · · · · · · · · · · · · · · · ·    |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               | Solubi             | lity of Elkosin in phosphate               |  |  |
|   | рН            |                    | rs at 37 <sup>°</sup> C                    |  |  |
|   |               | <br>mg%            | $10^3 \text{ mol } dm^{-3} a$              |  |  |
|   | 5.5           | 191.               | 0 6.862                                    |  |  |
|   | 6.5           | 209.               | 0 7.509                                    |  |  |
|   |               | 209.               |  |  |  |
|   | 7.5           | 297.               | 0 10.67                                    |  |  |
| -   |               | ·····              |  |  |  |
|   | a Ca          | alculat            | ed by compiler                             |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               | ILIARY             | INFORMATION                                |  |  |
| METHOD/APPARATUS/PROCEDURE  | :             |                    | SOURCE AND PURITY OF MATERIALS:            |  |  |
| Nothing specified.  |               |                    | Nothing specified.                         |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    | ESTIMATED ERROR:                           |  |  |
|   |               | Nothing specified. |  |  |  |
|   |               |                    |  |  |  |
|   |               | REFERENCES :       |  |  |  |
|   |               | ALLARIDED ;        |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |
|   |               |                    |  |  |  |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |  |  |
|--|--|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadi-midine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</li> <li>Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> <li>Phosphoric acid, monopotassium salt; KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ol> | Riess, W.<br>Intern. Congr. Chemotherapy, Proc.<br>3rd, Stuttgart <u>1963</u> , 1, 627–32. |  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:<br>R. Piekos  |  |  |
| VARIABLES:<br>One temperature: 20 <sup>0</sup> C; one pH: 7.4  |  |  |  |
| EXPERIMENTAL VALUES:   |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

Solubility of sulfadimidine in a M/15 Sörensen buffer solution (pH 7.4) at  $20^{\circ}$ C is 60 mg %(2.2 x  $10^{-3}$  mol dm<sup>-3</sup>, compiler ).

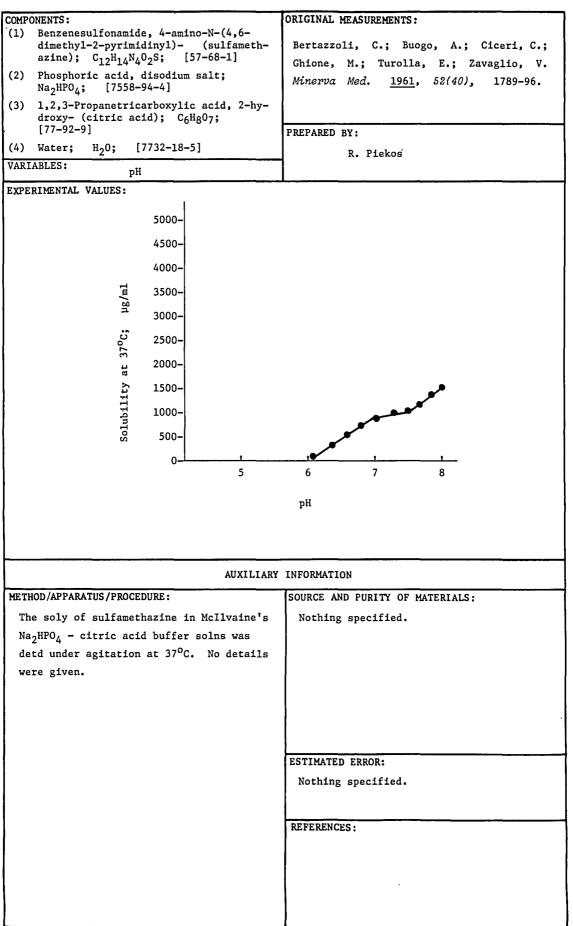
| METHOD/APPARATUS/PROCEDURE:                             | 3 |
|---|---|
| Sörensen buffer solns of pH varying                     |   |
| between 7 and 8 were prepd, satd with sulfa-            |   |
| dimidine at 20 <sup>0</sup> C, their pH was measured at |   |
| equilibrium, and the sulfadimidine was assay-           |   |
| ed colorimetrically. The measured pH values             |   |
| were plotted against concn, and the soly at             |   |
| pH 7.4 was detd by interpolation (personal              |   |
| communication).   |   |

SOURCE AND PURITY OF MATERIALS: Nothing specified.

ESTIMATED ERROR:

Nothing specified.

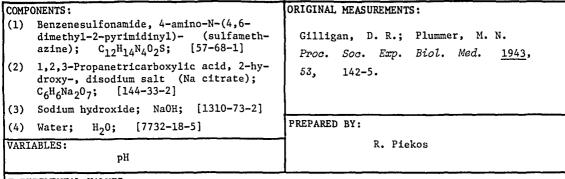
**REFERENCES:** 



| ·   |                                  |                                     |  |        |  |
|---|----------------------------------|-------------------------------------|--|--------|--|
| COMPONENTS:<br>(1) Benzenesulfonamid                              | e. 4-amino-N-(4.6-               | ORIGINAL MEASUREME                  | NTS:                                   |        |  |
| dimethy1-2-pyrimi   | dimethy1-2-pyrimidiny1)- (sulfa- |                                     | Portnov, M. A.; Zasosov, V. A.;        |        |  |
| dimezine); C <sub>12</sub> H                                      |                                  | Veselitskaya, T                     | . A.; Mikhalev, V.                     | Α.     |  |
| (2) Phosphoric acid,<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558- | .94-4]                           | Med. Prom. SSSI                     | R <u>1963</u> , <i>18(2)</i> , 3       | 36-9.  |  |
| (3) Phosphoric acid,<br>NaH <sub>2</sub> PO <sub>4</sub> ; [7558- |                                  |                                     |  |        |  |
| (4) Water; H <sub>2</sub> 0;                                      | 7732-1805]                       | PREPARED BY:                        |  |        |  |
| VARIABLES:  |                                  | R. Pie                              | kos                                    |        |  |
| EXPERIMENTAL VALUES:  |                                  | L                                   |  |        |  |
|   |                                  |                                     |  |        |  |
| - <b>F</b> - <b>r</b> ]   | pH                               | Solubilit                           | y at 20 <sup>0</sup> C                 |        |  |
| 01 pr   | osphate buffer                   | g/100 g solution                    | $10^2 \text{ mol kg}^{-1} \text{ a}$   |        |  |
|   | 0.7                              | 0.05                                | 0.2                                    |        |  |
|   | 1.5                              | 0.03                                | 0.1                                    |        |  |
|   | 8.5                              | 0.28                                | 1.0                                    |        |  |
|   |                                  |                                     |  |        |  |
| <u> </u>  | AUXILIARY                        | INFORMATION                         | <u> </u>                               |        |  |
| METHOD / APPARATUS / PROC   | EDURE:                           | SOURCE AND PURITY                   | OF MATERIALS:                          |        |  |
|   | excess of sulfadimezine          |                                     | source not specified                   | ) con- |  |
| in a buffer soln was  | s agitated for 6 h in a          | formed to the re                    | quirements of the Sta                  | ate    |  |
|   | nd allowed to stand for          | 1                                   | The buffer solns we                    |        |  |
| 2 h. If. after 30 r   | nin of agitation, the pH         |                                     | cally pure H <sub>3</sub> PO4 and      |        |  |
|   | equired value, it was            |                                     | ter was not specified                  |        |  |
|   | of a NaOH or HCl soln.           |                                     | •                                      |        |  |
|   | awn through a tube fitte         | a                                   |  |        |  |
| -   | ne sulfadimezine concn           | ]                                   |  |        |  |
|   | ation with potentiome-           |                                     | ······································ |        |  |
|   |                                  | ESTIMATED ERROR:<br>Soly and pH: no | t specified.                           |        |  |
| tric end point detection (1).                                     |                                  | Temp: ±0.2°C (                      |  |        |  |
|   |                                  | REFERENCES :                        |  |        |  |
|   |                                  |                                     |  |        |  |
|   |                                  |                                     |  |        |  |

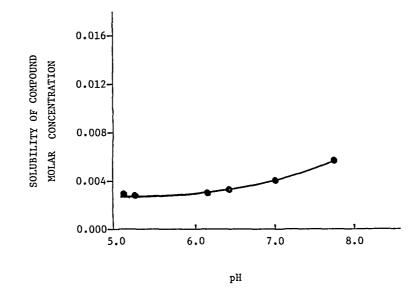
•

|  | OMPONENTS :   |   | ORIGINAL MEASUREMENTS:  |  |  |
|--|---|---|---|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfa-dimidine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</li> <li>Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> <li>Phosphoric acid, monopotassium salt; KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> <li>VARIABLES:</li> </ol> |   | (sulfa-<br>[57-68-1]<br>salt;<br>ssium salt;  | Hekster, Y. A.; Vree, T. B.;<br>Damsma, J. E.; Friesen, W. T.<br>J. Antimicrob. Chemother. 1981,<br>8, 133-44.<br>PREPARED BY:<br>R. Piekos |  |  |
| рН   |   |   |   |  |  |
| EXPERIMENTAL VALUES:   |   |   |   |  |  |
|  | pН  | Solubil   | Lity at 25 <sup>°</sup> C   |  |  |
|  |   | mg/l  | $10^2 \text{ mol } dm^{-3} a$   |  |  |
|  | 5.5   | 438   | 0.157   |  |  |
|  | 7.5   | 7000  | 2.515   |  |  |
|  | <sup>a</sup> Ca   | alculated by co   | ompiler   |  |  |
|  |   |   | •   |  |  |
|  |   | AUXILIARY   | INFORMATION   |  |  |
| METHOD/APPARATUS/PRO   | CEDURE :  | AUXILIARY   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:  |  |  |
| Satd solns of sulfa  | dimidine wer  | re prepd in   | SOURCE AND PURITY OF MATERIALS:<br>The source and purity of the materials   |  |  |
| Satd solns of sulface<br>phosphate buffers of<br>temp (25°C). The con-<br>measured by means of<br>high-performance lice<br>ped with a column or  | dimidine wer<br>f pH 5.5 and<br>oncn of sulf<br>f a Spectra<br>quid chromat<br>ven (Model 7   | re prepd in<br>1 7.5 at room<br>Fadimidine was<br>Physics 3500B<br>Cograph equip-<br>748) and a Pye-  | SOURCE AND PURITY OF MATERIALS:<br>The source and purity of the materials<br>were not specified.  |  |  |
| Satd solns of sulface<br>phosphate buffers of<br>temp (25°C). The co-<br>measured by means of<br>high-performance lice<br>ped with a column of<br>Unicam LC-UV spectro<br>The detector was con-  | dimidine wer<br>f pH 5.5 and<br>oncn of sulf<br>f a Spectra<br>quid chromat<br>ven (Model 7<br>ophotometric<br>nnected to a   | re prepd in<br>i 7.5 at room<br>fadimidine was<br>Physics 3500B<br>cograph equip-<br>748) and a Pye-<br>c detector.<br>a 1-mV recor-  | SOURCE AND PURITY OF MATERIALS:<br>The source and purity of the materials<br>were not specified.  |  |  |
| Satd solns of sulface<br>phosphate buffers of<br>temp (25°C). The co-<br>measured by means of<br>high-performance lice<br>ped with a column of<br>Unicam LC-UV spectro   | dimidine wer<br>f pH 5.5 and<br>oncn of sulf<br>f a Spectra<br>quid chromat<br>ven (Model 7<br>ophotometric<br>nnected to a<br>teel column<br>d with Lichr<br>hrompack. A | re prepd in<br>i 7.5 at room<br>fadimidine was<br>Physics 3500B<br>cograph equip-<br>748) and a Pye-<br>248) and a Pye-<br>258) and a Pye- | SOURCE AND PURITY OF MATERIALS:<br>The source and purity of the materials<br>were not specified.  |  |  |



EXPERIMENTAL VALUES:

Solubility of sulfamethazine in M/10 Na citrate + NaOH solution at 37°C



#### AUXILIARY INFORMATION

SOURCE AND PURITY OF MATERIALS: METHOD/APPARATUS/PROCEDURE: Sulfamethazine was supplied by Lederle Labs, An excess of sulfamethazine was shaken in Inc. The source and purity of the remain-M/10 Na citrate + NaOH solns of various pH values for 18 h in a water bath at 37°C, and ing materials were not specified. filtered in an incubator at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and  $37^{\rm O}{\rm C}$  were applied. The amt of dissolved compd was ESTIMATED ERROR: measured by the method of Bratton and Mar-Nothing specified. shall (1). **REFERENCES:** 1. Bratton, A. C.; Marshall, E. K., Jr. 1939, 128, 537. J. Biol. Chem.

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6-   | ORIGINAL MEASUREMENTS:  |
|--|---|
| dimethyl-2-pyrimidinyl)- (sulfadi-<br>mezine); $C_{12}H_{14}N_4O_2S$ ; [57-68-1]                                       | Likhol'ot, N. M. Farm. Zh. (Kiev)   |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]                                  | <u>1965</u> , 20(5), 44-6.  |
| (3) 1,2,3-Propanetricarboxylic acid, 2-h<br>droxy- (citric acid); C <sub>6</sub> H <sub>8</sub> 0 <sub>7</sub> ; [77-9 |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:  |
| VARIABLES: pH  | R. Piekos   |
| EXPERIMENTAL VALUES: ·   |   |
|  |   |
| рН   | Solubility at 20 <sup>0</sup> C   |
| of McIllvaine's buffer<br>solution g   | g/100  m1 10 <sup>3</sup> mol dm <sup>-3</sup> a  |
| 4.1  | 0.034 1.2   |
| 5.1  | 0.037 1.3   |
| 5.9  | 0.039 1.4   |
| 6.5  | 0.045 1.6   |
| 6.9  | 0.054 1.9   |
| 7.5  | 0.093 3.3   |
| <sup>a</sup> Calculated by com   | npiler  |
| AUXIL  | JARY INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| An earlier described method was employed   | i (1) Sulfadimezine: not specified.   |
| whereby a small excess of sulfadimezine  |   |
| equilibrated with 20 ml of the McIlvaine<br>buffer soln for 8 h in a 50-ml test tube                                   |   |
| Aliquots were withdrawn through a filter   |   |
| and sulfadimezine was assayed bromatomet   |   |
| cally.   |   |
|  |   |
|  | ESTIMATED ERROR:  |
|  | Soly: not specified.<br>Temp: ±0.1 <sup>0</sup> C (authors).  |
|  | pH : not specified.   |
|  | REFERENCES:   |
|  | <ol> <li>Gusyakov, V. P.; Likhol'ot, N. M.</li> <li>Farm. Zh. (Kiev) <u>1960</u>, 15(8),<br/>21.</li> </ol> |
|  |   |

| COMPONENTS:  |                |  | ORIGINAL MEA                | CHERNENT  | C .  |
|--|----------------|--|-----------------------------|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-di-   |                |  |                             |   | S:<br>Khalil, S. A. H.                                     |
| methyl-2-pyrimidinyl)- (sulfamethazine;<br>sulfadimidine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1]                          |                |  | J. Pharm.                   |   | -  |
| (2) Benzoic acid; C <sub>7</sub> H <sub>6</sub> O <sub>2</sub> ; [65-85-0]   |                |  |                             |   |  |
| (3) Water; H <sub>2</sub> O; [7732-18-5]   |                |  |                             |   |  |
| VARIABLES:   |                |  | PREPARED BY:                |   |  |
| Sulfamethazine cond  | entration, be  | nzoic acid   |                             | R. Piek   | 05   |
| concentration.   | concentration. |  |                             |   |  |
| EXPERIMENTAL VALUES  | 3:             | <u> </u>   |                             |   |  |
| Sulfamethazine Equilibrium solubility<br>concentration of sulfamethazine at<br>fixed benzoic acid con-<br>centration of 8.18<br>mmoles/1, at 24 <sup>o</sup> C |                | Initial<br>benzoic<br>acid con-<br>centra-<br>tion | Solubi.                     | lity of sulfamethazine <sup>b</sup>   |  |
| mmoles/1   | mmoles/1       | g dm <sup>-3</sup> a                               | mg%                         | mg%   | 10 <sup>3</sup> mol dm <sup>-3</sup> solution <sup>a</sup> |
| 2.16   | 0.076          | 0.0211   | 20                          | 38.8  | 1.39   |
| 3.60   | 0.083          | 0.0231   | 40                          | 38.2  | 1.37   |
| 7.20   | 0.173          | 0.0481   | 60                          | 36.1  | 1.30   |
| 10.80  | 1.400          | 0.3897   | 80                          | 13.0  | 0.467  |
| 14.40  | 1.442          | 0.4013   | 100                         | 4.8   | 0.17   |
| 36.00  | 1.417          | 0.3944   |                             |   |  |
| 72.00  | 1.457          | 0.4055   | <sup>a</sup> Calculat       | ed by co  | mpiler.  |
| 144.00 1.424 0.3963  |                |  |                             | hazine concentration  |  |
| 360.00   | 1.421          | 0.3955   |                             | 0.2 g%  |  |
|  |                |  |                             |   |  |
|  | <u></u>        |  |                             | <u> </u>  |  |
|  |                | AUXILIARI  | INFORMATION                 |   |  |
| METHOD/APPARATUS/PROCEDURE:<br>The concn of both benzoic acid and sulfame-   |                |  | SOURCE AND H<br>Sulfamethaz |   | a BP grade sulfadimidine                                   |
| razine were detd i   | ln a filtrate  | spectrophoto-                                      | (Imperial C                 | hemical   | Industries, England).                                      |
| metrically by appl   | ying equation  | s of Tinker  | Benzoic aci                 | d was of  | BP quality (British Drug                                   |
| and McBay (1) for  | two-component  | systems.   | Houses, Eng                 | land).  | Purity of the water was                                    |
| Measurements were  | made using a   | Unicam SP 500                                      | not specifi                 | .ed.  |  |
| spectrophotometer  | at 230 and 30  | 0 nm (in 0.05N                                     |                             |   |  |
| HC1). The validit  | y of the eqns  | was tested by                                      |                             |   |  |
| assaying known mixts of sulfamethazine and   |                |  |                             |   |  |
| benzoic acid.  |                | and<br>or r  | amethazi<br>±2.3%, r        | ne and benzoic acid ±1.9<br>esp. (not stated accuracy<br>bility - authors).<br>hors). |  |
|  |                |  | REFERENCES:                 |   |  |
|  |                | 1. Tinker  | , R.B.                      | ; McBay, A. J.  |  |
|  |                |  | J. Am                       | er. Pha   | rm. Assoc., Sci. Ed.                                       |
|  |                |  | <u>1954,</u>                | 43, 3   | 15.  |
|  |                |  |                             |   |  |
| L  |                |  | ۱ <u> </u>                  |   |  |

| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(4,6-di-<br/>methyl-2-pyrimidinyl)- (sulfadimezine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]<br/>(2) Ethanol; C<sub>2</sub>H<sub>6</sub>O; [64-17-5]</pre> | ORIGINAL MEASUREMENTS:<br>Shkadova, A. I.<br>Farm. Zh. (Kiev) <u>1969,</u> 24(3), 39-41. |
|--|--|
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [64-17-5]<br>(3) Water; H <sub>2</sub> O; [7732-18-5]  |  |
| VARIABLES:   | PREPARED BY:   |
| Concentration of ethanol   | R. Piekos  |

## EXPERIMENTAL VALUES:

| Concentration of ethanol |          | Solubility at 20 <sup>0</sup> C |                      |  |
|--------------------------|----------|---------------------------------|----------------------|--|
| mole %                   | weight % | $10^2 \text{ mol kg}^{-1}$      | g/100 g <sup>a</sup> |  |
| 0                        | 0        | 0.33                            | 0.092                |  |
| 10                       | 22.14    | 0.48                            | 0.13                 |  |
| 20                       | 39.01    | 1.07                            | 0.298                |  |
| 30                       | 52.31    | 2.18                            | 0.607                |  |
| 40                       | 63.04    | 2.85                            | 0.793                |  |
| 50                       | 71.90    | 3.12                            | 0.868                |  |
| 60                       | 79.33    | 3.07                            | 0.854                |  |
| 70                       | 85.65    | 2.96                            | 0.824                |  |
| 80                       | 91.10    | 2.38                            | 0.662                |  |
| 90                       | 95.83    | 0.98                            | 0.27                 |  |

<sup>a</sup> Calculated by compiler

| AUXILIARY   | INFORMATION   |
|---|---|
| METHOD/APPARATUS/PROCEDURE:<br>Sulfadimezine was equilibrated with the sol-<br>vent in a water thermostat at 20±0.1°C. The<br>concn of sulfadimezine was detd by alkalime-<br>tric titration. | SOURCE AND PURITY OF MATERIALS:<br>Purity of sulfadimezine conformed to the<br>requirements of the State Pharmacopiea IX.<br>The EtOH - water mixts were prepd from abs<br>EtOH (purity and source not specified) and<br>distd water. |
|   | ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.1 <sup>0</sup> C (author).   |
|   | REFERENCES :  |

| COMPONENTS   |   |                  | ORIGINAL MEASUREMENTS:   |
|--|---|------------------|--|
| methy  | Benzenesulfonamide, 4-amino-N-(4,6-di-<br>methyl-2-pyrimidinyl)- (sulfadimidine);<br>C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1] |                  | Gerencser-Németh, M.; Horbáth, M.<br><i>Gyógyszerészet</i> 1973, <i>17</i> , 417-21. |
|  | Sorbitan monooleate, polyoxyethylene<br>derivatives (Tween 80); [9005-65-6]   |                  | ;;   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |   |                  |  |
| VARIABLES:   | ;   | ·                | PREPARED BY:   |
| Concentration of Tween 80  |   |                  | R. Piekos  |
| EXPERIMENT   | TAL VALUES:   |                  |  |
|  | Concentration   | S                | olubility at 20 <sup>0</sup> C   |
|  | of Tween 80<br>Weight %   | g/100 g sol      | n <sup>a</sup> 10 <sup>3</sup> mol kg <sup>-1</sup> soln <sup>b</sup>                |
|  | 1   | 0.0530<br>0.0518 | 1.90<br>1.86   |
|  | 3   | 0.0734<br>0.0706 | 2.64<br>2.54   |
|  | 5   | 0.0922<br>0.0914 | 3.31<br>3.28   |
|  | 8 0.1078<br>0.1142  |                  | 3.873<br>4.103   |
| <sup>a</sup> Numerical values sup<br><sup>b</sup> Calculated by compil                     |   |                  |  |
|  |   | AUXILIARY        | INFORMATION  |
| METHOD / APPARATUS / PROCEDURE:  |   |                  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimidine (source and purity not speci-       |
| An excess of sulfadimidine in an aq Tween 80<br>soln was shaken in a lab shaker at 120 rpm |   |                  | fied) was dried at $100^{\circ}$ C for 3 h or over                                   |
| for 6 h. The soln was then filtered, the   |   |                  | concd $H_2SO_4$ for 72 h. Its mp was 196.5-8°C                                       |
| residue v  | vas washed first with t   | he filtrate      | Distd water was used. Source and purity of   |
| and finally with a small amt of water, dried and weighed.                                  |   |                  | Tween 80 were not specified.   |
|  |   |                  | ECTIMATED EDODA  |
|  |   |                  | ESTIMATED ERROR:   |
|  |   |                  | Nothing specified.   |
|  |   |                  | REFERENCES:  |
|  |   |                  |  |
|  |   |                  |  |
|  |   |                  |  |

| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-(4,6-di-methyl-2-pyrimidinyl)- (sulfamethazine; sulfadimidine); C12H14N202S; [57-68-1]</li> </ul> | Nasipuri, R. N.; Khalil, S. A. H.                                    |
| (2) 2-Pyrrolidinone, 1-etheny1-, polymers<br>(PVP); (C <sub>6</sub> H <sub>Q</sub> NO) <sub>x</sub> ; [9003-39-8]                            | J. Pharm. Sci. <u>1973,</u> 62(3), 473-5.                            |
| (3) Water; $H_20$ ; [7732-18-5]  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 24 <sup>0</sup> C   | R. Piekos  |
|  | Ki TEKOS   |
| EXPERIMENTAL VALUES:   |  |
| Solubility of sulfamethazine in an aq<br>5 mg% PVP, at 24 <sup>0</sup> C, is 40.1 mg% ( 1.44<br>compiler ).                                  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;                                      |
| Sulfamethazine was assayed spectrophotome-   | Sulfamethazine was a BP grade sulfadimidine                          |
| trically at 230 nm in a 0.05N HCl soln usin  | g (Imperial Chemical Industries, England).                           |
| a Unicam SP 500 spectrophotometer.   | PVP was a sample having an av mol wt of                              |
|  | 40,000 (Plasdone k 29-32, GAF Corp., New                             |
|  | York, N. Y.)   |
|  | Purity of the water was not specified.                               |
|  |  |
|  |  |
|  | ESTIMATED ERROR:   |
|  | Soly: ±1.9% (not stated accuracy or re-<br>producibility - authors). |
|  | Temp: ±0.2°C (authors).  |
|  | REFERENCES:  |
|  |  |
| · ·  |  |
|  |  |
|  |  |
|  |  |

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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(4,6-di-   | ORIGINAL MEASUREMENTS:  |
|---|---|
| methy1-2-pyrimidiny1)- (sulfamethazine;   | Nasipuri, R. N.; Khalil, S. A. H.   |
| sulfadimidine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1]                              | J. Pharm. Sci. <u>1973</u> , 62(3), 473-5.  |
| (2) Benzoic acid; C <sub>7</sub> H <sub>6</sub> O <sub>2</sub> ; [65-85-0]  |   |
| <pre>(3) 2-Pyrrolidinone, 1-etheny1-, polymers<br/>(PVP); (C<sub>6</sub>H<sub>9</sub>NO)<sub>x</sub>; [9003-39-8]</pre> |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:  |
| VARIABLES:  | R. Piekos   |
| Initial benzoic acid concentration  | K. Flekos   |
| EXPERIMENTAL VALUES:  |   |
|   | lity of sulfamethazine at 24 <sup>0</sup> C<br>plution containing 5 mg% of PVP  |
| concentration   |   |
| mg% mg%   | 10 <sup>3</sup> mol dm <sup>-3</sup> solution <sup>a</sup>  |
| 20 39.9   | 1.43  |
| 40 40.4   | 1.45  |
| 60 40.2   | 1.44  |
| 80 39.8   | 1.43  |
| 100 39.9  | 1.43  |
|   |   |
|   |   |
| AUXILIARY   | INFORMATION   |
|   | SOURCE AND PURITY OF MATERIALS:   |
| METHOD/APPARATUS/PROCEDURE:   | 1   |
| The concn of both benzoic acid and sulfamer-  | Sulfamethazine was a BP grade sulfadimidine   |
| azine were detd in a filtrate spectrophoto-   | _ · ·   |
| metrically by applying equations of Tinker  | Benzoic acid was of BP quality (British   |
| and McBay (1) for two-component systems.  | Drug Houses, England). PVP (Plasdone k  |
| Measurements were made using a Unicam SP 500  | 29-32, GAF Corp., New York, N. Y.) was a  |
| spectrophotometer at 230 and 300 nm ( in  | sample having an av mol wt of 40,000.   |
| 0.05N HCl ). The validity of the eqns was<br>tested by assaying known mixts of sulfameth-                               | Purity of the water was not specified.  |
| azine and benzoic acid.   | ESTIMATED ERROR:<br>Soly: sulfamethazine and benzoic acid ±1.9<br>and ±2.3%, resp. (not stated accuracy<br>or reproducibility - authors ).<br>Temp: ±0.2°C (authors). |
|   | REFERENCES:   |
|   | 1. Tinker, R. B.; McBay, A. J.  |
|   | J. Amer. Pharm. Assoc., Sci. Ed.  |
|   | 1954, 43, 315.  |
|   | ,,  |
|   | <u> </u>  |

| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(4,6-di-     methyl-2-pyrimidinyl)- (sulfamethazine);     C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1] (2) Ethanol, 2-ethoxy-; C<sub>4</sub>H<sub>10</sub>O<sub>2</sub>;     [110-80-5]</pre> | ORIGINAL MEASUREMENTS:<br>Sunwoo, C.; Eisen, H.<br>J. Pharm. Sci. <u>1971,</u> 60, 238-44.   |
|--|--|
| VARIABLES:   | PREPARED BY:   |
| One temperature: 25 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:<br>The mole fraction solubility of sulfame<br>is 0.0184 mol/dm <sup>3</sup> ( 5.47 g/100 g solut  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Soly was detd by the method reported by<br>Restaino and Martin (1). Sulfamethazine was<br>assayed on a Coleman-Hitachi 124 double-beam<br>spectrophotometer at 270 nm after diln of a<br>sample with 95% ethanol or water.              | <pre>SOURCE AND PURITY OF MATERIALS:<br/>The USP sulfamethazine (American Cyanamid<br/>Co., Pearl River, N.Y.), recrystd from warm<br/>alcohol and an industrial grade 2-ethoxy-<br/>ethanol (Cellosolve solvent, Union Carbide,<br/>New York, N. Y.) were used.</pre><br>ESTIMATED ERROR:<br>Temp: ±1.0°C (authors).<br>Soly: the mean of 3 runs was given<br>(authors).<br>REFERENCES:<br>1. Restaino, F. A.; Martin, A. N.<br>J. Pharm. Sci. <u>1964</u> , 53, 636. |

|  |  |             | ORIGINAL M  | EASUREMENTS                | ;                   |                                       |                             |
|--|--|-------------|---|----------------------------|---------------------|---------------------------------------|-----------------------------|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-di-   |  |             | Gutierrre:  | z, F.H.                    |                     |                                       |                             |
| met  | hyl-2-pyrim                                      | idinyl)- (s | ulfamethazin  | ne); Anales f              | is. auim.           | (Madrid)                              | 1945, <i>41</i> ,           |
| c <sub>12</sub>  | H <sub>14</sub> N <sub>4</sub> 0 <sub>2</sub> S; | [57-68-1]   |   | 537-60.                    | L L                 |                                       |                             |
| (2) 2-P  | ropanone (a                                      | cetone); C  | <sub>3</sub> н <sub>6</sub> 0;  |                            |                     |                                       |                             |
| [67  | ~64~1]   |             |   |                            |                     |                                       |                             |
| VARIABLE   | S:   |             |   | PREPARED B                 | Y:                  |                                       |                             |
|  | Tempera  | ture        |   |                            | R. Piek             | os                                    |                             |
| EXPERIME   | NTAL VALUES                                      | :           |   |                            |                     |                                       |                             |
| t/ <sup>o</sup> C  | G <sup>a</sup>                                   | Ep          | x <sub>g</sub> /1 <sup>c</sup>  | mol/1 <sup>d</sup> acetone | mmol/mol<br>acetone | l:Xg                                  | $1 + x_{cc}^{f}$            |
| 0  | 4.481  | 4.288       | 36.502  | 131.1                      | 9.39                | 22.31                                 | 27.66                       |
| 5  | 4.601  | 4.397       | 37.213  | 133.7                      | 9.59                | 21.73                                 | 26.86                       |
| 10   | 4.701  | 4.489       | 37.741  | 135.6                      | 9.80                | 21,27                                 | 26.49                       |
| 15   | 4.959  | 4.724       | 39.528  | 142.0                      | 10.35               | 20.16                                 | 25.29                       |
| 20   | 5.269  | 5.005       | 41.688  | 149.8                      | 10.99               | 18.98                                 | 23.98                       |
| 25   | 5.406  | 5.128       | 42.448  | 152.5                      | 11.28               | 18.49                                 | 23.56                       |
| 30   | 5.684  | 5.377       | 44.295  | 159.1                      | 11.86               | 17.59                                 | 22.57                       |
| 35   | 6.002  | 5.651       | 46.413  | 166.7                      | 12.52               | 16.66                                 | 21.54                       |
| 40   | 6.597  | 6,188       | 50.625  | 181.9                      | 13.76               | 15.19                                 | 19.75                       |
| 45   | 7.486  | 6.964       | 56.998  | 204.8                      | 15,62               | 13.36                                 | 17.54                       |
| 50   | 8.759  | 8,053       | 66.174  | 237.3                      | 18.27               | 11.42                                 | 15.11                       |
| $a_{\rm G} = \frac{p \ 100}{P - p}$ , where p and P are the weights of solute and solution, resp.<br>$b_{\rm E} = \frac{G \ 100}{G + 100}$ , $c_{\rm g}/l$ acetone; $d_{\rm should}$ be mmol/l acetone (compiler); |  |             |   |                            |                     |                                       |                             |
| <sup>e</sup> g of acetone required to dissolved 1 g of solute; <sup>f</sup> volume (cm <sup>3</sup> ) of acetone required to dissolve 1 g of solute.   |  |             |   |                            |                     |                                       |                             |
|  |  |             | AUXILI  | ARY INFORMATION            | 1                   | · · · · · · · · · · · · · · · · · · · |                             |
| ,  |  |             |   | PURITY OF                  |                     |                                       |                             |
| A special all-glass app was constructed ena-   |  |             |   |                            | s not specif:       |                                       |                             |
| bling the prepn of satd solns, agitation by  |  | Í           | -   |                            | ed. The absen       |                                       |                             |
| bubbling a stream of acetone-satd N, filtra-   |  |             |   |                            | confirmed by        |                                       |                             |
|  |  |             | nt without o  | 1-                         |                     |                                       | acopeia VI a                |
| tact with air. Two exchangeable dissoln ves-   |  |             | Spanish Pharmacopeia VIII.<br>The purity of sulfamethazine was not speci- |                            |                     |                                       |                             |
| sels of 15 and 8 $cm^3$ working capacity were  |  |             | y ot sulfam   | ethazine w                 | as not speci•       |                                       |                             |
|  |  |             |   |                            |                     |                                       |                             |
|  |  |             | tat. The vo   |                            |                     |                                       |                             |
|  |  |             | cm <sup>3</sup> , and the   | LOITWALED                  |                     |                                       |                             |
|  |  |             | h. The satd   |                            |                     |                                       | ted until 2<br>the second o |
|  |  | -           | the solvent   | cir                        | nal were ob         |                                       |                             |
| _  |  |             | ere dried at  | Temp: =0                   |                     | hor).                                 |                             |
| 105°C,   | weighed, an                                      | d examd for | the presence  | e REFERENCES               | :                   |                                       |                             |

of solvated acetone.

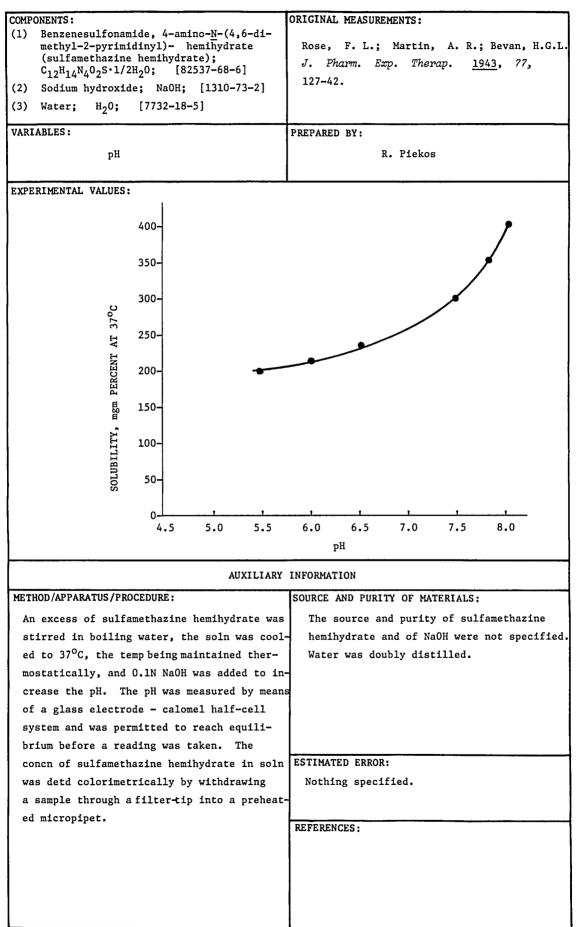
| 344  | •  |
|--|--|
| <ul> <li>COMPONENTS:</li> <li>(1) Benzenesulfonamide, 4-amino-N-(4,6-di-methy1-2-pyrimidiny1)- (sulfadimidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [57-68-1]</li> <li>(2) Methane, trichloro- (chloroform);<br/>CHCl<sub>3</sub>; [67-66-3]</li> </ul> | ORIGINAL MEASUREMENTS:<br>Riess, W.<br>Intern. Congr. Chemotherapy, Proc.<br>3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 20 <sup>0</sup> C   | R. Piekos  |
| Solubility of sulfadimidine in chlorof<br>mol dm <sup>-3</sup> solution, compiler).  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| Nothing specified.   | Nothing specified.   |

ESTIMATED ERROR:

Nothing specified.

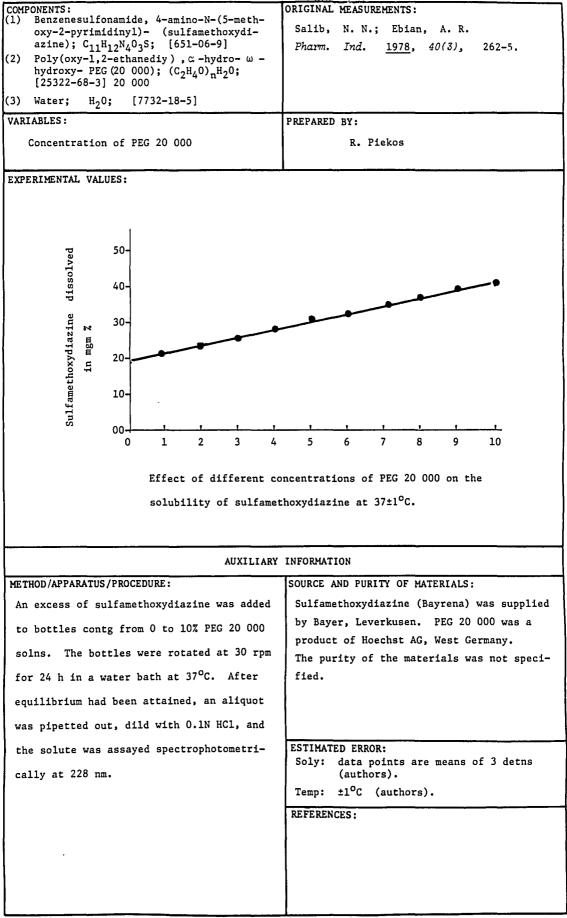
REFERENCES:

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                    |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-di-<br/>methyl-2-pyrimidinyl)- (sulfadimezine);</li> </ol> | Gusyakov, V. P.; Likhol'ot, N. M.;                        |
| $C_{12}H_{14}N_4O_2S;$ [57-68-1]   | Kutna, I. M. Farm. Zh. (Kiev)                             |
| (2) Poly(oxy-1,2-ethanediy1), $\alpha$ -hydro- $\omega$ -  | <u>1968,</u> 23(6), 56-61.                                |
| (2) Foly( $0xy-1,2-echaned1y1$ ), $\alpha = hydro = hydroxy-$ (PEG 400); $(C_2H_40)_nH_20$ ;           |   |
| [25322-68-3] 400   |   |
| VARIABLES :  | PREPARED BY:  |
| One temperature: 21-25°C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfadimezine in $\alpha$ -hydro-  | $\omega$ -hydroxypoly(oxy-1,2-ethanediy1)                 |
| 400 at room temperature (21-25 <sup>0</sup> C) is 10   | .4% by weight ( 0.417 mol kg $^{-1}$                      |
| PEG 400, compiler ).   |   |
| rad 400, compiler ).   |   |
|  |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;                           |
| Small quantities (2-4 mg) of sulfadimezine   | Sulfadimezine: neither source nor purity                  |
| were added to a known quantity of PEG 400  | was specified. PEG 400: source not specified;             |
| under stirring until satn was attained.  | sp gr 1.127 g cm <sup>-3</sup> ; temp of solidification   |
|  | approx 6 <sup>o</sup> C; refractive index 1.466 (temp not |
|  | indicated).   |
|  | 1   |
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|  | ESTIMATED ERROR:  |
|  |   |
|  | Nothing specified.  |
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|  | REFERENCES:   |
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:  |
|---|---|
| (1) Cobalt, bis[4-amino-N-(4,6-dimethy1-2-  | Tskitishvili, M. G.; Mikadze, I. I.                             |
| pyrimidinyl)benzenesulfonamidato-N <sup>N</sup> ,0]-,   | Soobshch. Akad. Nauk Gruz. SSR                                  |
| hydrate; C <sub>24</sub> H <sub>26</sub> CoN <sub>8</sub> 0 <sub>4</sub> S <sub>2</sub> •nH <sub>2</sub> 0;   |   |
| [86729-24-0]  | <u>1978</u> , 89(3), 589-92.                                    |
|   |   |
| (2) Hydrochloric acid; HC1; [7647-01-0]   |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:  |
| VARIABLES:  |   |
| PH  | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
| K <sub>so</sub> over the HCl concentration range 2<br>at 25 <sup>o</sup> C, is 3.35 x 10 <sup>-13</sup> .   | $2.5 \times 10^{-2} - 2.5 \times 10^{-5} \text{ mol dm}^{-3}$ , |
|   | INFORMATION   |
|   |   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                                 |
| In a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute was placed and shaken for 6 h in a water thermostat at $25^{\circ}$ C. After attaining equilibrium, the pH of the soln was measured and the Co <sup>2+</sup> and S content was detd to calculate K <sub>so</sub> . | Nothing specified.  |
| 1   | ESTIMATED ERROR:  |
|   |   |
|   | Nothing specified.  |
|   | REFERENCES :  |
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| ONENTS | ::   |        |      |    |
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| Ronzo  | neer | 11 fon | amic | 14 |



| COMPONENTS :   | ORIGINAL MEASUREMENTS:   |
|--|--|
| <ol> <li>Copper, bis[4-amino-<u>N</u>-(4,6-dimethy]-2-<br/>pyrimidinyl)benzenesulfonamidato-<u>N</u><sup>N</sup>,0]-,<br/>hydrate; C<sub>24</sub>H<sub>26</sub>CuN<sub>8</sub>0<sub>4</sub>S<sub>2</sub>•nH<sub>2</sub>0;<br/>[86729-23-9]</li> <li>Hydrochloric acid; HC1; [7647-01-0]</li> <li>Water; H<sub>2</sub>0; [7732-18-5]</li> </ol> | Tskitishvili, M.G.; Mikadze, I.I.<br>Soobshch. Akad. Nauk Gruz. SSR<br><u>1978,</u> 89(3), 589-92. |
|  |  |
| PH pH  | PREPARED BY:<br>R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| $K_{so}$ over the HCl concentration range<br>at 25°C, is 1.77 x 10 <sup>-16</sup> .  | 2.5 x $10^{-2}$ - 2.5 x $10^{-5}$ mol dm <sup>-3</sup> ,   |
|  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| In a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute was placed and shaken for 6 h in a water thermostat at $25^{\circ}$ C. After attaining equilibrium , the pH of the soln was measured and the Cu <sup>2+</sup> and S content was detd to calculate K <sub>so</sub> .   | Nothing specified.   |
|  | ESTIMATED ERROR:   |
|  | Nothing specified.   |
|  | REFERENCES:  |

| 350  |         |                  |
|------|---------|------------------|
| COMP | ONENTS: |                  |
| (1)  |         | bis[4-amino-N-(4 |

2-pyrimidinyl)benzenesulfonamidato-<u>N</u>,0 hydrate; C<sub>24</sub>H<sub>26</sub>MnN<sub>8</sub>0<sub>4</sub>S<sub>2</sub>•nH<sub>2</sub>0; [84812-75-9] Tskitishvili, M. G.; Shvelashvili, A. E.; Mikadze, I. I.; Zhorzholiani, N. B.; Chrelashvili, M. V. Izv. Akad. Nauk (2) Hydrochloric acid; HC1; [7647-01-0] Gruz. SSR, Ser. Khim. 1981, 7(4), (3) Water; H<sub>2</sub>0; [7732-18-5] 300-4. VARIABLES: PREPARED BY: pН R. Piekos EXPERIMENTAL VALUES: Concentration of HC1 pH 10<sup>9</sup> K<sub>so</sub> at 25°C (mo1/1)  $1.0 \times 10^{-2}$ 6.40 7.91  $5.0 \times 10^{-3}$ 6.77 7.94  $2.5 \times 10^{-3}$ 6.96 7.91  $1.0 \times 10^{-3}$ 7.92 7.54  $5.0 \times 10^{-4}$ 7.82 7.90  $2.5 \times 10^{-4}$ 7.90 7.92  $1.0 \times 10^{-4}$ 8,10 7.94

ORIGINAL MEASUREMENTS:

| $5.0 \times 10^{-5}$ | 8.12          | 7.97 |
|----------------------|---------------|------|
| $1.5 \times 10^{-5}$ | 8.15          | 8.00 |
|                      | Mean          | 7.94 |
| To be continued on   | the next page | 2.   |

### AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                              | SOURCE AND PURITY OF MATERIALS:                            |
|--|--|
| The earlier described apparatus and method               | 0.1M solutions of chem pure Mn(OAc) <sub>2</sub> ,         |
| was used (1): in a glass vessel, a mixt of               | monosodium salt of sulfadimezine, HCl as                   |
| 100 ml of HCl of appropriate concn and the               | well as doubly distd water were used. The                  |
| solute were placed and shaken for 6 h in a               | source of the materials was no specified.                  |
| water thermostat at 25°C. After attaining                |  |
| equilibrium , the pH of the soln was measured            |  |
| and the $Mn^{2+}$ and S content was determined to        |  |
| calculate K <sub>so</sub> . The pH was measured on a pH- |  |
| 673 pH meter.  | ESTIMATED ERROR:   |
|  | $K_{so}$ : std deviation 3 x 10 <sup>-11</sup> (compiler). |
|  | Temp and pH: not specified.                                |
|  |  |
|  | REFERENCES:  |
|  | 1. Tskitishvili, M. G.; Mikadze, I. I.                     |
|  | Soobshch. Akad. Nauk Gruz. SSR                             |
|  | <u>1978,</u> 89(3), 589.                                   |
|  | 1  |
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|  | 30   |
|--|--|
| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
| <ol> <li>Nickel,bis[4-amino-<u>N</u>-(4,6-dimethyl-2-<br/>pyrimidinyl)benzenesulfonamidato-<u>N</u><sup>N</sup>,0]-</li> </ol> | Tskitishvili, M. G.; Shvelashvili, A. E.                                       |
| dihydrate; C <sub>24</sub> H <sub>26</sub> N <sub>8</sub> N10 <sub>4</sub> S <sub>2</sub> ·2H <sub>2</sub> 0;<br>[84812-74-8]  | Mikadze, I. I.; Zhorzholiani, N. B.;   |
| (2) Hydrochloric acid; HC1; [7647-01-0]  | Chrelashvili, M. V. Izv. Akad. Nauk  |
| (3) Water; H <sub>2</sub> O; [7732-18-5]   | Gruz. SSR. Ser. Khim. <u>1981,</u> 7(4),                                       |
| •<br>•   | 300-4.   |
| VARIABLES:<br>pH   | PREPARED BY:<br>R. Piekos  |
| F  |  |
| EXPERIMENTAL VALUES:   | I  |
|  |  |
| Concentration of HCl   | pH 10 <sup>14</sup> K <sub>so</sub> at 25 <sup>0</sup> C                       |
| (mol/l)  | pH 10 <sup>14</sup> K <sub>so</sub> at 25 <sup>5</sup> C                       |
|  |  |
|  |  |
|  | 1.63   |
|  | 1.37 1.66  |
| $2.5 \times 10^{-3}$   | 3.29 1.60  |
| $1.0 \times 10^{-3}$   | .85 1.60   |
| $5.0 \times 10^{-4}$ 9   | .10 1.66   |
| $2.5 \times 10^{-4}$ 9   | 1.64   |
| $1.0 \times 10^{-4}$ 9   | .34 1.67   |
| <b>r</b>   |  |
| . 5  |  |
| 2.5 x 10 - 9   |  |
|  | Mean 1.64  |
|  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| The earlier described apparatus and method   | 0.1M solns of chem. pure Ni(OAc)2, mono-                                       |
| was used (1): in a glass vessel, a mixt of   | sodium salt of sulfadimezine, and HCl as                                       |
| 100 ml of HCl of appropriate concn and the   | well as doubly distd water were used. The                                      |
| solute were placed and shaken for 6 h in a   | source of the materials was not specified.                                     |
| water thermostat at 25°C. After attaining  |  |
| equilibrium, the pH of the soln was meas-  |  |
| ured and the Ni <sup>2+</sup> and S content was deter-   |  |
| mined to calculate K <sub>so</sub> . The pH was meas-  |  |
| ured on a pH-673 pH meter.   | ESTIMATED ERROR:<br>$K_{so}$ : std deviation 3 x 10 <sup>-16</sup> (compiler)/ |
|  | Temp and pH: not specified.  |
|  |  |
|  | REFERENCES:  |
|  | 1. Tskitishvili, M. G.; Mikadze, I. I.   |
|  | Soobshch. Akad. Nauk Gruz. SSR   |
|  | <u>1978</u> , <i>89(3)</i> , 589.  |
|  | 1  |
|  | I  |

| COMP   | ONENTS:  |   |   | ORIGINAL MEASUR   | EMENTS:                  |     |
|--|--|---|---|---|--------------------------|-----|
| (1)  |  |   | Nesbitt, R. U   | ., Jr.; Sandmann,   | B. J.<br>1012-17.        |     |
|  |  |   | e; KNO <sub>3</sub> ; [7757-79-1]   |   |                          |     |
|  | Water  |   | [7732-18-5]   |   |                          |     |
| VARI   | ABLES:   |   |   | PREPARED BY:  |                          |     |
|  |  | рH  |   | R. P  | iekos                    |     |
| EXPE   | RIMENT   | AL VALUES:  |   | 1   |                          |     |
|  | the M<br>Determ  | ethod of Kno<br>mined by Din  | tal Silver Sulfamethazin<br>own Subtraction with the<br>rect Potentiometry on Id<br>ric Acid Buffer | Molar Concentra   | tion of the Silver I     | Ion |
|  |  |   | pH 2.186  |   | pH 3.970                 |     |
|  |  | S x 10 <sup>3</sup>   | $[Ag^+] \times 10^3$  | S x 10 <sup>4</sup>   | $[Ag^{+}] \times 10^{4}$ |     |
|  |  | 1.194   | 1.185   | 0.9920  | 1.028                    |     |
|  |  | 1.191   | 1.185   | 0.9689  | 1.003                    |     |
|  |  | 1.191   | 1.171   | 0.9813  | 1.041                    |     |
|  |  | 1.218   | 1.194   | 1.1010  | 1.170                    |     |
|  |  | 1.194   | 1.157   | 0.9945  | 1.053                    |     |
|  |  | 1.204   | 1.166   | -   | -                        |     |
|  | Mean   | 1.198   | 1.176   | 1.0100  | 1.059                    |     |
|  |  | ••••••••••••••••••••••••••••••••••••••  | AUXILIARY   | INFORMATION   |                          |     |
|  |  | ARATUS/PROCI  |   |   | TY OF MATERIALS:         |     |
|  |  |   | sulfamethazine and 25 or<br>acid buffer were placed   |   | sed were anal or USP     | -   |
|  | in paraffin-coated vials, adjusted to an ionic strength 0.1M with KNO3 and rotated   |   |   | Ag sulfamethazine was prepd by the method o<br>Rosenzweig and Fuchs (1) and recrystd from |                          |     |
| end over end in a themostated bath until e-<br>quilibrium soly was obtained (3-7 days). Af-<br>ter filtration through 20M glass filtering<br>crucibles, the solns were analyzed at 25±<br>0.1°C in paraffin-coated beakers for Ag <sup>+</sup><br>ions with a silver-ion selective electrode<br>(No. 94-16, Orion Res., Cambridge, Mass) |  | f ammonia (2). Water had a sp cond of (1-10 x 10 <sup>-7</sup> ohm <sup>-1</sup> cm <sup>-1</sup> .<br>The source of the reagents was not specifi |   | of (1-10)   |                          |     |
| 10   | standardized at the temp indicated and 0.1M<br>ionic strength. The pH was measured with<br>a triple-purpose pH electrode (Corning Sci. |   | ESTIMATED ERROR:  |   |                          |     |

#### ESTIMATED ERROR: Soly: when tested by one-way analysis of variance, the means displayed in the 1st Table were found not to be statistically different at the 1% confidence level (authors).

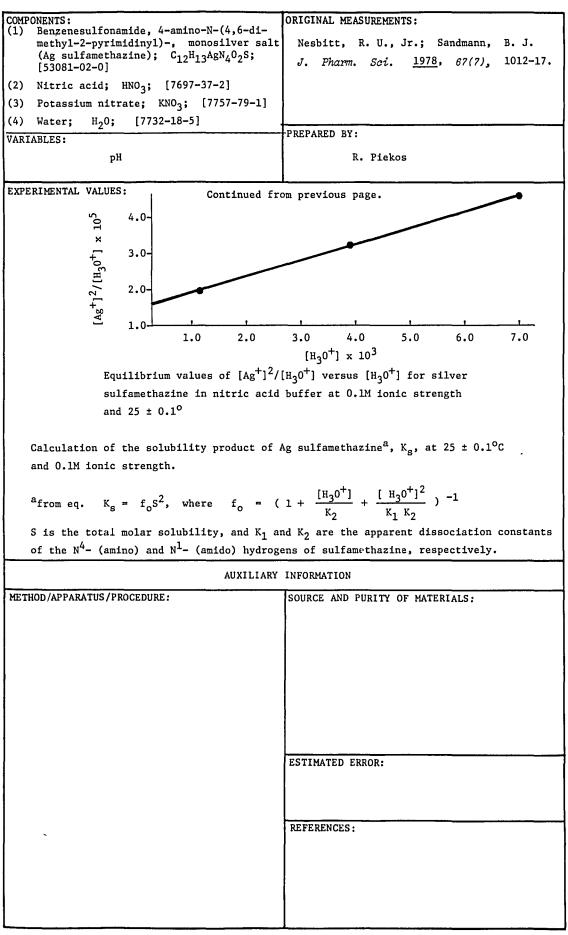
**REFERENCES:** 

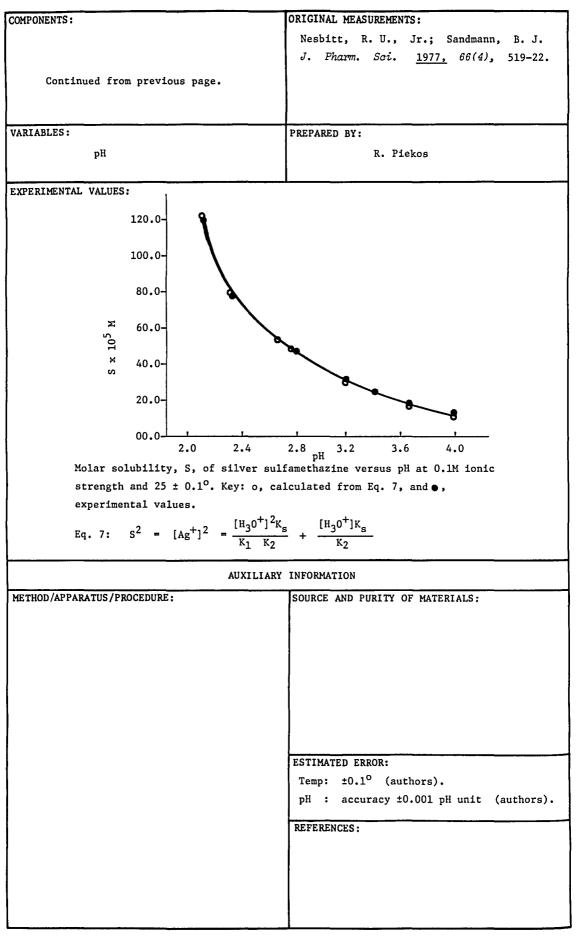
Instruments, Medfield, Mass) standardized

nitric acid buffers were prepd by diln of 0.1M  $\rm HNO_3$  and were adjusted to an ionic strength of 0.1M with  $\rm KNO_3.$ 

using buffers meeting NBS requirements. The

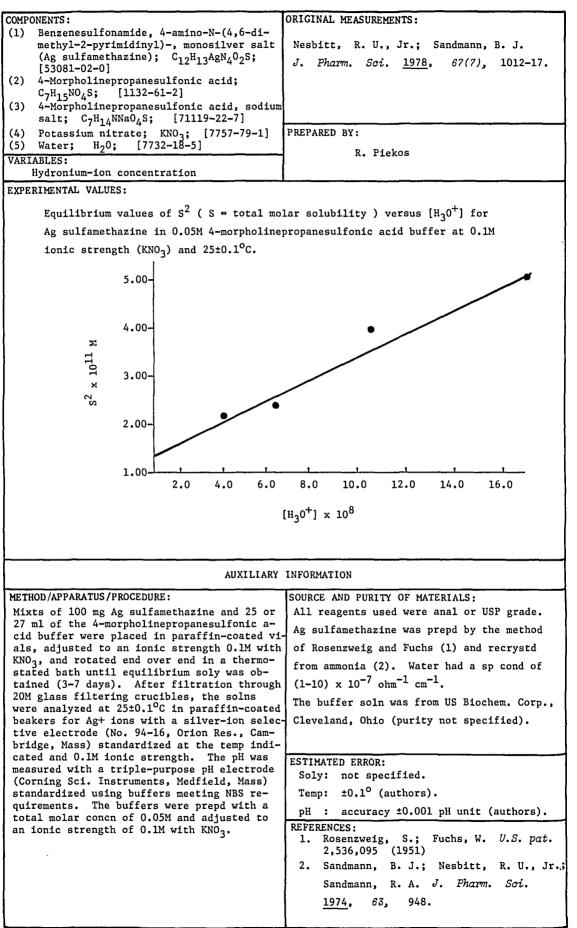
- Rosenzweig, S.; Fuchs, W. U. S. pat. 2,536,095 (1951).
- (2) Sandmann, B. J.; Nesbitt, R. U., Jr.; Sandmann, R. A. J. Pharm. Sci. <u>1974</u>, 63, 948.





| COMPONENTS:         | <u></u>                | ORIGINAL MEASUREME       | INTS:   |
|---------------------|------------------------|--------------------------|---|
| Continued from      | previous page.         |                          | Jr.; Sandmann, B. J.<br><u>1978</u> , 67(7), 1012-17. |
| VARIABLES:          | <u></u>                | PREPARED BY:             |   |
| pH                  |                        | R. F                     | Piekos  |
| EXPERIMENTAL VALUES | :                      | L                        |   |
| рН                  | fo                     | s <sup>2</sup>           | к <sub>s</sub> a                                      |
| 2.174               | $2.551 \times 10^{-6}$ | $1.477 \times 10^{-6}$   | $3.77 \times 10^{-12}$                                |
| 2.421               | $6.323 \times 10^{-6}$ | 5.897 x 10 <sup>-7</sup> | $3.72 \times 10^{-12}$                                |
| 2.668               | $1.455 \times 10^{-5}$ | $2.606 \times 10^{-7}$   | $3.79 \times 10^{-12}$                                |
| 2.934               | $3.265 \times 10^{-5}$ | $1.151 \times 10^{-7}$   | $3.76 \times 10^{-12}$                                |
|                     |                        | Mear                     | a $(3.76 \pm 0.03)10^{-12}$                           |
|                     |                        |                          |   |
|                     | AUXIL                  | IARY INFORMATION         |   |
| METHOD/APPARATUS/PR | OCEDURE :              | SOURCE AND PURITY        | OF MATERIALS:   |
|                     |                        | ESTIMATED ERROR:         |   |
|                     |                        | REFERENCES :             |   |

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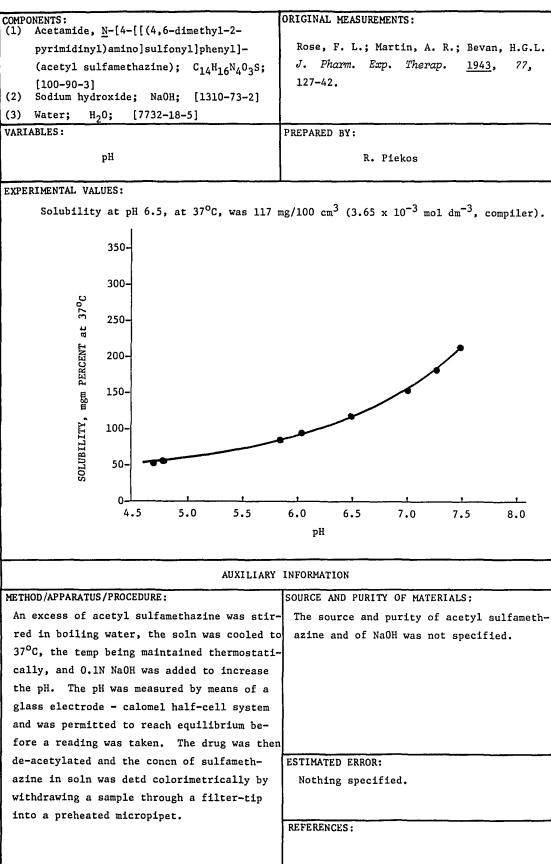


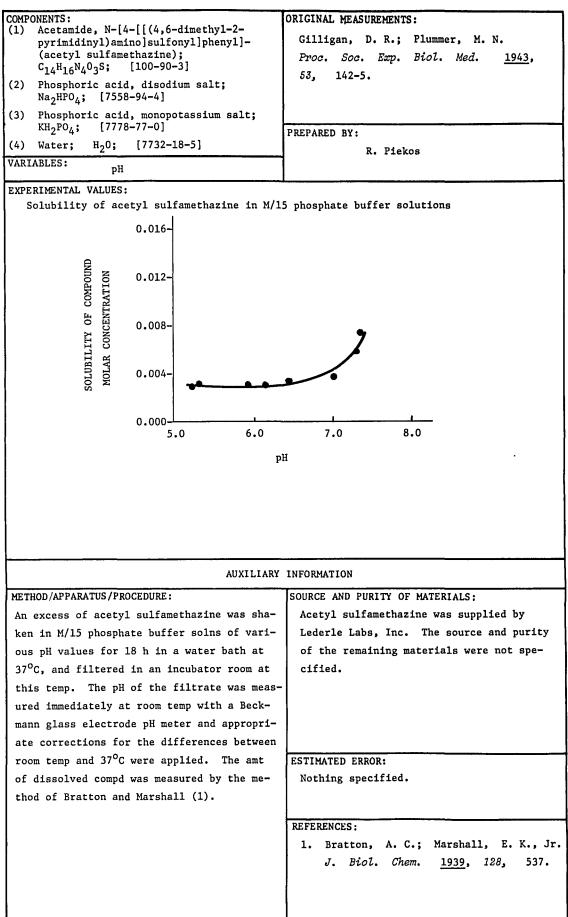
| <pre>COMPONENTS:<br/>.(1) Zinc, (<u>T</u>-4)-bis[4-amino-<u>N</u>-(4,6-dimethyl-<br/>2-pyrimidinyl)benzenesulfonamidato-N<sup>N</sup>,0}<br/>(Zn(II) sulfamethazine);<br/>C<sub>24</sub>H<sub>24</sub>N<sub>8</sub>0<sub>4</sub>S<sub>2</sub>Zn; [71261-83-1]<br/>(2) Water; H<sub>2</sub>0; [7732-18-5]</pre> | FOX. UN. L. JI. HOUAR, S. |
|--|---------------------------|
| VARIABLES:<br>One temperature: 28-30 <sup>0</sup> C  | PREPARED BY:<br>R. Piekos |
| EXPERIMENTAL VALUES:   |                           |

Solubility of Zn(II) sulfamethazine in water at room temperature  $(28-30^{\circ}C)^{a}$  is 8.6 mg% ( 1.4 x  $10^{-4}$  mol dm<sup>-3</sup> solution, compiler ).

 $^{\rm a}{\rm Value}$  given by one of the authors ( S.M. ) in personal communication.

| AUXILIARY   | INFORMATION  |
|---|--|
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:  |
| Satd soln of Zn(II) sulfamethazine was<br>prepd in water and after 24 h aliquots from<br>the clear supernatant were assayed for<br>sulfamethazine content using the colorime-<br>tric method of Bratton and Marshall (1).<br>The soly value was then calcd from the<br>molecular formula. | The Zn(II) sulfamethazine was prepd by the<br>authors as follows: an inorg Zn salt was<br>reacted with Na salt of sulfamethazine and<br>the ppt was analyzed and characterized.<br>No details were given, however.<br>Purity of the materials was not specified. |
|   | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 120, 537.   |





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|--|--|---|
| COMPONENTS:  |  | ORIGINAL MEASUREMENTS:                    |
| <ol> <li>Acetamide, N-[4-[[(4,6<br/>pyrimidinyl)amino]sulf</li> </ol>                        | -dimethy1-2-   | Meier, R; Allemann, O., von Meyenburg, H. |
| (acetyl Elkosin); C <sub>1</sub>   | 4 <sup>H</sup> 16 <sup>N</sup> 4 <sup>0</sup> 3 <sup>S</sup> ; | Schweiz. Med. Wochenschr. <u>1944</u> ,   |
| [100-90-3]<br>(2) Phosphoric acid, disod.<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | ium salt;  | 74(42), 1091-5.                           |
| <ul> <li>(3) Phosphoric acid, monop<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> | otassium salt;   |   |
| (4) Water; $H_20$ ; [7732-   | 18-51  | PREPARED BY:                              |
| VARIABLES:   |  | R. Piekos                                 |
| рН   |  |   |
| EXPERIMENTAL VALUES:   |  |   |
|  |  |   |
|  |  |   |
|  | So   | Lubility of acetyl Elkosin                |
|  |  | phosphate buffers at 37 <sup>°</sup> C    |
|  | mį   | $10^3 \text{ mol dm}^{-3} \text{ a}$      |
|  | 5.5 11   | 5.0 3.590                                 |
|  | 6.5 112  | 3.652                                     |
|  | 7.5 176  | 5.0 5.494                                 |
|  | ·····  |   |
|  | <sup>a</sup> Calculate   | ed by compiler.                           |
|  |  |   |
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|  | AUXILI   | ARY INFORMATION                           |
| METHOD/APPARATUS/PROCEDURE:  | ·····  | SOURCE AND PURITY OF MATERIALS:           |
| Nothing specified.   |  | Nothing specified.                        |
|  |  |   |
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|  |  |   |
|  |  |   |
|  |  |   |
|  |  | ESTIMATED ERROR:                          |
|  |  | Nothing specified.                        |
|  |  |   |
|  |  | REFERENCES:                               |
|  |  |   |
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| <pre>COMPONENTS:<br/>(1) Acetamide, N-[4-[[(4,6-dimethyl-2-<br/>pyrinidinyl)amino]sulfonyl]phenyl]-<br/>(N<sup>4</sup>-acetylsulfadimidine);<br/>C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>0<sub>3</sub>S; [100-90-3]<br/>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]<br/>(3) Phosphoric acid, monopotassium salt;</pre> | ORIGINAL MEASUREMENTS:<br>Hekster, Y. A.; Vree, T. B.<br>Damsma, J. E.; Friesen, W. T.<br>J. Antimicrob, Chemother. <u>1981</u> , 8,<br>133-44. |
|--|---|
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]<br>(4) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES: pH   | PREPARED BY:<br>R. Piekos   |

**EXPERIMENTAL VALUES:** 

| рH  | Solubility at 25 <sup>0</sup> C |                               |  |
|-----|---------------------------------|-------------------------------|--|
| pn  | mg/l                            | $10^3 \text{ mol } dm^{-3} a$ |  |
| 5.5 | 752                             | 2.35                          |  |
| 7.5 | 1340                            | 4.18                          |  |

<sup>a</sup> Calculated by compiler.

#### AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: Satd solns of N<sup>4</sup>- acetylsulfadimidine were The source and purity of the materials prepd in phosphate buffers of pH 5.5 and were not specified. 7.5 at room temp ( $25^{\circ}C$ ). The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a column oven (Model 748) and a Pye-Unicam LC-UV spectrophotometric detector. The detector was connected to a 1-mV recorder. A stainless steel co-ESTIMATED ERROR: The detection limit of the solute by HPLC lumn (10 cm x 4.6 mm i.d.) was packed with was 0.5 mg/1 (authors. Lichrosorb RPS, 5 µm, obtained from Chrom-The error in temperature and pH was not pack. An injection loop of 100 µl was used. specified. **REFERENCES:** The oven temp was 40°C. Detection of the solute was performed at 260 nm.

| 362  |  |
|--|--|
| <ul> <li>COMPONENTS:</li> <li>(1) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>S; [100-90-3]</li> <li>(2) 1,2,3-Propanetricarboxylic acid, 2-hy-droxy-, disodium salt (Na citrate)C<sub>6</sub>H<sub>6</sub>Na<sub>2</sub>O<sub>7</sub>; [144-33-2]</li> </ul> | ORIGINAL MEASUREMENTS:<br>Gilligan, D. R.; Plummer, M. N.<br><i>Proc. Soc. Exp. Biol. Med.</i> <u>1943,</u><br>53, 142-5.  |
| <ul> <li>(3) Sodium hydroxide; NaOH; [1310-73-2]</li> <li>(4) Water; H<sub>2</sub>0; [7732-18-5]</li> </ul>  | PREPARED BY:   |
| VARIABLES:   | R. Piekos  |
| pH   | L  |
| EXPERIMENTAL VALUES:<br>Solubility of acetyl sulfamethazine in   | M/10 Na citrate + NaOH solutions at 37 <sup>0</sup> C  |
| 0.016-   |  |
| MOLAR CONFOUND<br>SOLUBILITY OF COMPOUND<br>MOLAR CONCENTRATION<br>MOLAR CONCENTRATION   | and a second sec |
| 0.000  |  |
| 5.0 6.0  | 7.0 8.0<br>рН  |
|  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| An excess of acetyl sulfamethazine was sha-<br>ken in M/10 Na citrate + NaOH solns of va-<br>rious pH values for 18 h in a water bath<br>at 37°C, and filtered in an incubator room<br>at this temp. The pH of the filtrate was<br>measured immediately with a Beckmann glass<br>electrode pH meter and appropriate correct-                 |  |
| ions for the differences between room temp<br>and 37°C were applied. the amt of dissolved<br>compd was measured by the method of Bratton<br>and Marshall (1).  |  |
|  | <pre>I. Bratton, A. C.; Marshall, E. K., Jr.<br/>J. Biol. Chem. <u>1939</u>, 128, 537.</pre>   |

| COMPO | DNENTS:  | ORIGINAL MEASUREMENTS:  |
|-------|--|---|
| (1)   | Acetamide, $\underline{N}$ -[[4-(acetylamino)phenyl]-<br>sulfonyl]- $N$ -(4,6-dimethyl-2-pyrimidin-<br>yl)- (N <sup>1</sup> , $\overline{N}^4$ -diacetylsulfamidine);<br>C <sub>16</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub> S; [59224-69-0] | Hekster, Ch. A.; Vree, T. B.<br>Antibiotics Chemother. <u>1982</u> , 31,<br>22-118. |
| (2)   | Phosphoric acdi, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  |   |
| (3)   | Phosphoric acid, monopotassium salt;   |   |
|       | кн <sub>2</sub> ро <sub>4</sub> ; [7778-77-0]  | PREPARED BY:  |
| (4)   | Water; H <sub>2</sub> 0; [7732-18-5]   | R. Piekos   |
| VARI  | ABLES: pH  |   |
| EXPE  | RIMENTAL VALUES:   |   |

| рH               | Solubility at 25 <sup>0</sup> C |                                      |  |
|------------------|---------------------------------|--------------------------------------|--|
| pn               | mg/l                            | $10^5 \text{ mol dm}^{-3} \text{ a}$ |  |
| 5.5              | 11.8                            | 3.25                                 |  |
| 7.5 <sup>b</sup> | 9.3                             | 2.6                                  |  |
|                  |                                 |                                      |  |

<sup>a</sup> Calculated by compiler

<sup>b</sup> Erroneous pH value of 7.0 is given in the article.

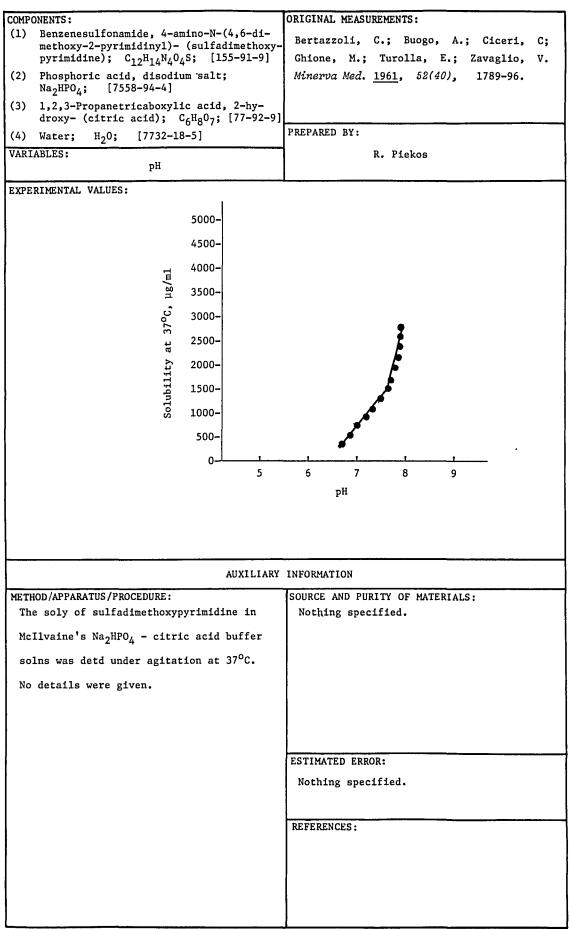
## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
|---|--|
| The earlier developed method (1) was used                           | Neither source nor the purity of the mate-   |
| (personal communication). Satd solns of                             | rials was specified.   |
| N <sup>1</sup> ,N <sup>4</sup> -diacetylsulfadimidine were prepd in |  |
| phosphate buffers of pH 5.5 and 7.5 at 25 <sup>0</sup> C.           |  |
| The concn of the solute was measured by                             |  |
| means of a Spectra Physics 3500B high-perfor-                       |  |
| mance liquid chromatograph equipped with a                          |  |
| Model 748 column oven and a Pye-Unicam LC-UV                        |  |
| spectrophotometric detector.  | ESTIMATED ERROR:<br>Soly: the detection limit of the solute by<br>HPLC was 0.5 mg/l (authors). |
|   | The errors in temp and pH were not specified.  |
|   | REFERENCES:  |
|   | 1. Hekster, Y. A; Vree, T. B.;   |
|   | Damsma, J. E.; Friesen, W. T.  |
|   | J. Antimicrob. Chemother. <u>1981</u> ,  |
|   | 8, 133.  |
|   |  |

| COMPONENTS :  | ORIGINAL MEASUREMENTS:                                   |  |
|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-   | Caldwell, W. T.; Kornfeld, E. C.;                        |  |
| <pre>methyl-5-n-pentyl-2-pyrimidinyl)-;</pre>                                 | Donnell, C. K. J. Am. Chem. Soc.                         |  |
| C <sub>16</sub> H <sub>22</sub> N <sub>4</sub> O <sub>2</sub> S; [71119-35-2] | <u>1941,</u> 63, 2188-90.                                |  |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                      | <u></u> ,  |  |
| (-,   |  |  |
| VARIABLES:  | PREPARED BY:   |  |
| One temperature: 29 <sup>0</sup> C  | R. Piekos  |  |
| one cemperature. 29 0   | A. LIEROS  |  |
| EXPERIMENTAL VALUES:  | ····   |  |
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| Solubility of 4-amino-N-(4-methyl-5-n-p                                       | entyl-2-pyrimidinyl)benzenesulfon-                       |  |
| amide in water at 29 <sup>0</sup> C is 2.8 mg/100 ml                          |  |  |
| amide in water at 29°C is 2.6 mg/100 mi                                       | solution (8.4 x 10 mol dm -                              |  |
| compiler ).   |  |  |
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| AUXILIARY INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                          |  |
| Soly was detd by weighing the residue ob-                                     | The sulfonamide, mp 188-90 <sup>0</sup> C (cor, recrystd |  |
| tained by evapg to dryness a known volume of                                  | from aq EtOH), was prepd by condensing                   |  |
| soln satd at 29 <sup>0</sup> C.   | 2-amino-4-methyl-5-n-pentylpyrimidine with               |  |
|   | acetylsulfanilyl chloride followed by hy-                |  |
|   | drolysis with aq NaOH and pptn at pH 6.                  |  |
|   | Anal: %N 16.67 (calcd 16.75). Purity                     |  |
|   | of the water was not specified.                          |  |
|   |  |  |
|   | ESTIMATED ERROR:   |  |
|   | Nothing specified.                                       |  |
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|   | REFERENCES:  |  |
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COMPONENTS: ORIGINAL MEASUREMENTS: (1) Benzenesulfonamide, 4-amino-N-(2-Roblin, R. O., Jr.; Winnek, P. S.; English, J. P.; J. Am. Chem. Soc. methyl-4-pyrimidinyl)-; 1942, 64, 567-70. [599-84-8]  $C_{11}H_{12}N_4O_2S;$ (2) Water; H<sub>2</sub>0; [7732-18-5] VARIABLES: PREPARED BY: One temperature: 37°C R. Piekos EXPERIMENTAL VALUES: Solubility of 4-amino-N-(2-methy1-4-pyrimidiny1)benzenesulfonamide in water at  $37^{\circ}C$  is 623 mg/100 cm<sup>3</sup> solution (2.36 x  $10^{-2}$  mol dm<sup>-3</sup>, compiler ). AUXILIARY INFORMATION METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS: The sulfonamide, mp 207-8°C (cor), was prepd Excess sulfonamide in water was heated and stirred on a steam bath for 30 min. The sus-by the authors. Anal: %C 50.2 (calcd 50.0); pension was then agitated for 24 h in a ther- %H 4.6 (4.6); %N 21.4 (21.2). mostat at 37°C. A sample of the satd soln Purity of the water was not specified. was withdrawn through a glass filter, dild, and analyzed by the Marshall method (1) using a General electric recording spectrophotometer for comparing the colors developed with those of the standards. ESTIMATED ERROR: Nothing specified. **REFERENCES:** 1. Bratton, A. C.; Marshall, E. K., Jr. J. Pharmacol. 1939, 66, 4.

| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2-6-di-<br/>methyl-4-pyrimidinyl)- (sulfasomidine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</pre> |       | EVALUATOR:<br>Anthony N. Paruta<br>Department of Pharmaceutics<br>University of Rhode Island<br>Kingston, Rhode Island, USA<br>and |
|---|-------|--|
| (2)   | Water | Ryszard Piekos<br>Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986   |

### CRITICAL EVALUATION:

The value of  $6.86 \times 10^{-3} \text{ mol dm}^{-3}$  at 310K as given by Kaneniwa et al. (1) is based on 3-5 days equilibration and accurate spectrophotometric analytical method. The temperature variation was well controlled, t0.05K. Five years later, Goto et al. (2), also using several days of equilibration and a spectrophotometric analysis provided a value of  $6.75 \times 10^{-3} \text{ mol dm}^{-3}$ , in good agreement with the earlier one. The recommended value is given as  $6.80 \times 10^{-3} \text{ mol dm}^{-3}$  in water at 310K.

The two solubility values (3,4) in ethanol are also in close agreement. In 1977, Mauger et al. (3) using a 24 hour equilibrium period and spectrophotometric analysis to report a value of  $9.45 \times 10^{-3}$  mol dm<sup>-3</sup> in ethanol at 298K. Martin and Miralles (4) determined a value of  $9.52 \times 10^{-3}$  mol dm<sup>-3</sup> at 298K, in excellent agreement with the earlier value. The solubilities in water and ethanol at 310K are 6.8 and 13.9 x  $10^{-3}$ mol dm<sup>-3</sup>, roughly a two fold increase in ethanol.

#### **REFERENCES:**

(1) Kaneniwa, N.; Watari, N.; Iijima, H. Chem. Pharm. Bull. 1978, 26(9), 2603-14.

- (2) Goto, S.; Komatsu, M.; Tagawa, K.; Kawata, M. Chem. Pharm. Bull. <u>1983</u>, 31(1), 256-61.
- (3) Mauger, J.W.; Paruta, A.N.; Gerraughty, R.J.; J. Pharm. Sci. <u>1972</u>, 61(1), 94-7.
- (4) Martin, A.; Miralles, M.J. J. Pharm. Sci. <u>1982</u>, 71(4), 439-42.

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-                                     | Yamazaki, M.; Aoki, M.; Kamada, A.;  |
| dimethyl-4-pyrimidinyl)- (sulfisomidine);                                   | Yata, N. Yakuzaigaku <u>1967,</u> 27(1),   |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | 37-40.   |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                    |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| One temperature: 30 <sup>0</sup> C  | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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|   | 20 <sup>0</sup> 0 do 5 65 mm 1/2 ( 1 57 ) -3   |
| Solubility of sulfisomidine in water at                                     | 50 C 18 5.05 mmol/L (1.5/ g dm ~,  |
| compiler ).   |  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| Sulfisomidine (0.5 g ) was placed in an L-                                  | Nothing specified.   |
| shaped tube together with 20 ml of water.                                   | Nothing specified.   |
| The mixt was shaken in a thermostat until                                   |  |
| equilibrium was attained. The sulfisomidine                                 |  |
| was assayed in the supernatant spectrophoto-                                |  |
| metrically at 545 nm on a Beckmann DU spec-                                 |  |
| trophotometer. The results were taken from                                  |  |
| a calibration graph.  |  |
|   | ESTIMATED ERROR:   |
|   | Soly: not specified.   |
|   | Temp: ±1 <sup>0</sup> C (authors)  |
|   |  |
|   | REFERENCES:  |
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|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-(2,6-<br/>dimethyl -4-pyrimidinyl)- (sulfiso-<br/>midine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</li> <li>(2) Water; H<sub>2</sub>O; [7732-18-5]</li> </ul>  | Kaneniwa, N.; Watari, N.; Iijima, H.<br><i>Chem. Pharm. Bull.</i> <u>1978</u> , <i>26(9)</i> ,<br>2603-14. |
|   |  |
| VARIABLES:<br>One temperature: 37°C   | PREPARED BY:<br>R. Piekos  |
| EXPERIMENTAL VALUES:  |  |
| Solubility of sulfisomidine in water (<br>( 6.86 x 10 <sup>-3</sup> mol dm <sup>-3</sup> , compiler ).  | at 37 <sup>0</sup> C is 1.91 mg/ml solution  |
| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of sulfisomidine was placed in a<br>flask contg 25 ml of water. The flask was<br>shaken (2 strokes/s at the amplitude of 3 cm)<br>in a thermostatically controlled water bath<br>at $37^{\circ}$ C. One-ml sample was withdrawn every<br>6 h (total equilibration period was 3-5 days)<br>using a warmed Millipore filter syringe with<br>a filter pore size of 0.45 $\mu$ (Millipore HAWP<br>01300) and the filtrate was dild with water<br>and assayed spectrophotometrically (1). |  |

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| <ul> <li>COMPONENTS:</li> <li>(1) Benzenesulfonamide<br/>dimethyl-4-pyrimide<br/>dine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub></li> <li>(2) Water; H<sub>2</sub>O; [7]</li> </ul> |   | GOLO, S.; KOMALSU, M.;  |
|---|---|---|
| VARIABLES:  |   | PREPARED BY:  |
| Temperature   |   | R. Piekos   |
| EXPERIMENTAL VALUES:  | - <u></u>   | ,,,,,,,,,,,,,,,,,,  |
|   | t/°C  | Solubility  |
|   | g/1   | $10^3 \text{ mol } dm^{-3} a$   |
|   | 37 1.8  | 3 6.75  |
|   | 55 3.3  | 5 12.0  |
|   | <sup>a</sup> Calcula  | ated by compiler  |
|   |   | ILIARY INFORMATION  |
| METHOD/APPARATUS/PROCEDU<br>A 3 g sample of sulfis  |   | SOURCE AND PURITY OF MATERIALS:<br>was Sulfisomidine had mp 245-9°C (decomp).         |
| accurately weighed int<br>10 ml of water was add<br>sealed, placed in a co<br>bath and allowed to st<br>The equilibrium concn<br>measured spectrophotom<br>after diazotization w                  | o a 20-ml ampu<br>ed. The ampul<br>nst temp (37 <sup>0</sup> o<br>and for several<br>of the solute v<br>etrically at 53 | and The purity of water was not specified.<br>was<br>or 55°C)<br>days.<br>was<br>8 nm |
| reagent (1).  |   | ESTIMATED ERROR:  |
|   |   | Nothing specified.  |
|   |   | REFERENCES:<br>1. Tsuda, K.; Matsunaga, S.<br>Yakugaku Zasshi <u>1942,</u> 62, 362.   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                         |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-                                       | Ogata, H.; Shibazaki, T.; Inoue, T.;           |
| dimethyl-4-pyrimidinyl)- (sulfisomidine);                                     | Ejima, A. Chem. Pharm. Bull. <u>1979</u> ,     |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]   | 27(6), 1281-6.                                 |
| (2) Hydrochloric acid; HCl; [7647-01-0]                                       | 27(0), 1201-0.                                 |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]                                      |  |
| VARIABLES:  | PREPARED BY:                                   |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                                      |
| one cemperature. 57 C   | K. FIEROS                                      |
| EXPERIMENTAL VALUES:  |  |
|   |  |
| Solubility of sulfisomidine in 0.1N HCl<br>mol dm <sup>-3</sup> , compiler ). | at 37 <sup>0</sup> C is 49.418 mg/ml ( 0.17755 |
|   |  |
| AUXILIARY   | INFORMATION                                    |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:                |
| A centrifuge tube contg 30 ml of 0.1N HCl                                     | Comm available 500-mg uncoated tablets of      |
| and 0.5-3.0 g of the sulfisomidine powder                                     | sulfisomidine were used.                       |
| was tightly sealed and shaken at 37°C. The                                    | Hydrochloric acid was of reagent grade.        |
| concn of the dissolved drug was detd spec-                                    |  |
| trophotometrically following filtration                                       |  |
| through a Millipore filter (type EH, pore                                     |  |
| size 0.5 $\mu\text{m})$ , and the procedure was re-                           |  |
| peated every 24 h until a const concn was                                     |  |
| obtained.   | ESTIMATED ERROR:                               |
|   | Nothing specified.                             |
|   | ······································         |
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|   | REFERENCES:                                    |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-                | ORIGINAL MEASUREMENTS:  |  |
|--|---|--|
| methyl-4-pyrimidinyl)- (sulfisomidine);                                  | Takubo, T.; Matsumaru, H.   |  |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]<br>(2) Carbonic acid, monosodium salt; | Tsuchiya, S.; Hiura, M.<br>Chem. Pharm. Bull. <u>1973,</u> 21(7), |  |
| NaHCO <sub>3</sub> ; [144-55-8]  | 1440-5.   |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]                                 | 1440-5.   |  |
| VARIABLES:   | PREPARED BY:  |  |
| One temperature: 37 <sup>0</sup> C; one pH: 8.4                          | R. Piekos   |  |
|  | NY TEROD  |  |
| EXPERIMENTAL VALUES:   |   |  |
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| Solubility of sulfisomidine in a NaHCO3                                  | solution ( 1.680 g NaHCO <sub>2</sub> /100 ml                     |  |
| water ) of pH 8.4 at 37 <sup>o</sup> C is 9.32 mg/ml                     |   |  |
| water ) of pH 8.4 at 37°C is 9.32 mg/ml                                  | solution" ( 3.35 x 10 - mol dm -                                  |  |
| solution, compiler ).  |   |  |
|  |   |  |
| <sup>a</sup> Numerical value to the graphical data g                     | diven by one of the authors (S. T. )                              |  |
|  |   |  |
| in personal communication.   |   |  |
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| AUXILIARY  | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                                   |  |
| Aliquots of the NaHCO3 solution were placed                              |   |  |
| in glass-stoppered flask with excess of sul-                             | grade. The source and purity of NaHCO3 were                       |  |
| fisomidine. The flasks were allowed to                                   | not specified.  |  |
| stand at 37±1 <sup>0</sup> C and shaken vigorously for                   | Distd water was used.   |  |
| 4 h until equilibrium was established. One                               |   |  |
| ml of the supernatant was removed by means                               |   |  |
| of a filter pipet and sulfisomidine was                                  |   |  |
| assayed by the previously reported method                                |   |  |
| (1).   | ESTIMATED ERROR:  |  |
|  | Soly and pH: not specified.                                       |  |
|  | Temp: ±1 <sup>0</sup> C (authors).                                |  |
|  |   |  |
|  | REFERENCES:   |  |
|  | 1. Takubo, T.; Tsuchiya, S.; Hiura, M.                            |  |
|  | Yakuzaigaku <u>1971</u> , 31, 298.                                |  |
|  |   |  |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br>methyl-4-pyrimidinyl)- (sulfisomidine);<br>$C_{12}H_{14}N_4O_2S$ ; [515-64-0]<br>(2) Carbonic acid, disodium salt;<br>$Na_2CO_3$ ; [497-19-8]<br>(3) Water; $H_2O$ ; [7732-18-5]<br>VARIABLES:<br>One temperature: $37^{\circ}C$ ; one pH: 11.3 | ORIGINAL MEASUREMENTS:<br>Takubo, T.; Matsumaru, H.;<br>Tsuchiya, S.; Hiura, M.<br><i>Chem. Pharm. Bull.</i> <u>1973</u> , 21(7),<br>1440-5.<br>PREPARED BY:<br>R. Piekos |  |
|--|---|--|
|  |   |  |
| EXPERIMENTAL VALUES:<br>Solubility of sulfisomidine in a Na <sub>2</sub> CO <sub>3</sub><br>water ) of pH 11.3 at 37°C is 37.38 mg/m<br>solution, compiler ).<br><sup>a</sup> Numerical value to the graphical data w<br>( S. T. ) in personal communication.  | nl solution <sup>a</sup> ( 0.1343 mol dm <sup>-3</sup>  |  |
| AUXILIARY  | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |  |
| Aliquots of the Na <sub>2</sub> CO <sub>3</sub> soln were placed in  | The sulfisomidine was of pharmaceutical   |  |
| glass-stoppered flasks with excess of sulfi-   |   |  |
| somidine. The flasks were allowed to stand   | were not specified.   |  |
| at 37±1°C and shaken vigorously for 4 h un-  | Distd water was used.   |  |
| til equilibrium was established. One ml of   |   |  |
| the supenatant was removed by means of a   |   |  |
| filter pipet and sulfisomidine was assayed   |   |  |
| by the previously reported method (1).   |   |  |
|  | ESTIMATED ERROR:  |  |
|  | Soly and pH: not specified.<br>Temp: ±1 <sup>0</sup> C (authors).   |  |
|  | REFERENCES:   |  |
|  | 1. Takubo, T.; Tsuchiya, S.; Hiura, M.<br><i>Yakuzaigaku <u>1971</u>, 31,</i> 298.  |  |

| COMPONENTS:   |   |                            | ORIGINAL MEASUREMENT | ۶.  |   |
|---|---|----------------------------|----------------------|---|---|
| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</pre> |   |                            |                      | sumaru, H.;   |   |
|   | <pre>(2) Carbonic acid, disodium salt;<br/>Na<sub>2</sub>CO<sub>3</sub>; [497-19-8]</pre> |                            |                      | Chem. Pharm. Bull. <u>1973,</u> 21(7),<br>1440-5.                   |   |
| (3)   |   | monosodium salt;<br>-55-8] |                      |   |   |
| (4)   | Water; H <sub>2</sub> 0;  | [7732-18-5]                |                      | PREPARED BY:  |   |
| VARI  | ABLES:  | рН                         |                      | R. Piekos   |   |
| EXPE  | RIMENTAL VALUES:  | <u></u>                    |                      |   |   |
|   |   |                            |                      |   |   |
|   | Na <sub>2</sub> CO <sub>3</sub>   |                            |                      |   |   |
| <u></u>   |   | NaHC03                     | рН                   | Solubility at 37 <sup>0</sup> C                                     |   |
| g/  | 100 ml water  | g/100 ml water             |                      | mg/ml soln <sup>a</sup>   | 10 mol dm <sup>-3</sup> soln <sup>b</sup> |
|   | 0.212   | 1.512                      | 9.1                  | 11.82   | 0.4247                                    |
|   | 0.848   | 1.008                      | 9.8                  | 25.70   | 0.9234                                    |
|   | 1.908   | 0.168                      | 10.7                 | 34.36   | 1.2345                                    |
|   | a   |                            | i/a                  |   |   |
|   |   | lues to the graphic        | cal data             | a were given by one o   | of the authors                            |
|   | ( S. T. ) in  | personal communica         | ation.               |   |   |
|   | <sup>b</sup> Calculated   | by compiler.               |                      |   |   |
|   |   |                            |                      |   |   |
|   |   | AUX                        | KILIARY              | INFORMATION   |   |
| METH  | HOD/APPARATUS/PRO   | OCEDURE:                   |                      | SOURCE AND PURITY OF  | F MATERIALS:                              |
| Aliquots of the carbonate buffer solns were   |   |                            |                      | The sulfisomidine was of pharmaceutical                             |   |
| pla   | ced in glass-sto  | ppered flasks with         | excess               | grade. The source and purity of Na <sub>2</sub> CO <sub>3</sub> and |   |
| of  | of sulfisomidine. The flasks were allowed   |                            |                      | NaHCO <sub>2</sub> were not sp                                      | ecified.                                  |

NaHCO3 were not specified. Distd water was used.

fisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported method (1). ESTIMATED ERROR: Soly and pH: not specified. Temp: ±1°C (authors). REFERENCES: 1. Takubo, T.; Tsuchiya, S.; Hiura, M. Yakuzaigaku <u>1971,</u> 31, 298.

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  | ORIGINAL MEASUREMENTS:                  |
|--|---|
| methyl-4-pyrimidinyl)- (sulfaisodi-  | Riess, W.                               |
| midine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0]       | Intern. Congr. Chemotherapy, Proc.      |
| (2) Phosphoric acid, disodium salt;  | (                                       |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]<br>(3) Phosphoric acid, monopotassium salt; | 3rd, Stuttgart <u>1963</u> , 1, 627-32. |
| кн <sub>2</sub> ро <sub>4</sub> ; [7778-77-0]  |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                            |
| VARIABLES:   | R. Piekos                               |
| One temperature: 20°C; one pH: 7.4   |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfaisodimidine in a M/   | 15 Sörensen buffer solution (pH 7.4)    |
| at 20 <sup>°</sup> C is 190 mg% ( $6.83 \times 10^{-3}$ mol d                              | <sup>-3</sup> solution, compiler ).     |
|  | . Solution, complete /.                 |
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|  | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |
| Sörensen buffer solns of pH varying between  | Nothing specified.                      |
| 7 and 8 were prepd, satd with sulfaisodi-  |   |
| midine at 20°C, their pH was measured at   |   |
| -  |   |
| equilibrium, and the sulfaisodimidine was  |   |
| assayed colorimetrically. The measured pH  |   |
| values were then plotted against concn, and  |   |
| the soly at pH 7.4 was detd by interpolation   |   |
| (personal communication).  |   |
| (personal communication).  | ESTIMATED ERROR:                        |
|  |   |
|  | Nothing specified.                      |
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|  | REFERENCES:                             |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:                  |  |
|--|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-   | Yamazaki, M.; Aoki, M.;                 |  |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>2</sub>S; [515-64-0]</pre> | Kamada, A.; Yata, N.                    |  |
| (2) Phosphoric acid, disodium salt;  | Yakuzaigaku <u>1967</u> , 27(1), 37-40. |  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | 1akuzatyaku <u>1907</u> , 27(1), 37-40. |  |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]                                  |   |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                            |  |
| VARIABLES:   | R. Piekos                               |  |
| One temperature: 30 <sup>o</sup> C; one pH: 7.4  |   |  |
| EXPERIMENTAL VALUES:   |   |  |
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| Solubility of sulfisomidine in a phosph  | ate buffer solution of pH 7.4           |  |
| $(\mu = 0.17)$ at 30°C is 8.53 mmol/L (3   | $2.27 \pm 4-3$                          |  |
| $(\mu = 0.17)$ at 50 C is 8.55 mmol/L (  | 2.37 g dm <sup>-</sup> , compiler).     |  |
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| AUXILIARY  | INFORMATION                             |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:         |  |
| Sulfisomidine (0.5 g ) was placed in an L-   | Nothing specified.                      |  |
| shaped tube together with 20 ml of the buf-  |   |  |
| fer soln. The mixt was shaken in a thermo-   |   |  |
| stat until equilibrium was attained. The   |   |  |
| sulfisomidine was assayed in the supernatant   |   |  |
| spectrophotometrically at 545 nm on a Beck-  |   |  |
| mann DU spectrophotometer. The results were  | 1                                       |  |
| taken from a calibration graph.  |   |  |
|  |   |  |
|  | ESTIMATED ERROR:                        |  |
|  | Soly and pH: not specified.             |  |
|  | Temp: ±1 <sup>0</sup> C (authors).      |  |
|  | REFERENCES:                             |  |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-                |                     |             | ORIGINAL MEASUREMENTS:   |
|--|---------------------|-------------|--|
| methyl-4-pyrimidinyl)- (sulfisomidine);                                  |                     |             | Hekster, Ch. A.; Vree, T. B.   |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]  |                     |             | Antibiotics Chemother. <u>1982,</u> 31,  |
| (2) Phosphoric acid, dis<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94- |                     | ;           | 22-118.  |
| (3) Phosphoric acid, mor<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0 | opotassium<br>)]    | salt;       |  |
| (4) Water; H <sub>2</sub> 0; [773  | 32-18-5]            |             | PREPARED BY:   |
| VARIABLES: pH  | 1                   |             | R. Piekos  |
| EXPERIMENTAL VALUES:   |                     |             |  |
| EXIERTENTAL VALUES.  |                     |             |  |
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|  |                     |             |  |
|  |                     | Solu        | ubility at 25 <sup>0</sup> C   |
|  | рН                  |             |  |
|  |                     | mg/l        | $10^3 \text{ mol } dm^{-3} a$  |
|  | 5.5                 | 1,580       | 5.677  |
|  | 7.5 <sup>b</sup>    | 2,480       | 8.910  |
|  |                     |             |  |
|  |                     | lated by co |  |
|  | <sup>b</sup> Errone | eous pH val | lue of 7.0 is given  |
|  | in the              | article.    |  |
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| · · · · · · · · · · · · · · · · · · ·                                    |                     |             |  |
|  |                     | AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDU   | RE:                 |             | SOURCE AND PURITY OF MATERIALS:  |
| The earlier developed me   |                     |             | Neither source nor the purity of the mate-   |
| (personal communication)   | . Satd sol          | lns of      | rials was specified.   |
| sulfisomidine were prepd   |                     |             | 1  |
| of pH 5.5 and 7.5 at 25 <sup>c</sup>                                     |                     |             | ]  |
| solute was measured by m   |                     | -           |  |
| Physics 3500B high-perfo   |                     |             | 1  |
| tograph equipped with a Model 748 column                                 |                     |             |  |
| oven and a Pye-Unicam LC-UV spectrophoto-                                |                     |             |  |
| metric detector.   |                     |             | ESTIMATED ERROR:<br>Soly: the detection limit of the solute by<br>HPLC was 0.5 mg/l (authors). |
|  |                     |             | The errors in temp and pH were not speci-<br>fied.   |
|  |                     |             | REFERENCES:  |
|  |                     |             | 1. Hekster, Y. A.; Vree, T. B.;  |
|  |                     |             | Damsma, J. E.; Friesen, W. T.  |
|  |                     |             | J. Antimicrob. Chemother. <u>1981</u> , 8,   |
|  |                     |             | 133.   |
|  |                     |             |  |

| COMPONENTS:                               |  |                                       | ORIGINAL     | MEASUREMENTS:                                 |  |
|---|--|---------------------------------------|--------------|---|--|
| (1)                                       | Benzenesulfonamide, 4-amino-N-(2,6-di-<br>methyl-4-pyrimidinyl)- (sulfisomidine);<br>C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] |                                       |              | T.; Matsuman<br>a, S.; Hiura                  | ru, H.;<br>1. M.                                       |
| (2)                                       |  | · ·                                   | Pharm. Bull. | <u>1973,</u> 21(7),                           |  |
| (3)                                       | 4 7  |                                       |              |   |  |
| (4)                                       | Water; H <sub>2</sub> 0; [7732-  | -18-5]                                | PREPARED     | BY:   |  |
| VARI                                      | ABLES:   |                                       | 1            | R. Piekos                                     |  |
|   | pH   |                                       | l            |   |  |
| EXPERIMENTAL VALUES:                      |  |                                       |              |   |  |
| -   | Citric acid  | Ma <sub>2</sub> HPO <sub>4</sub>      | рH           | <u> </u>                                      | ubility at 37°C  |
|   | g/100 ml water   | g/100 ml water                        |              | mg/ml soln <sup>a</sup>                       | 10 <sup>2</sup> mol dm <sup>-3</sup> soln <sup>b</sup> |
|   | 1.680  | 0.572                                 | 3.1          | 2.98  | 1.071  |
|   | 1.260  | 1.144                                 | 4.2          | 1.92  | 0.690  |
|   | 0.840  | 1.716                                 | 5.8          | 1.48  | 0.532  |
|   | 0.420  | 2.228                                 | 6.8          | 1.81  | 0.650  |
|   | <sup>b</sup> Calculated  | by compiler.                          |              |   |  |
|   |  | AUXILIARY                             | INFORMATI    | ON  |  |
| METH                                      | OD/APPARATUS/PROCEDURE   | · · · · · · · · · · · · · · · · · · · | SOURCE A     | ND PURITY OF M                                | ATERIALS:  |
| A1:                                       | iquots of the buffer so  | oln were placed in                    | The sul      | lfisomidine was                               | s of pharmaceutical                                    |
| -   | ass-stoppered flasks w   |                                       | grade.       | The source an                                 | nd purity of the citric                                |
|   | omidine. The flasks we   |                                       |              | - 1   | e not specified.                                       |
|   | and at 37±1 <sup>0</sup> C and shake<br>until equilibrium was e  |                                       | Distd v      | vater was used.                               |  |
|   | of the supernatant was   |                                       |              |   |  |
| of a filter pipet and sulfisomidine was   |  |                                       |              |   |  |
| assayed by the previously reported method |  |                                       |              |   |  |
| (1).                                      |  |                                       | ESTIMATE     |   |  |
|   |  |                                       |              | id pH: not spe<br>±1 <sup>0</sup> C (authors) |  |
|   |  |                                       | remp.        | -1 0 (authors)                                | •  |
|   |  |                                       |              | ES:   | ••   |
|   |  |                                       |              |   | nchiya, S.; Hiura, M.<br>7 <u>1,</u> <i>31</i> , 298.  |
|   |  |                                       |              |   |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                |
|---|---|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</pre> | Takubo, T.; Matsumaru, H.;<br>Tsuchiya, S.; Hiura, M. |
| <pre>(2) 1,2,3-Propanetricarboxylic acid, 2-hy-<br/>droxy- (citric acid); C<sub>6</sub>H<sub>8</sub>0<sub>7</sub><br/>[77-92-9]</pre>                                     | Chem. Pharm. Bull. <u>1973,</u> 21(7),<br>1440-5.     |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C; one pH: 2.1   | R. Fiekos   |
| EXPERIMENTAL VALUES:  |   |

Solubility of sulfisomidine in a citric acid solution ( 2.100 g citric acid per 100 ml water ) of pH 2.1 at  $37^{\circ}$ C is 6.21 mg/ml solution<sup>a</sup> ( 2.23 x  $10^{-2}$  mol dm<sup>-3</sup> solution, compiler ).

<sup>a</sup>Numerical value to the graphical data given by one of the authors ( S. T. ) in personal communication.

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                          | SOURCE AND PURITY OF MATERIALS:   |
|--|---|
| Aliquots of the citric acid soln were pla-           | The sulfisomidine was of pharmaceutical   |
| ced in glass-stoppered flasks with excess            | grade. The source and purity of the citric  |
| of sulfisomidine. The flasks were allowed            | acid were not specified.  |
| to stand at $37\pm1^{\circ}$ C and shaken vigorously | Distd water was used.   |
| for 4 h until equilibrium was established.           |   |
| One ml of the supernatant was removed by             |   |
| means of a filter pipet and sulfisomidine            |   |
| was assayed by the previously reported pro-          |   |
| cedure (1).  | ESTIMATED ERROR:<br>Soly and pH: not specified.<br>Temp: ±1 <sup>0</sup> C (authors). |
|  | REFERENCES:   |
|  | 1. Takubo, M; Tsuchiya, S; Hiura, M.  |
|  | Yakuzaigaku <u>1971,</u> 31, 298.   |
|  |   |

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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |  |
|--|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</li> <li>Ethanol; C<sub>2</sub>H<sub>6</sub>O; [64-17-5]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> | Martin, A,; Miralles, M. J.<br><i>J. Pharm. Sci.</i> <u>1982,</u> 71(4), 439-42. |  |
| (J) water, 1120, [//J2-10-J]   |  |  |
| VARIABLES:   | PREPARED BY:   |  |
| One temperature: 25 <sup>0</sup> C   | R. Piekos  |  |
|  |  |  |
| EXPERIMENTAL VALUES:   |  |  |
| EXTERITE VALUE:  |  |  |
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| Mole fraction solubility of sulfisomidin   | ne in 94.94% (v/v) ethanol at $25^{\circ}$ C                                     |  |
|  |  |  |
| is 0.001110 (numerical value given in pe   | ersonal communication to compiler ).   |  |
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| AUXILIARY  | INFORMATION  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |  |
| About 20 ml of 95% (label) ethanol was in-   | Sulfisomidine, mp 515.6 K, was from Sigma  |  |
|  | 1  |  |
| troduced into screw-capped vials contg an  | Chemical, St. Louis, Mo. The 94.94% (v/v)  |  |
| excess of sulfisomidine. The vials were  | ethanol (labeled 95%), $d = 0.8139 \text{ g cm}^{-3}$                            |  |
| agitated for 72 h in a shaker bath main-   | at 25 <sup>0</sup> C, was from Fisher Scientific, Fair                           |  |
| tained at 25±0.2°C. After equilibrium was  | Lawn, N. J. Its purity was not specified.  |  |
| obtained, a filtered aliquot was pipetted,   |  |  |
| using an automatic micropipet, into a volu-  |  |  |
| metric flask and appropriately dild with   |  |  |
| MeOH. The solns were analyzed in a Beck-   | ESTIMATED ERROR:   |  |
| mann Model 25 spectrophotometer at 281.5 nm.   |  |  |
|  | Soly: detns were run in triplicate   |  |
|  | (authors).   |  |
|  | Temp: ±0.2°C (authors).  |  |
|  | REFERENCES :   |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |  |  |
|---|--|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);</li> </ol>  | Martin, A.; Miralles, M. J.  |  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0]   | J. Pharm. Sci. <u>1982</u> , 71(4), 439-42.  |  |  |
| (2) Ethanol; $C_2H_60$ ; [64-17-5]  |  |  |  |
| (3) Formic acid; $H_2CO_2$ ; [64-18-6]  |  |  |  |
| (4) Sodium formate; HCNa0 <sub>2</sub> ; [141-53-7]   |  |  |  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES:  | PREPARED BY:   |  |  |
| Concentration of ethanol  | R. Piekos  |  |  |
| EXPERIMENTAL VALUES:  |  |  |  |
|   |  |  |  |
| % Ethanol in  | Mole fraction solubility <sup>b</sup>  |  |  |
| aqueous buffer <sup>a</sup>   | at 25 <sup>0</sup> C   |  |  |
| 95  | 0.001320   |  |  |
| 90  | 0.001460   |  |  |
| 80  | 0.001660   |  |  |
| 50  | 0.000858   |  |  |
|   |  |  |  |
| (personal communication to compile<br><sup>b</sup> Numerical values given in personal   |  |  |  |
|   | r).  |  |  |
| <sup>b</sup> Numerical values given in personal   | r).  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY  | r).<br>communication to compiler.<br>INFORMATION   |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma   |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated  | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25±0.2°C. After equilibrium was obtained, a  | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.<br>The source and purity of formic acid were   |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.<br>The source and purity of formic acid were   |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25±0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto  | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.<br>The source and purity of formic acid were<br>not specified.<br>Distilled water was used.  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25±0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns  | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.<br>The source and purity of formic acid were<br>not specified.<br>Distilled water was used.  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an exces<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25±0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask   | r).<br>communication to compiler.<br>INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine, mp 515,6 K, was from Sigma<br>Chemicals, St. Louis, Mo. Ethanol (94.94%<br>v/v) and NaOH were from Fisher Scientific,<br>Fair Lawn, N. J.<br>The source and purity of formic acid were<br>not specified.<br>Distilled water was used.<br>ESTIMATED ERROR:<br>Soly: detns were run in triplicate  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).</pre>  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).<br/>TEmp: ±0.2<sup>o</sup>C (authors).</pre> |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).</pre>  |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).<br/>TEmp: ±0.2<sup>o</sup>C (authors).</pre> |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).<br/>TEmp: ±0.2<sup>o</sup>C (authors).</pre> |  |  |
| <sup>b</sup> Numerical values given in personal<br>AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>About 20 ml of the solvent mixt was intro-<br>duced into screw-capped vials contg an excess<br>of sulfisomidine. The vials were agitated<br>for 72 h in a shaker bath maintained at<br>25t0.2°C. After equilibrium was obtained, a<br>filtered aliquot was pipetted, using an auto<br>matic micropipette, into a volumetric flask<br>and appropriately dild with MeOH. The solns<br>were analyzed in a Beckmann Model 25 spectro | <pre>r).<br/>communication to compiler.<br/>INFORMATION<br/>SOURCE AND PURITY OF MATERIALS:<br/>Sulfisomidine, mp 515,6 K, was from Sigma<br/>Chemicals, St. Louis, Mo. Ethanol (94.94%<br/>v/v) and NaOH were from Fisher Scientific,<br/>Fair Lawn, N. J.<br/>The source and purity of formic acid were<br/>not specified.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: detns were run in triplicate<br/>(authors).<br/>TEmp: ±0.2<sup>o</sup>C (authors).</pre> |  |  |

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di                                   |  |
| methyl-4-pyrimidinyl)- (sulfisomidin  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | 94-7.  |
| (2) Methanol; CH <sub>4</sub> 0; [67-56-1]                                  |  |
|   |  |
| VARIABLES:  | PREPARED BY:   |
| Temperature   | R. Piekos  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
|   |  |
|   |  |
|   |  |
|   |  |
| t/ <sup>o</sup> C Mole frac   | tion solubility ( $\times 10^4$ )                                      |
|   |  |
| 25  | 11.2   |
| 30  | 12.7   |
| 37  | 16.5   |
|   |  |
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|   | ······································                                 |
| AUXILIA   | RY INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:  |
| A const temp bath contg screw-capped bottl                                  |  |
| with sulfisomidine in excess and methanol                                   | ceutical Co.   |
| was rotated for 24 h. Samples were with-                                    | Methanol: spectrophotometric grade solvent,                            |
| drawn through a pledget of glass wool into                                  | •  |
| a pipet, which was wiped clean and allowed                                  |  |
| to drain into a volumetric flask. Solute                                    |  |
| concns were detd by spectrophotometric ass                                  |  |
| at predetd wavelengths using a Cary model                                   |  |
| spectrophotometer (1).  | ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors). |
|   | Temp: ±0.1°C (authors).  |
|   | REFERENCES :   |
| }   | 1. Paruta, A. N.; Mauger, J. W.  |
|   | J. Pharm. Sci. <u>1971</u> , 60, 432.                                  |
|   |  |
| 1   |  |

| Alexander, K. S.; Paruta, A. N.<br>Drug. Dev. Ind. Pharm. <u>1977</u> , 3(2),<br>163-83. |  |
|--|--|
| PREPARED BY:<br>R. Piekos  |  |
|  |  |

| t/ <sup>4</sup> | °c ——— | Solub                          | ility                                  | _ |
|-----------------|--------|--------------------------------|--|---|
|                 | mg/ml  | 10 <sup>3</sup> X <sup>a</sup> | 10 <sup>2</sup> mol dm <sup>-3</sup> b |   |
| 25              | 7.64   | 1.12                           | 2.74                                   |   |
| 30              | 8.67   | 1.27                           | 3.15                                   |   |
| 37              | 11.2   | 1.65                           | 4.02                                   |   |

- <sup>a</sup> X = mole fraction
- <sup>b</sup> Calculated by compiler

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:                    |
|--|--|
| A const temp bath contg screw-capped bottles | Sulfisomidine: lot E2498, Ciba Pharmaceuti-        |
| with sulfisomidine in excess and methanol    | cal Co. Its mp agreed with the literature          |
| was rotated for 24 h. Samples were with-     | value. Methanol was a spectrograde solvent         |
| drawn through a pledget of glass wool into a | from the Mallinckrodt Chemical Works.              |
| pipet, which was wiped clean and allowed to  |  |
| drain into a volumetric flask. Soly was detd |  |
| from absorbance and previously ascertained   |  |
| Beer's law plots detd on a Cary model 16     |  |
| spectrophotometer (1).                       | ESTIMATED ERROR:                                   |
|  | Soly: av of at least 3 detn is reported (authors). |
|  | Temp: ±0.1 <sup>0</sup> C (authors).               |
|  | REFERENCES:  |
|  | 1. Mauger, J. W.; Paruta, A. N.;                   |
|  | Gerraughty, R. J. J. Pharm. Sci.                   |
|  | <u>1972</u> , <i>61(1)</i> , 94.                   |
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|--|---|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | ORIGINAL MEASUREMENTS:                          |  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);</li> </ol> | Mauger, J. W.; Paruta, A. N.;                   |  |
|  | Gerraughty, R. J. J. Pharm. Sci.                |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0]                            | 1972, 61(1), 94-7.                              |  |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> 0; [64-17-5]  |   |  |
| VARIABLES:   | PREPARED BY:                                    |  |
| Temperature  | R. Piekos                                       |  |
| EXPERIMENTAL VALUES:   | L   |  |
|  |   |  |
|  |   |  |
|  |   |  |
|  |   |  |
| t/ <sup>0</sup> C Mole fractio   | on solubility ( x 10 <sup>4</sup> )             |  |
| 25   | 5.53  |  |
| 30   | 6.38  |  |
| 37   | 8.20  |  |
|  |   |  |
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| AUXILIARY  | INFORMATION                                     |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                 |  |
| A const temp bath contg screw-capped bottles   |   |  |
| with sulfisomidine in excess and ethanol was   | ceutical Co.                                    |  |
| rotated for 24 h. Samples were withdrawn   | Ethanol was from the U. S. Industrial Chem-     |  |
| through a pledget of glass wool into a pipet   | , icals Co. (purity not specified).             |  |
| which was wiped clean and allowed to drain   |   |  |
| into a volumetric flask. Solute concns were  |   |  |
| detd by spectrophotometric assay at predetd  |   |  |
| wavelengths using a Cary model 16 spectro-   |   |  |
| photometer (1).  | ESTIMATED ERROR:                                |  |
|  | Soly: av values of 3 detns are given (authors). |  |
|  | Temp: ±0.1 <sup>o</sup> C (authors).            |  |
|  | REFERENCES :                                    |  |
|  | 1. Paruta, A. N.; Mauger, J. W.                 |  |
|  | J. Pharm. Sci. <u>1971</u> , 60, 432.           |  |
|  |   |  |
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|--|--|---------------|---|--|
| COMPONEN   |  | 1 - 1 - 2     | 10 6 14                                     | ORIGINAL MEASUREMENTS:                         |
|  |  |               |   | Mauger, J. W.; Petersen, H., Jr.;              |
|  | thy1-4-pyrimidin   |               | omidine);                                   | 1  |
| c <sub>1:</sub>  | 2 <sup>H</sup> 14 <sup>N</sup> 4 <sup>0</sup> 2 <sup>S</sup> ; [51 | 5-64-0]       |   | Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),       |
| (2) Etl  | hanol; C <sub>2</sub> H <sub>6</sub> O;                            | [64-17-5]     |   | 163-83.  |
| 1  | 20   |               |   |  |
| VARIABLE   | S :  |               |   | PREPARED BY:                                   |
| VARIADDO   |  |               |   |  |
|  | Temperature  |               |   | R. Piekos                                      |
|  |  | <del></del>   |   | L  |
| EXPERIME   | NTAL VALUES:   |               |   |  |
|  |  |               |   |  |
|  |  |               |   |  |
|  |  |               |   |  |
|  |  |               |   |  |
|  |  |               | Solubi                                      | ility  |
|  | t/°C   |               |   |  |
|  |  | mg/ml         | 10 <sup>4</sup> X                           | a $10^2 \text{ mol } \text{dm}^{-3} \text{ b}$ |
|  |  |               |   |  |
|  | 25   | 2.63          | 5.53  | 0.945  |
|  | 30   | 3.02          | 6.38  | 1.08   |
|  | 37   | 3.86          | 8.20  | 1.39   |
|  |  |               |   |  |
|  | b Calc   | ulated by con | mpiler.                                     |  |
|  | ·····  |               | AUXILIARY                                   | INFORMATION                                    |
| METHOD /A  | PPARATUS / PROCEDU   |               |   | SOURCE AND PURITY OF MATERIALS:                |
|  | temp bath contg  |               | d bottles                                   | Sulfisomidine: lot E2498, Ciba Pharmaceuti-    |
|  |  | • •           |   | cal Co. Its mp agreed with the literature      |
| with sulfisomidine in excess and ethanol was<br>rotated for 24 h. Samples were withdrawn |  |               | value. Ethanol was from the U.S. Industrial |  |
|  | -  |               |   | Chemicals Co. Its refractive index value       |
|  |  |               |   | and density agreed with literature values.     |
| which was wiped clean and allowed to drain   |  |               | and density agreed with interature values.  |  |
| into a volumetric flask. Soly was detd from  |  |               |   |  |
|  | nce and previous   |               |   |  |
| _  | ts detd on a Car   | y model 16 sp | pectropho-                                  | •  |
| tometer (1).   |  |               |   | ESTIMATED ERROR:                               |
|  |  |               |   | Soly: av of at least 3 detns is reported       |
|  |  |               |   | (authors).                                     |
|  |  |               |   | Temp: ±0.1°C (authors).                        |
|  |  |               |   | REFERENCES :                                   |
|  |  |               |   | 1. Mauger, J. W.; Paruta, A. N.;               |
|  |  |               |   | Gerraughty, R. J. J. Pharm. Sci.               |
|  |  |               |   | 1972, 61(1), 94.                               |
|  |  |               |   |  |
|  |  |               |   |  |
|  |  |               |   |  |

|  | ORIGINAL MEASUREMENTS:                      |  |  |
|--|---|--|--|
| (1) Benzenesulfonamide, 4-amino- <u>N</u> -(2,6-di-                              | Martin, A.; Miralles, M. J.                 |  |  |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);</pre>                               |   |  |  |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]  | J. Pharm. Sci. <u>1982</u> , 71(4), 439-42. |  |  |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> 0; [64-17-5]                          |   |  |  |
| VARIABLES:   | PREPARED BY:                                |  |  |
| One temperature: 25 <sup>0</sup> C   | R. Piekos                                   |  |  |
| EXPERIMENTAL VALUES:   |   |  |  |
| Mole fraction solubility of sulfisomid<br>0.000557 ( numerical value given in pe |   |  |  |
| AUXILIARY  | INFORMATION                                 |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS;             |  |  |
| About 20 ml of abs ethanol was introduced  | Sulfisomidine, mp 515.6 K, was from Sigma   |  |  |
| into screw-capped vials contg an excess of                                       | Chemicals, St. Louis, Mo., and abs ethanol  |  |  |
| sulfisomidine. The vials were agitated for                                       |   |  |  |
| 72 h in a shaker bath maintained at  | Ind., and contained 0.57% (v/v) water.      |  |  |
| 25±0.2 <sup>o</sup> C. After equilibrium was obtained,                           | The reagents were tested for identity and   |  |  |
| a filtered aliquot was pipetted, using an  | purity.                                     |  |  |
| automatic micropipette, into a volumetric  |   |  |  |
| flask and appropriately dild with MeOH. The                                      |   |  |  |
| solns were analyzed in a Beckmann Model 25                                       | ESTIMATED ERROR:                            |  |  |
| spectrophotometer at 281.5 nm.   | Soly: detns were run in triplicate          |  |  |
|  | (authors).                                  |  |  |
|  | Temp: ±0.2 <sup>0</sup> C (authors).        |  |  |
|  | REFERENCES :                                |  |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                          |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  | Sunwoo, C.; Eisen, H.                           |
| <pre>methyl-4~pyrimidinyl)- (sulfisomidine);</pre>                          | J. Pharm. Sci. <u>1971</u> , 60, 238-44.        |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] |   |
| (2) Ethanol, 2-ethoxy-, C <sub>4</sub> H <sub>10</sub> O <sub>2</sub> ;     |   |
| [110-80-5]  |   |
| VARIABLES:  | PREPARED BY:                                    |
| One temperature: 25°C   | R. Piekos                                       |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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|   |   |
| The mole fraction solubility of sulfise                                     | omidine in 2-ethoxyethanol at 25 <sup>0</sup> C |
| is 0.0111 ( 3.35 g/100 g solution, comp                                     | oiler)  |
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| AUXILIARY   | INFORMATION                                     |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                 |
| Soly was detd by the method reported by                                     | Sulfisomidine (Ciba Pharmaceutical Co.,         |
| Restaino and Martin (1). Sulfisomidine was                                  | Summit, N. J.) was recrystd from warm alco-     |
| assayed on a Coleman-Hitachi 124 double-beam                                |   |
| spectrophotometer at 270 nm after diln of a                                 | grade (Cellosolve solvent, Union Carbide,       |
|   |   |
| sample with 95% alcohol or water.   | New York, N. Y.).                               |
|   |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:                                |
|   | Temp: ±1.0 <sup>0</sup> C (authors).            |
|   | Soly: the mean of 3 runs was given              |
|   | (authors).                                      |
|   | REFERENCES:                                     |
|   | 1. Restaino, F. A.; Martin, A. N.               |
|   | J. Pharm. Sci. <u>1964</u> , 53, 636.           |
|   | 5. 11atur. D52. <u>1704</u> , 00, 030.          |
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|  | OPTOTNAL MILLOUPPLETVER                    |  |  |
|--|--|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | ORIGINAL MEASUREMENTS:                     |  |  |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);</pre>         | Mauger, J. W.; Paruta, A. N.;              |  |  |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]                          | Gerraughty, R. J. J. Pharm. Sci.           |  |  |
|  | <u>1972</u> , <i>61(1)</i> , 94-7.         |  |  |
| (2) 1-Propanol; C <sub>3</sub> H <sub>8</sub> 0; [71-23-8] |  |  |  |
|  |  |  |  |
| VARIABLES:   | PREPARED BY:                               |  |  |
| Temperature  | R. Piekos                                  |  |  |
|  |  |  |  |
| EXPERIMENTAL VALUES:                                       |  |  |  |
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|  | <i>,</i>                                   |  |  |
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|  |  |  |  |
| t/ <sup>0</sup> C Mole                                     | fraction solubility (x 10 <sup>4</sup> )   |  |  |
|  |  |  |  |
| 25   | 4.23                                       |  |  |
| 30   | 4.89                                       |  |  |
| 37   | 6.48                                       |  |  |
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| AUXILIARY  | INFORMATION                                |  |  |
| METHOD/APPARATUS/PROCEDURE:                                | SOURCE AND PURITY OF MATERIALS:            |  |  |
| A const temp bath contg screw-capped bottles               | Sulfisomidine: lot E2498 from Ciba Pharma- |  |  |
| with sulfisomidine in excess and 1-propanol                | ceutical Co.                               |  |  |
| was rotated for 24 h. Samples were with-                   | 1-Propanol was a Baker Analyzed Reagent,   |  |  |
| drawn through a pledget of glass wool into a               | J. T. Baker Chemical Co.                   |  |  |
| pipet, which was wiped clean and allowed to                |  |  |  |
| drain into a volumetric flask. Solute con-                 |  |  |  |
| cns were detd by spectrophotometric assay at               |  |  |  |
| predetd wavelengths using a Cary model 16                  |  |  |  |
| spectrophotometer (1).                                     | ESTIMATED ERROR:                           |  |  |
|  | Soly: av values of 3 detns are given       |  |  |
|  | (authors).                                 |  |  |
|  | Temp: ±0.1 <sup>0</sup> C (authors).       |  |  |
|  | REFERENCES:                                |  |  |
|  | 1. Paruta, A. N.; Mauger, J. W.            |  |  |
|  | J. Pharm. Sci. <u>1971,</u> 60, 432.       |  |  |
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|  |                                      | 303  |  |  |
|--|--------------------------------------|--|--|--|
| COMPONENTS:<br>(1) Benzenesulfonamide,<br>methyl-4-pyrimidinyl<br>C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-<br>(2) 1-Propanol; C <sub>3</sub> H <sub>8</sub> O;   | )- (sulfisomidine);<br>64-0]         | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.<br>Alexander, K. S.; Paruta, A. N.<br>Drug. Dev. Ind. Pharm. <u>1977</u> , 3(2),<br>163-83.   |  |  |
| VARIABLES:   |                                      | PREPARED BY:   |  |  |
| Temperature  |                                      | R. Piekos  |  |  |
| EXPERIMENTAL VALUES:   |                                      | L  |  |  |
|  |                                      |  |  |  |
| t/°C -   | Solut                                | bility   |  |  |
|  | mg/ml 10 <sup>4</sup> x <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3</sup> b   |  |  |
| 25   | 1.57 4.23                            | 5.64   |  |  |
| 30   | 1.81 4.89                            | 6.50   |  |  |
| 37   | 2.39 6.48                            | 8.59   |  |  |
|  | mole fraction<br>ated by compiler    |  |  |  |
|  | AUXILIARY                            | INFORMATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfisomidine in excess and 1-propanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into a<br>pipet, which was wiped clean and allowed to<br>drain into a volumetric flask. Soly was<br>detd from absorbance and previously ascer-<br>tained Beer's law plots detd on a Cary model |                                      | SOURCE AND PURITY OF MATERIALS:<br>Sulfisomidine: lot E2498, Ciba Pharmaceuti-<br>cal Co. Its mp agreed with the literature<br>value. 1-Propanol was Baker Analyzed Rea-<br>gent ( J.T. Baker Chemical Co.). Its re-<br>fractive index value and density agreed<br>with literature values. |  |  |
| 16 spectrophotometer (1).  |                                      | ESTIMATED ERROR:<br>Soly: av of at least 3 detns is reported<br>(authors).<br>Temp: ±0.1 <sup>O</sup> C (authors).<br>REFERENCES:<br>1. Mauger, J. W.; Paruta, A. N.;  |  |  |
|  |                                      | Gerraughty, R. J. <i>J. Pharm. Sci.</i><br><u>1972</u> , <i>61(1)</i> , 94.  |  |  |

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                  |  |  |
|---|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  |   |  |  |
| methyl-4-pyrimidinyl)- (sulfisomidine);                                     | Mauger, J. W.; Paruta, A. N.;                           |  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | Gerraughty, R. J. J. Pharm. Sci.                        |  |  |
| (2) 1-Butanol; C <sub>4</sub> H <sub>10</sub> 0; [71-36-3]                  | <u>1972,</u> 61(1), 94-7.                               |  |  |
|   |   |  |  |
| VARIABLES:  | PREPARED BY:  |  |  |
| Temperature   | R. Piekos   |  |  |
|   |   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
| t/ <sup>0</sup> C Mole fra  | action solubility (x 10 <sup>4</sup> )                  |  |  |
| 25  | 3.44  |  |  |
| 30  | 4.17  |  |  |
| 37  | 5.56  |  |  |
|   |   |  |  |
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| AUXILIARY   | INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                         |  |  |
| A const temp bath contg screw-capped bottles                                |   |  |  |
| with sulfisomidine in excess and 1-butanol                                  | ceutical Co.  |  |  |
| was rotated for 24 h. Samples were with-                                    | 1-Butanol was from the Mallinckrodt Chem-               |  |  |
| drawn through a pledget of glass wool into a                                | ical Works.   |  |  |
| pipet, which was wiped clean and allowed to                                 |   |  |  |
| drain into a volumetric flask. Solute con-                                  |   |  |  |
| cns were detd by spectrophotometric assay                                   |   |  |  |
| at predtd wavelengths using a Cary model 16 spectrophotometer (1).          |   |  |  |
| apectiophotometer (1).  | ESTIMATED ERROR:<br>Soly: av values of 3 runs are given |  |  |
|   | (authors).  |  |  |
|   | Temp: $\pm 0.1^{\circ}C$ (authors).                     |  |  |
|   | REFERENCES:   |  |  |
|   | 1. Paruta, A. N.; Mauger, J. W.                         |  |  |
|   | J. Pharm. Sci. <u>1971</u> , 60, 432.                   |  |  |
| 1   |   |  |  |
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| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0] (2) 1-Butanol; C<sub>4</sub>H<sub>10</sub>O; [71-36-3]</pre>   |    |           | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),<br>163-83.  |   |  |
|--|----|-----------|--|---|--|
| VARIABLES:   |    |           | REPARED BY:  |   |  |
| Temperatur   | re |           | R. Piekos  |   |  |
| EXPERIMENTAL VALUES:   |    |           |  |   |  |
| t/°C   |    |           | 4.53<br>6.00   |   |  |
|  |    | AUXILIARY | VFORMATION   |   |  |
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfisomidine in excess and 1-butanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into<br>a pipet, which was wiped clean and allowed<br>to drain into a volumetric flask. Soly was<br>detd from absorbance and previously ascer-<br>tained Beer's law plots detd on a Cary model<br>16 spectrophotometer (1). |    |           | cal Co. Its mp agre<br>value. 1-Butanol wa<br>Chemical Works. Its<br>and density agreed v<br>SSTIMATED ERROR:<br>Soly: av of at leas<br>(authors).<br>Temp: ±0.1°C (auth<br>REFERENCES:<br>1. Mauger, J. W.; | 2498, Ciba Pharmaceuti-<br>eed with the literature<br>as from the Mallinckrodt<br>as refractive index value<br>with literature values.<br>at 3 detns is reported<br>mors).<br>Paruta, A. N.;<br>J. J. Pharm. Sci. |  |

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |  |  |
|---|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  | Mauger, J. W.; Paruta, A. N.;             |  |  |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);</pre>                          | Gerraughty, R. J. J. Pharm. Sci.          |  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | <u>1972,</u> 61(1), 94-7.                 |  |  |
| (2) 1-Pentanol; C <sub>5</sub> H <sub>12</sub> 0; [71-41-0]                 |   |  |  |
|   |   |  |  |
| VARIABLES:  | PREPARED BY:                              |  |  |
| Temperature   | R. Piekos                                 |  |  |
|   |   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |
|   |   |  |  |
| t/ <sup>0</sup> C Mole frac   | tion solubility ( $\times 10^4$ )         |  |  |
|   |   |  |  |
| 25  | 2.84                                      |  |  |
| 30  | 3.43                                      |  |  |
| 37  | 4.54                                      |  |  |
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| AUXILIARY   | INFORMATION                               |  |  |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:           |  |  |
| A const temp bath contg screw-capped bottles                                |   |  |  |
| with sulfisomidine in excess and 1-pentanol                                 | ceutical Co.                              |  |  |
| was rotated for 24 h. Samples were with-                                    | 1-Pentanol was from Fisher Scientific Co. |  |  |
| drawn through a pledget of glass wool into a                                |   |  |  |
| pipet, which was wiped clean and allowed to                                 |   |  |  |
| drain into a volumetric flask. Solute con-                                  |   |  |  |
| cns were detd by spectrophotometric assay                                   | ESTIMATED ERROR:                          |  |  |
| at predetd wavelengths using a Cary model 16                                |   |  |  |
| spectrophotometer (1).  | (authors).                                |  |  |
|   | Temp: ±0.1°C (authors).<br>REFERENCES:    |  |  |
|   | 1. Paruta, A. N.; Mauger, J. W.           |  |  |
|   | J. Pharm. Sci. <u>1971</u> , 60, 432.     |  |  |
|   |   |  |  |
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|--|---|--|--|
| <ul> <li>COMPONENTS:         <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</li> <li>1-Pentanol; C<sub>5</sub>H<sub>12</sub>O; [71-41-0]</li> </ol> </li> </ul> | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug. Dev. Ind. Pharm. <u>1977</u> , 3(2),<br>163-83. |  |  |
| VARIABLES:<br>Temperature  | PREPARED BY:<br>R. Piekos   |  |  |
| EXPERIMENTAL VALUES:   |   |  |  |
|  |   |  |  |
| t/ <sup>0</sup> C  | Solubility  |  |  |
| mg/m1 10 <sup>4</sup>  | $x^a$ 10 <sup>3</sup> mol dm <sup>-3 b</sup>  |  |  |
| 25 0.73 2.0  | 34 2.62   |  |  |
| 30 0.88 3.4  | 3 3.16  |  |  |
| 37 1.16 4.   | 54 4.17   |  |  |
| <sup>a</sup> X = mole fract  | tion  |  |  |
| <sup>b</sup> Calculated by   | compiler  |  |  |
|  | RY INFORMATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |  |  |
| A const temp bath contg screw-capped bott:   |   |  |  |
| with sulfisomidine in excess and 1-pentance  |   |  |  |
| was rotated for 24 h. Samples were with-   | value. 1-Pentanol was from Fisher Scienti-<br>a fic Co. Its refractive index value and  |  |  |
| drawn through a pledget of glass wool into<br>pipet, which was wiped clean and allowed t   |   |  |  |
| drain into a volumetric flask. Soly was  |   |  |  |
| detd from absorbance and previously ascer-   |   |  |  |
| tained Beer's law plots detd on a Cary mod   | .e1   |  |  |
| 16 spectrophotometer (1).  | ESTIMATED ERROR:<br>Soly: av of at least 3 detns is reported  |  |  |
|  | (authors).  |  |  |
|  | Temp: ±0.1 <sup>0</sup> C (authors).  |  |  |
|  | REFERENCES:   |  |  |
|  | <ol> <li>Mauger, J. W.; Paruta, A. N.;<br/>Gerraughty, R. J. J. Pharm. Sci.<br/><u>1972,</u> 61(1), 94.</li> </ol>                                      |  |  |
|  |   |  |  |

| COMPONENTS:   |                            | ORIGINAL MEASUREMENTS:                              |  |  |
|---|----------------------------|---|--|--|
| (1) Benzenesulfonamide, 4-  | amino-N-(2,6-di-           | Mauger, J. W.; Paruta, A. N.;                       |  |  |
| methyl-4-pyrimidinyl)-  | (sulfisomidine);           | Gerraughty, R. J. J. Pharm. Sci.                    |  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64- | -0]                        | <u>1972,</u> 61(1), 94-7.                           |  |  |
| (2) 1-Octanol; C <sub>8</sub> H <sub>18</sub> O;                          | [111-87-5]                 |   |  |  |
| VARIABLES:  |                            | PREPARED BY:  |  |  |
| Temperature   |                            | R. Piekos   |  |  |
|   |                            |   |  |  |
| EXPERIMENTAL VALUES:  |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   | t/ <sup>0</sup> C Mole fra | ction solubility (x 10 <sup>4</sup> )               |  |  |
| -   | 25                         | 1.36  |  |  |
|   |                            |   |  |  |
|   | 30                         | 1.83  |  |  |
|   | 37                         | 2.44  |  |  |
| -   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |
|   | AUXILIARY                  | INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   |                            | SOURCE AND PURITY OF MATERIALS:                     |  |  |
| A const temp bath contg scr   | ew-capped bottles          | Sulfisomidine: lot E2498 from Ciba Pharma-          |  |  |
| with sulfisomidine in exces   |                            | ceutical Co.  |  |  |
| was rotated for 24 h. Samp  |                            | 1-Pentanol was from Fisher Scientific Cp.           |  |  |
| drawn through a pledget of  |                            |   |  |  |
| pipet, which was wiped clea   |                            |   |  |  |
| drain into a volumetric fla   |                            |   |  |  |
| cns were detd by spectropho   | -                          |   |  |  |
| at predetd wavelengths usir   | ig a Cary model 16         |   |  |  |
| spectrophotometer (1).  |                            | ESTIMATED ERROR:                                    |  |  |
|   |                            | Soly: av values of 3 runs are given                 |  |  |
|   |                            | (authors).  |  |  |
|   |                            | Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES: |  |  |
|   |                            | 1. Paruta, A. N.; Mauger, J. W.                     |  |  |
|   |                            | J. Pharm. Sci. <u>1971</u> , 60, 432.               |  |  |
|   |                            | voj voz.  |  |  |
|   |                            |   |  |  |
|   |                            |   |  |  |

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| COMPONENTS :   |                       |                           | ORIC                           | GINAL MEASUREMENTS:  |
|--|-----------------------|---------------------------|--------------------------------|--|
| <ol> <li>Benzenesulfon,<br/>methyl-4-pyrin<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S;</li> <li>1-Octanol;</li> </ol> | nidinyl)-<br>[515-64- | (sulfisomidi<br>0]        | ne); Ale<br>Dru                | ager, J. W.; Petersen, H., Jr.;<br>exander, K. S.; Paruta, A. N.<br>ag Dev. Ind. Pharm. <u>1977,</u> 3(2)<br>2-83. |
| VARIABLES:   |                       |                           | PREI                           | PARED BY:  |
| Temperato  | ıre                   |                           |                                | R. Piekos  |
| EXPERIMENTAL VALUES  |                       |                           |                                |  |
|  | t/°CSolu              |                           | Solubilit                      | у  |
|  | •                     | mg/ml                     | 10 <sup>4</sup> X <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3</sup> b   |
|  | 25                    | 0.24                      | 1.36                           | 0.86   |
|  | 30                    | 0.32                      | 1.83                           | 1.15   |
|  | 37                    | 0.43                      | 2.44                           | 1.55   |
|  |                       | ■ mole fr<br>alculated by |                                | · · · · · · · · · · · · · · · · · · ·  |
|  |                       |                           |                                |  |

with sulfisomidine in exc anol value. 1-Octanol was from Fisher Scientific was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into Co. Its refractive index value and density agreed with literature values. a pipet, which was wiped clean and allowed to drain into a volumetric flask. Soly was detd from absorbance and previously ascertained Beer's law plots detd on a Cary model 16 spectrophotometer (1).

ESTIMATED ERROR: Soly: av of a least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES ;

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. J. Pharm. Sci. <u>1972,</u> 61(1), 94.

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |  |  |
|---|--|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  | ~  |  |  |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);</pre>                          | Mauger, J. W.; Paruta, A. N.;                |  |  |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [515-64-0] | Gerraughty, R. J.; J. Pharm. Sci.            |  |  |
| (2) 1-Decanol; C <sub>10</sub> H <sub>22</sub> 0 [112-30-1]                 | <u>1972,</u> 61(1), 94-7.                    |  |  |
| (2) 1 5000002, 0100220 (222 50 2)   |  |  |  |
| VARIABLES:  | PREPARED BY:                                 |  |  |
|   |  |  |  |
| Temperature   | R. Piekos                                    |  |  |
| EXPERIMENTAL VALUES:  |  |  |  |
| EALINING VALUES.  |  |  |  |
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|   |  |  |  |
| t/ <sup>0</sup> C Mole  | fraction solubility ( x 10 <sup>4</sup> )    |  |  |
|   |  |  |  |
| 25  | 1.80   |  |  |
| 30  | 2.04   |  |  |
| 37  | 2.53   |  |  |
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| AUXILIARY   | INFORMATION                                  |  |  |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:              |  |  |
|   | s Sulfisomidine: lot E2498 from Ciba Pharma- |  |  |
| with sulfisomidine in excess and 1-decanol                                  | ceutical Co.                                 |  |  |
| was rotated for 24 h. Samples were with-                                    | 1-Decanol was from Matheson, Coleman and     |  |  |
| drawn through a pledget of glass wool into                                  | Bell.  |  |  |
| a pipet, which was wiped clean and allowed                                  |  |  |  |
| to drain into a volumetric flask. Solute                                    |  |  |  |
| concns were detd by spectrophotometric assa                                 | )<br>7                                       |  |  |
| at predetd wavelengths using a Cary model                                   |  |  |  |
| 16 spectrophotometer (1).   | ESTIMATED ERROR:                             |  |  |
|   | Soly: av values of 3 runs are given          |  |  |
|   | (authors).                                   |  |  |
|   | Temp: ±0.1 <sup>0</sup> C (authors).         |  |  |
|   | REFERENCES:                                  |  |  |
|   | 1. Paruta, A. N.; Mauger, J. W.              |  |  |
|   | J. Pharm. Sci. <u>1971</u> , 60, 432.        |  |  |
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| COMPONENTS .  |  | OPTOTNAT  | MEASUREMENTS:   |                                       |   |
|---|--|-----------|---|---------------------------------------|---|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-                             |  |           |   |                                       | - ··· ·                                 |
| (1) Benzenesulfonamide, 4-amino-N-(2,0-di-<br>methyl-4-pyrimidinyl)- (sulfisomidine); |  |           |   | J. W.; Petersen                       |   |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]   |  |           | Alexander, K. S.; Paruta, A. N.   |                                       |   |
|   |  |           | Drug De<br>163 <b>-</b> 83.   | v. Ind. Pharm.                        | <u>1977,</u> 3(2),                      |
| (2) 1-Decanol; C <sub>10</sub> H <sub>22</sub> O;                                     | (2) 1-Decanol; C <sub>10</sub> H <sub>22</sub> 0; [112-30-1] |           |   |                                       |   |
| VARIABLES:  |  |           | PREPARED  | BY:                                   | <u> </u>                                |
| Temperature   |  |           |   | R. Piekos                             |   |
|   |  |           |   | · · · · · · · · · · · · · · · · · · · |   |
| EXPERIMENTAL VALUES:  |  |           |   |                                       |   |
|   |  |           |   |                                       |   |
|   |  |           |   |                                       |   |
|   | t/ <sup>o</sup> C  | So        | olubility   |                                       |   |
|   |  | mg/ml     | 10 <sup>4</sup> X <sup>a</sup>  | $10^3$ mol dm <sup>-3</sup> a         |   |
|   | 25   | 0.26      | L <b>.</b> 80   | 0.93                                  |   |
|   | 30   | 0.30      | 2.04  | 1.08                                  |   |
|   | 37   | 0.37      | 2.53  | 1.33                                  |   |
| <sup>a</sup> X = mole fra<br><sup>b</sup> Calculated by                               |  |           |   |                                       |   |
|   |  |           |   |                                       |   |
|   |  | AUXILIARY | INFORMATI   | ON                                    | <b>.</b>                                |
| METHOD/APPARATUS/PROCEDURE:   |  |           |   | D PURITY OF MATE                      |   |
| A const temp bath contg screw-capped bottles  |  |           |   |                                       | B, Ciba Pharmaceuti-                    |
| with sulfisomidine in exce  |  |           | cal Co. Its mp agreed with the literature value. 1-Decanol was from Matheson, Cole- |                                       |   |
| was rotated for 24 h. Sar   | -  |           |   |                                       |   |
| drawn through a pledget of  |  |           | 1   |                                       | ctive index value<br>Literature values. |
| pipet, which was wiped cla<br>drain into a volumetric f                               |  |           | 1   | ity agreed with i                     | literature values.                      |
|   |  |           | 1   |                                       |   |
| from absorbance and previously ascertained  |  |           |   |                                       |   |
| Beer's law plots detd on a Cary model 16  |  |           | ļ   |                                       |   |
| spectrophotometer (1).  |  |           | ESTIMATEI<br>Solv: a  |                                       | letne is reported                       |
|   |  |           | Soly: av of at least 3 detns is reported (authors).                                 |                                       |   |
|   |  |           |   |                                       |   |
|   |  |           | Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:                                 |                                       |   |
|   |  |           | 1   | er, J. W.; Paru                       | ita, A. N.:                             |
|   |  | -         | aughty, R. J.   |                                       |   |
|   |  |           | 1972  |                                       |   |
|   |  |           | <u></u>   | <u> </u>                              |   |
|   |  |           |   |                                       |   |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |
|---|---|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-                                  | Martin, A.; Miralles, M. J.                 |
| <pre>methyl-4-pyrimidinyl)- (sulfisomidine);</pre>                          |   |
| C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | J. Pharm. Sci. <u>1982</u> , 71(4),         |
| (2) n-Hexane; C <sub>6</sub> H <sub>14</sub> ; [110-54-3]                   | 439-42.                                     |
|   |   |
| VARIABLES:  | PREPARED BY:                                |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                   |
| one temperature: 25 C   | A. LIEKUS                                   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Mole fraction solubility of sulfisomidi                                     | ne in n-hexane at 25 <sup>0</sup> C is      |
| 0.000038 (numerical value given in pers                                     | onal communication - compiler ).            |
| 0.000000 (numerical value given in pers                                     |   |
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| AUXILIARY   | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| About 20 ml of n-hexane was introduced into                                 | Sulfisomidine, mp 515.6 K, was from Sigma   |
| screw-capped vials contg an excess of sulfi-                                | Chemicals, St. Louis, Mo., and n-hexane was |
| somidine. The vials were agitated for 72                                    | from Aldrich Chemical, Milwaukee, Wis.      |
| h in a shaker bath maintained at $25\pm0.2^{\circ}$ C.                      | They were tested for identity and purity.   |
| After equilibrium was obtained, a filtered                                  |   |
| -   | 1   |
| aliquot was pipetted, using an automatic                                    |   |
| micropipette, into a volumetric flask and                                   |   |
| appropriately dild with MeOH. The solns                                     |   |
| were analyzed in a Beckmann Model 25 spec-                                  | ESTIMATED ERROR:                            |
| trophotometer at 281.5 nm.  | Soly: the detn was made in triplicate       |
|   | (authors).                                  |
|   | Temp: ±0.2 <sup>0</sup> C (authors).        |
|   | REFERENCES :                                |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-   | Riess, W.   |
| methyl-4-pyrimidinyl)- (sulfaisodi-  | Intern. Congr. Chemotherapy, Proc.,   |
| midine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [515-64-0] | 3rd, Stuttgart <u>1963</u> , 1, 627-32.   |
| (2) Methane, trichloro- (chloroform);  | 1 51 ag 55 av 5 gai v 1903 gai v 1 |
| CHC1 <sub>3</sub> ; [67-66-3]  |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 20 <sup>0</sup> C   | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfaisodimidine in chl  | oroform at $20^{\circ}$ C is 38 mgZ   |
| $(1.4 \times 10^{-3} \text{ mol dm}^{-3} \text{ solution, com})$                     |   |
| (1.4 x 10 mol dm solution, com   | piler).   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| Nothing specified.   | Nothing specified.  |
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|  | ESTIMATED ERROR:  |
|  | Nothing specified.  |
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| ]  | REFERENCES:   |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |  |
|---|---|--|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);<br/>C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>S; [515-64-0]</pre> | Yamazaki, M.; Aoki, M.; Kamada, A.;<br>Yata, N. <i>Yakuzaigaku <u>1967</u>, 27(1)</i> , |  |
| (2) Methane, trichloro- (chloroform);   | 37-40.  |  |
| CHC1 <sub>3</sub> ; [67-66-3]   |   |  |
| VARIABLES:  | PREPARED BY:  |  |
| One temperature: 30 <sup>0</sup> C  | R. Piekos   |  |
| one temperature. 50 C   | A. TIEKUS   |  |
| EXPERIMENTAL VALUES:  |   |  |
|   |   |  |
|   |   |  |
|   |   |  |
| Solubility of sulfisomidine in chloroform at 30 <sup>0</sup> C is 1.63 mmol/L   |   |  |
| $(0.454 \text{ g dm}^{-3}, \text{ compiler}).$  |   |  |
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| AUXILIARY   | INFORMATION   |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |  |
| Sulfisomidine (0.5 g) was placed in an L-   | Nothing specified.  |  |
| shaped tube together with 20 ml of chloro-  |   |  |
| form. The mixt was shaken in a thermostat   |   |  |
| until equilibrium was attained. The sulfi-  |   |  |
| somidine was assayed in the supernatant   |   |  |
| spectrophotometrically at 545 nm on a Beck-   |   |  |
| mann DU spectrophotometer. The results were   |   |  |
| taken from a calibration graph.   |   |  |
|   | ESTIMATED ERROR:<br>Soly: not specified.  |  |
|   | Temp: ±1°C (authors).   |  |
|   |   |  |
|   | REFERENCES:   |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |  |
| <ol> <li>Benzenesulfonamide, 4-amino-<u>N</u>-(2,6-di-<br/>methyl-4-pyrimidinyl)- (sulfisomidine);</li> </ol> | Martin, A.; Miralles, M. J.                 |  |
| $C_{12}H_{14}N_4O_2S;$ [515-64-0]   | J. Pharm. Sci. <u>1982</u> , 71(4), 439-42. |  |
| (2) Ethanol; $C_2H_60$ ; [64-17-5]  |   |  |
|   |   |  |
| (3) n-Hexane; C <sub>6</sub> H <sub>14</sub> ; [110-54-3]<br>VARIABLES:                                       | PREPARED BY:                                |  |
| Concentration of n-hexane   | R. Piekos                                   |  |
|   |   |  |
| EXPERIMENTAL VALUES:  |   |  |
|   |   |  |
| % n-Hexane Mole   | fraction solubility <sup>a</sup>            |  |
|   | at 25°C                                     |  |
| 75  | 0.000037                                    |  |
| 60  | 0.00088                                     |  |
| 40  | 0.000207                                    |  |
| 20  | 0.000392                                    |  |
| 10  | 0.000473                                    |  |
|   |   |  |
|   |   |  |
| <sup>a</sup> Numerical values gi  | ven in personal communication               |  |
| to compiler.  |   |  |
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| AUXILIARY   | INFORMATION                                 |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |  |
| About 20 ml of the solvent mixt was intro-  | Sulfisomidine, mp 515.6 K, was from Sigma   |  |
| duced into screw-capped vials contg an ex-  | Chemicals, St. Louis, Mo., and abs ethanol  |  |
| cess of sulfisomidine. The vials were agi-  | was from Commercial Solvent, Terre Haute,   |  |
| tated for 72 h in a shaker bath maintained<br>at 25±0.2°C. After equilibrium was obtained                     |   |  |
| a filtered aliquot was pipetted, using an   | Wis. The reagents were tested for identity  |  |
| automatic micropipette, into a volumetric   | and purity.                                 |  |
| flask and appropriately dild with MeOH. The   |   |  |
| solns were analyzed in a Beckmann Model 25  | ESTIMATED ERROR:                            |  |
| spectrophotometer at 281.5 nm.  | Soly: detns were made in triplicate         |  |
|   | (authors).                                  |  |
|   | Temp: ±0.2°C (authors).<br>REFERENCES:      |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |  |  |
|---|---|--|--|
| (1) Zinc, $(\underline{T}-4)$ -bis[4-amino- <u>N</u> -(2,6-dimethyl-  | FUX, UI, L., JE, FIOUAR, S.,  |  |  |
| 4-pyrimidinyl)benzenesulfonamidato- <u>N<sup>N</sup>,0</u> }  | Stanford, J. W.; Fox, P. L.   |  |  |
| (Zn(II) sulfisomidine);   | Scand. J. Plast. Reconstr. Surg. <u>1979,</u>                                     |  |  |
| $C_{24}H_{24}N_8O_4S_2Zn;$ [71261-88-6]   | 13(1), 89-94.   |  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |  |
| VARIABLES:  | PREPARED BY:  |  |  |
| One temperature: 28-30 <sup>0</sup> C   | R. Piekos   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
| Solubility of Zn(II) sulfisomidine in water at room temperature (28-30 <sup>0</sup> C) <sup>4</sup><br>is 171.0 mg% (2.758 x 10 <sup>-3</sup> mol dm <sup>-3</sup> solution, compiler ).<br><sup>a</sup> Value given by one of the authors ( S. M. ) in personal communication. |   |  |  |
| AUXILIARY   | INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |  |  |
| Satd soln of Zn(II) sulfisomidine was prepd   | The Zn(II) sulfisomidine was prepd by the   |  |  |
| in water and after 24 h aliquots from the   | authors as follows: an inorg Zn salt was  |  |  |
| clear supernatant were assayed for sulfi-   | reacted with Na salt of sulfisomidine and   |  |  |
| somidine content using the colorimetric   | the ppt was analyzed and characterized. No  |  |  |
| method of Bratton and Marshall (1). The   | details were given, however.  |  |  |
| soly was then calculated from the molecular formula.  | Purity of the materials was not specified.  |  |  |
|   | ESTIMATED ERROR:  |  |  |
|   | Nothing specified.  |  |  |
|   |   |  |  |
|   | REFERENCES:   |  |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.   |  |  |
|   | I. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 120, 537. |  |  |

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|  | DNENTS:  |                      |                      | ORIGINAL MEASUREMENTS:   |
| (1)  | Acetamide, N-[4-[[(2 midinyl)amino]sulfon  | ,6-dimet<br>v1]phenv | :hyl-4-pyri-<br>/1]- | Hekster, Ch. A.; Vree, T. B.   |
|  | (N <sup>4</sup> -acetylsulfisomid  | ine);                |                      | Antibiotics Chemother. 1982, 31,   |
|  | $C_{14}H_{16}N_{4}O_{3}S;$ [3163-31-3]   |                      |                      | 22–118.  |
|  | <ol> <li>Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ol> |                      |                      |  |
|  | Phosphoric acid, mon<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-                                | opotassi<br>01       | lum salt;            |  |
| 1  | 2 4  | 32 <b>-</b> 18-5]    | l                    | PREPARED BY:   |
|  | ABLES: pH  |                      |                      | R. Piekos  |
| EXPE   | RIMENTAL VALUES:   |                      |                      |  |
|  |  |                      |                      |  |
|  |  |                      |                      | _  |
|  |  | pН                   | Solubil              | ity at 25°C  |
|  |  | ·····                | mg/1                 | $10^4 \text{ mol dm}^{-3} \text{ a}$   |
|  |  | 5.5                  | 53                   | 1.65   |
|  |  | 7.5 <sup>b</sup>     | 128                  | 3.99   |
|  |  | <sup>a</sup> Calc    | culated by c         | ompiler.   |
|  |  | <sup>b</sup> Erra    | neous pH va          | ue of 7.0 is given in  |
|  |  |                      | article.             | , and the second s |
|  |  |                      |                      |  |
|  |  |                      |                      |  |
|  |  |                      | AUXILIAR             | Y INFORMATION  |
| METH   | OD/APPARATUS/PROCEDUR  | Е:                   |                      | SOURCE AND PURITY OF MATERIALS:  |
|  | earlier developed me   |                      |                      | Neither source nor the purity of the mate-   |
|  | sonal communication)   |                      |                      | riarb wab opcorricut   |
|  | acetylsulfisomidine were prepd in phosphate  |                      |                      |  |
| 1  | ers of pH 5.5 and 7.   |                      |                      |  |
| 1  | of the solute was measured by means of a   |                      |                      |  |
|  | Spectra Physics 3500B high-performance liq-  |                      |                      |  |
| uid chromatograph equipped with a Model 748<br>column oven and a Pye-Unicam LC-UV spectro- |  |                      |                      |  |
| 1  |  | icam LC-             | •uv spectro-         |  |
| phot   | ometric detector.  |                      |                      | ESTIMATED ERROR:<br>Soly: the detection limit of the solute by<br>HPLC was 0.5 mg/l (authors).<br>The errors in temp and pH were not specified   |
|  |  |                      |                      | REFERENCES :   |
| l  |  |                      |                      | 1. Hekster, Y. A.; Vree, T. B.;  |
| [  |  |                      |                      | Damsma, J. E.; Friesen, W. T.  |
|  |  |                      |                      | J. Anitmicrob. Chemother. 1981,  |
|  |  |                      |                      | 8, 133.  |
|  |  |                      |                      |  |

| COMPONENTS:   | EVALUATOR:   |
|---|--|
| <pre>(1) Benzenesulfonamide, 4-amino-N-(2-6-<br/>dimethoxy-4-pyrimidiny1)<br/>(sulfadimethoxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S;<br/>[122-11-2]</pre> | Anthony N. Paruta<br>Department of Pharmaceutics<br>University of Rhode Island<br>Kingston, Rhode Island, USA<br>and |
| (2) Water or  | Ryszard Piekos   |
| Aqueous HCl   | Faculty of Pharmacy, University of Gdansk<br>Gdansk, Poland 1986   |

#### CRITICAL EVALUATION:

The solubility of sulfadimethoxine in water at 310K was reported by Watari, Hanano and Kaneniwa in two different journals (1,2); the determined value of the solubility for sulfadimethoxine given as 1.49 x  $10^{-4}$  mol dm<sup>-3</sup>. Except for the source of the material all experimental conditions were identical. With the assumption that the commercial grade (1), purified by crystallization, was equivalent to the pharmacopeial grade (2), the recommended value of solubility in water at 310K is 1.49 x  $10^{-4}$  mol dm<sup>-3</sup>

The reported solubilities at 310K in 0.1 mol  $L^{-1}$  HCl solution are divergent (1,3). Watari (1) gave a value of  $0.793 \times 10^{-3}$  mol dm<sup>-3</sup> which is some four tenths of that given by Ogata et al. (3). The latter (3) value refers to commercial tablets of sulfadimethoxine which may contain water-soluble non-active components that could interfere with the analysis. Though both methods and procedures were quite similar, Watari et al. (1) used a different pore sized millipore filter and the recommended technique of withdrawal to prevent thermal shock. It would seem that both reported equilibrium data, a 3-5 day period by Watari et al. (1) and the invarient asymptope of a dissolution profile by Ogata et al. (3). While it would be difficult to ascertain a recommended value with this limited data, an approximate range of  $1-2 \times 10^{-3}$  mol dm<sup>-3</sup> in aqueous 0.1 mol L<sup>-1</sup>HCl at 310K can be given. It is instructive to note that the solubility value of the protonated compound is about 10 times greater than that of pure water. Although 1-2 x  $10^{-3}$  mol dm<sup>-3</sup> is a low level of solubility, it is 10 times greater than the solubility in the absence of a high concentration of protons.

### **REFERENCES:**

- 28(7), 2221-5.
- Watari, N.; Hanano, M.; Kaneniwa, N. Chem. Pharm. Bull. <u>1980</u>,
   Watari, N.; Kaneniwa, N.; Hanano, M. Int. J. Pharm. <u>1980</u>, 6 6(2), 155-66. (3) Ogata, H.; Shibazaki, T.; Inoue, T.; Ejima, A. Chem. Pharm. Bull. 1979, 27(6). 1281-6.

|   | ···                                       |
|---|---|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                    |
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | Yamazaki, M.; Aoki, M.; Kamada, A.;       |
| methoxy-4-pyrimidinyl)- (sulfadimeth-   | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [122-11-2] | 37-40.                                    |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
|   |   |
| VARIABLES:  | PREPARED BY:                              |
| One temperature: 30°C   | R. Piekos                                 |
| EXPERIMENTAL VALUES:  | I   |
| EXPERIMENTAL VALUES.  |   |
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| Solubility of sulfadimethoxine in wata  | er at $30^{\circ}$ C is 0.10 mmol/L       |
|   |   |
| ( $3.1 \times 10^{-2} \text{ g dm}^{-3}$ , compiler ).                              |   |
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| AUXILIARY   | INFORMATION                               |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:           |
| Sulfadimethoxine (0.5 g) was placed in an   | Nothing specified.                        |
| L-shaped tube together with 20 ml of water.   |   |
| The mixt was shaken in a thermostat until   |   |
| equilibrium was attained. The sulfadimeth-  |   |
| oxine was assayed in the supernatant spec-  |   |
| trophotometrically at 545 nm on a Beckmann  |   |
| DU spectrophotometer. The results were ta-  |   |
| ken from a calibration graph.   |   |
|   | ESTIMATED ERROR:                          |
|   | Soly: not specified.                      |
|   | Temp: ±1 <sup>0</sup> C (authors).        |
|   |   |
|   | REFERENCES:                               |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-   |  |
| methoxy-4-pyrimidiny1)-  | Watari, N.; Hanano, M.; Kaneniwa, N.<br>Chem. Pharm. Bull. <u>1980,</u> 28(7), |
| (sulfadimethoxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> 0 <sub>4</sub> S; | 2221-5.  |
| [122-11-2]   |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
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| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfadimethoxine in water  | at 37 <sup>0</sup> C is 4.63 mg/100 ml   |
| $(1.49 \times 10^{-4} \text{ mol dm}^{-3}, \text{ compiler }).$                      |  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| The earlier reported app and procedure was   | Comm sulfadimethoxine was recrystd from  |
| employed (1): an excess of sulfadimethoxine,   |  |
| required to saturate the medium, was placed  | sieve shaker.  |
| in a flask contg 25 ml of water. The flask   | Distd water was used.  |
| was shaken (2 strokes/s) at the amplitude  |  |
| of 3 cm in a thermostatically controlled water bath at 37±0.05°C. One-ml sample was  |  |
| removed every 6 h (total equilibration pe-   |  |
| riod was 3-5 days) using a warmed Millipore  |  |
| filter syringe with a filter pore size of  | ESTIMATED ERROR:<br>Soly: not specified.                                       |
| 0.45 $\mu$ (Millipore HAWP 01300), and the fil-                                      | Temp: ±0.05°C (authors).   |
| trate was dild with water and assayed spec-  |  |
| trophotometrically.  | REFERENCES :   |
|  | l. Kaneniwa, N.; Watari, N.  |
|  | Chem. Pharm. Bull. <u>1974,</u> 22,  |
| 1  | 1699.  |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | ORIGINAL MEASUREMENTS:<br>Watari, N.; Kaneniwa, N.; Hanano, M.  |
| methoxy-4-pyrimidinyl)-<br>(sulfadimethoxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S;<br>[122-11-2]  | Int. J. Pharm. <u>1980</u> , 6(2), 155-66.  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |
| Solubility of sulfadimethoxine in water (1.49 x $10^{-4}$ mol dm <sup>-3</sup> , compiler ).   | r at 37 <sup>0</sup> C is 4.63 mg/100 ml  |
| ſ<br>Ħ <u>ĦĦŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢŢ</u>   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>The earlier developed method was employed<br>(1), whereby an excess of sulfadimethoxine,<br>required to saturate medium, was placed in<br>a flask contg 25 ml of water. The flask was<br>stroken (2 strokes/s) at an amplitude of 3<br>cm, in a thermostatically controlled bath.<br>One-ml sample was removed every 6 h (total<br>equilibration time was 3-5 days) using a<br>warmed Millipore filter syringe with a fil-<br>ter pore size of $0.45 \mu$ (Millipore HAWP<br>01300) and the filtrate was dild with water<br>and assayed spectrophotometrically. | <pre>SOURCE AND PURITY OF MATERIALS:<br/>Sulfadimethoxine was of the Japanese Phar-<br/>macopeia grade.<br/>Distilled water was used.<br/>ESTIMATED ERROR:<br/>Soly: not specified.<br/>Temp: ±0.05<sup>o</sup>C (authors).<br/>REFERENCES:<br/>1. Kaneniwa, N.; Watari, N.<br/>Chem. Pharm. Bull. <u>1974</u>, 22, 1699.</pre> |

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|---|---|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-                           | ORIGINAL MEASUREMENTS:                  |
| methoxy-4-pyrimidinyl)- (sulfadimeth-   | Ogata, H.; Shibazaki, T.;               |
| oxime); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [122-11-2] | Inoue, T.; Ejima, A.                    |
| (2) Hydrochloric acid; HC1; [7647-01-0]   | Chem. Pharm. Bull. <u>1979</u> , 27(6), |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  | 1281-6.                                 |
|   |   |
| VARIABLES:  | PREPARED BY:                            |
| One temperature: 37 <sup>0</sup> C  | R. Piekos                               |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sulfadimethoxine in 0.1   | N HC1 at 37°C is 0.606 mg/ml            |
| $(1.95 \times 10^{-3} \text{ mol dm}^{-3}, \text{ compiler}).$                      |   |
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| AUXILIARY   | INFORMATION                             |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:         |
| A centrifuge tube contg 30 ml of 0.1N HCl   | Comm available 250-mg uncoated tablets  |
| and 0.5-3.0 g of the sulfadimethoxine powder  | of sulfadimethoxine were used.          |
| was tightly sealed and shaken at 37 <sup>0</sup> C. The                             | Hydrochloric acid was of reagent grade. |
| concn of the dissolved drug was detd spectro  |   |
| photometrically following filtration through  | 1                                       |
| a Millipore filter (type EH, pore size 0.5  |   |
| $\mu$ m ), and the procedure was repeated until                                     |   |
| a const concn was obtained.   |   |
| contin was obtained.  | ESTIMATED ERROR:                        |
|   |   |
|   | Nothing specified.                      |
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|   | REFERENCES :                            |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | ORIGINAL MEASUREMENTS:   |
| <pre>methoxy-4-pyrimidiny1)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S; [122-11-2]</pre> | Watari, N.; Hanano, M.; Kaneniwa, N.;  |
| (2) Hydrochloric acid; HCl; [7647-01-0]  | Chem. Pharm. Bull. <u>1980</u> , 28(7),<br>2221-5.                                   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
|  |  |
| VARIABLES:   | PREPARED BY:   |
| One temperature: 37 <sup>0</sup> C   | R. Piekos  |
| EXPERIMENTAL VALUES:   | ·  |
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| Solubility of sulfadimethoxine in 0.1N   | HCl solution at 37°C is 24.6   |
| $mg/100 m1$ (7.93 x $10^{-4} mol dm^{-3} - co$   | mpiler ).  |
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| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| The earlier reported app and procedure was<br>employed (1): an excess of sulfadimethoxine,                                       | Comm sulfadimethoxine was recrystd from<br>EtOAc and sieved through a Ro-Tap testing |
| required to saturate the medium, was placed  | sieve shaker.  |
| in a flask contg 25 ml of 0.1N HCl soln.   | Source and purity of the 0.1N HCl soln were  |
| The flask was shaken (2 strokes/s) at the  | not specified.   |
| amplitude of 3 cm in a thermostatically con-   |  |
| trolled water bath at 37±0.05°C. One-ml  |  |
| sample was removed every 6 h (total equili-  |  |
| bration period was 3-5 days) using a warmed<br>Millipore filter syringe with a filter pore                                       | ESTIMATED ERROR:<br>Soly: not specified.   |
| size of 0.45 $\mu$ (Millipore HAWP 01300), and   | Temp: $\pm 0.05^{\circ}C$ (authors).   |
| the filtrate was dild with water and assayed   | -  |
| spectrophotometrically.  | REFERENCES:  |
|  | l. Kaneniwa, N.; Watari, N.  |
|  | Chem. Pharm. Bull. <u>1974,</u> 22, 1699.  |
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| NENTS:              |          |
|---------------------|----------|
| Benzenesulfonamide. | 4-amino- |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                 |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-   |  |
| <pre>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2]</pre> | Riess, W.                              |
| (2) Phosphoric acid, disodium salt;  | Intern. Congr. Chemotherapy, Proc.     |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | 3rd, Stuttgart <u>1963,</u> 1, 627-32. |
| (3) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                           |
| VARIABLES:   | R. Piekos                              |
| One temperature: 20°C; one pH 7.4  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of sulfadimethoxine in a M/1  | 5 Sörensen buffer solution (pH 7.4)    |
| at $20^{\circ}$ C is 28 mg% ( 9.0 x $10^{-4}$ mol dm <sup></sup>   | 3  colution constlar )                 |
|  | solution, compiler ).                  |
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| AUXILIARY  | INFORMATION                            |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:        |
| SUrensen buffer solns of pH varying between  | Nothing specified.                     |
| 7 and 8 were prepd, satd with sulfadimeth-   |  |
| oxine at 20°C, their pH was measured at equi-  |  |
| librium, and the sulfadimethoxine was assay-   |  |
| ed colorimetrically. The measured pH values  |  |
| were plotted against concn, and the soly at  | $\sim$                                 |
| pH 7.4 was detd by interpolation (personal   |  |
| communication).  |  |
|  | ESTIMATED ERROR:                       |
|  | Nothing specified.                     |
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|  | REFERENCES :                           |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:  |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2]</li> </ol> | Yamazaki, M.; Aoki, M.; Kamada, A.;<br>Yata, N. <i>Yakuzaigaku</i> 1967, 27(1), |
| (2) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | 37-40.  |
| <ul> <li>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>2</sub>; [7778-77-0]</li> </ul>   |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:  |
| VARIABLES:   | R. Piekos   |
| One temperature: 30 <sup>o</sup> C; one pH: 7.4  |   |
| EXPERIMENTAL VALUES:   |   |
| . Solubility of sulfadimethoxine in a ph ( $\mu$ = 0.17 ) at 30°C is 1.73 mmol/L (   |   |
| AUXILIARY  | INFORMATION   |
|  | SOURCE AND PURITY OF MATERIALS:   |
| METHOD/APPARATUS/PROCEDURE:  |   |
| Sulfadimethoxine (0.5 g) was placed in an L<br>shaped tube together with 20 ml of the buf-   |   |
| fer soln. The mixt was shaken in a thermo-   |   |
| stat until equilibrium was attained. The   |   |
| sulfadimethoxine was assayed in the superna  | _   |
| tant spectrophotometrically at 545 nm on a   |   |
|  |   |
| Beckmann DU spectrophotometer. The results   | {   |
| were taken from a calibration graph.   | ESTIMATED ERROR:  |
| 1  | Soly and pH: not specified.   |
|  | Temp: ±1°C (authors).   |
| }  | +cmp+ o (authoro).  |
|  | REFERENCES :  |
| }  |   |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-a                               |                             | ORIGINAL MEASUREMENTS:                             |
|--|-----------------------------|--|
| methoxy-4-pyrimidinyl)-  | - (sulfadimeth-             | Mauger, J. W.; Paruta, A. N.;                      |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; | [122-11-2]                  | Gerraughty, R. J. J. Pharm. Sci.                   |
| (2) Methanol; CH <sub>4</sub> 0; [67                                     | 7-56-1]                     | <u>1972,</u> 61(1),                                |
| -  |                             |  |
|  |                             |  |
| VARIABLES:   |                             | PREPARED BY:                                       |
| Temperature  |                             | R. Piekos  |
|  |                             |  |
| EXPERIMENTAL VALUES:   |                             |  |
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| -  | t/ <sup>0</sup> C Mole frac | tion solubility (x 10 <sup>4</sup> )               |
|  | 25                          | 11.6   |
|  | 30                          | 13.9   |
|  | 37                          | 17.7   |
|  | 57                          | 1/./   |
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|  | AUXILIARY                   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  |                             | SOURCE AND PURITY OF MATERIALS:                    |
| A const temp bath contg scre   | w-capped bottles            | Sulfadimethoxine: lot 203057, Hoffmann-            |
| with sulfadimethoxine and me   | thanol was rota-            | La Roche, Inc.                                     |
| ted for 24 h. Samples were   | withdrawn through           | Methanol: spectrophotometric grade solvent,        |
| a pledget of glass wool into   | a pipet, which              | Mallinckrodt Chem Works.                           |
| was wiped clean and allowed  | to drain into a             |  |
| volumetric flask. Solute co  | oncns were detd             |  |
| by spectrophotometric assay  | at predetd wave-            |  |
| lengths using a Cary model 1   |                             |  |
| ter (1).   |                             | ESTIMATED ERROR:                                   |
|  |                             | Soly: av values of 3 detns are given<br>(authors). |
|  |                             | Temp: ±0.1 <sup>0</sup> C (authors).               |
|  |                             | REFERENCES:  |
|  |                             | 1. Paruta, A. N.; Mauger, J. W.                    |
|  |                             | J. Pharm. Sci. <u>1971</u> , 60, 432.              |
|  |                             |  |
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| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S; [122-11-2]<br/>(2) Methanol; CH<sub>4</sub>0; [67-56-1]</pre> | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Fharm. <u>1977,</u> 3(2),<br>163-83. |
|--|---|
| VARIABLES:   | PREPARED BY:  |
| Temperature  | R. Piekos   |

EXPERIMENTAL VALUES:

| . 100             |       | Solubility                     |  |
|-------------------|-------|--------------------------------|--|
| t/ <sup>0</sup> C | mg/ml | 10 <sup>3</sup> x <sup>a</sup> | 10 <sup>2</sup> mol dm <sup>-3 b</sup> |
| 25                | 8.84  | 1.16                           | 2.85                                   |
| 30                | 10.5  | 1.39                           | 3.38                                   |
| 37                | 13.4  | 1.77                           | 4.32                                   |

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<sup>a</sup> X = mole fraction

<sup>b</sup> Calculated by compiler.

| AUXILIARY   | INFORMATION  |
|---|--|
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfadimethoxine in excess and methanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into a<br>pipet, which was wiped clean and allowed to<br>drain into a volumetric flask. Soly was<br>detd from absorbance and previously ascer-<br>tained Beer's law plots detd on a Cary model | La Roche, Inc. Its mp agreed with the<br>literature value. Methanol was a spectro-   |
| 16 spectrophotometer (1).   | <pre>ESTIMATED ERROR:<br/>Soly: av of at least 3 detns is reported<br/>(authors).<br/>Temp: ±0.1<sup>o</sup>C (authors).<br/>REFERENCES:<br/>1. Mauger, J. W.; Paruta, A. N.;<br/>Gerraughty, R. J. J. Pharm. Sci.<br/><u>1972,</u> 61(1), 94.</pre> |

| 201/D01/D1/D2  |                            |  |
|--|----------------------------|--|
| COMPONENTS:<br>(1) Benzenesulfonamide, 4-                                | amino-N-(2.6-              | ORIGINAL MEASUREMENTS:   |
| dimethoxy-4-pyrimidiny   |                            | Mauger, J. W.; Paruta, A. N.;  |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; |                            | Gerraughty, R. J. J. Pharm. Sci.   |
|  |                            | 1972, 61(1), 94-7.   |
| (2) Ethanol; C <sub>2</sub> H <sub>6</sub> O; [6                         | 4-17-5]                    |  |
|  |                            |  |
| VARIABLES:   |                            | PREPARED BY:   |
| Temperature  |                            | R. Piekos  |
|  |                            |  |
| EXPERIMENTAL VALUES:   |                            |  |
|  |                            |  |
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|  |                            |  |
|  | t/ <sup>0</sup> C Mole fra | ction solubility (x 10 <sup>4</sup> )  |
|  |                            |  |
|  | 25                         | 7.14   |
|  | 30                         | 8.58   |
|  | 37                         | 11.00  |
| _  |                            |  |
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|  |                            | INFORMATION  |
|  |                            |  |
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg scr               | ew-capped bottles          | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann - La |
| with sulfadimethoxine in ex  | ••                         | Roche, Inc.  |
| was rotated for 24 h. Samp   |                            | Ethanol ( purity not specified) was from                                       |
| drawn through a pledget of   |                            |  |
| pipet, which was wiped clea  | -                          | order industrial onemptais out   |
| drain into a volumetric fla  |                            |  |
| cns were detd by spectropho  |                            |  |
| predetd wavelengths using a  |                            |  |
| spectrophotometer (1).   | cary moder to              |  |
| spectrophotometer (1).   |                            | ESTIMATED ERROR:<br>Soly: av values of 3 detns are given                       |
|  |                            | (authors).   |
|  |                            | Temp: ±0.1 <sup>0</sup> C (authors).   |
|  |                            | REFERENCES :   |
|  |                            |  |
|  |                            | 1. Paruta, A. N.; Mauger, J. W.  |
|  |                            | J. Pharm. Sci. <u>1971,</u> 60, 432.   |
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|---|-------------------|------------------------|--|--|---|--|
| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S; [122-11-2] (2) Ethanol; C<sub>2</sub>H<sub>6</sub>0; [64-17-5] VARIABLES:</pre>  |                   |                        | 5-d1-<br>neth-   | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977</u> , 3(2),<br>163-83.<br>PREPARED BY:   |   |  |
| Temperatu   | ire               |                        |  | R. Piekos  |   |  |
|   |                   |                        |  |  |   |  |
| EXPERIMENTAL VALUES   | •                 |                        |  |  |   |  |
|   | t/ <sup>o</sup> C |                        | Solubili   |  |   |  |
|   | . <u></u>         | mg/ml                  | 10 <sup>4</sup> x  | <sup>a</sup> 10 <sup>2</sup> mol dm <sup>-3 b</sup>  |   |  |
|   | 25                | 3.78                   | 7.14   | 1.22   |   |  |
|   | 30                | 4.52                   | 8.58   | 1.46   |   |  |
|   | 37                | 5.74                   | 11.00  | 1.85   |   |  |
|   | a                 | X = mole<br>Calculated |  | ler.   |   |  |
|   |                   | AUX                    | ILIARY INF   | ORMATION   |   |  |
| METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfadimethoxine in excess and ethanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into a<br>pipet, which was wiped clean and allowed to<br>drain into a volumetric flask. Soly was<br>detd from absorbance and previously ascer-<br>tained Beer's law plots detd on a Cary model<br>16 spectrophotometer (1). |                   |                        | oottles S<br>chanol L<br>Lth- a<br>into a I<br>ved to i<br>vas a<br>scer-<br>7 model<br>ES | URCE AND PURITY OF MAT<br>ulfadimethoxine: lot 2<br>a Roche, Inc. Its mp<br>ture value. Ethanol<br>ndustrial Chemicals Co<br>ndex value and density<br>ture values.<br>TIMATED ERROR:<br>Soly: av of at least<br>(authors).<br>Femp: ±0.1 <sup>o</sup> C (autho<br>FERENCES: | 03027, Hoffmann<br>agreed with the liter<br>was from the U. S.<br>. Its refractive<br>agreed with liter-<br>3 detns is reported |  |

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|   |                                       | 1   |       |
|---|---------------------------------------|---|-------|
| COMPONENTS:   |                                       | ORIGINAL MEASUREMENTS:                              |       |
| (1) Benzenesulfonamide,   |                                       | Mauger, J. W.; Paruta, A. N.;                       |       |
| methoxy-4-pyrimidiny  |                                       | Gerraughty, R. J. J. Pharm. Sci                     | •     |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S | ; [122-11-2]                          | 1972, 61(1), 94-7.                                  |       |
| (2) 1-Propanol; C <sub>3</sub> H <sub>8</sub> 0;                        | [71-23-8]                             |   |       |
| VARIABLES:  |                                       | PREPARED BY:  |       |
| Temperature   |                                       | R. Piekos   |       |
|   | · · · · · · · · · · · · · · · · · · · |   |       |
| EXPERIMENTAL VALUES:  |                                       |   |       |
|   |                                       |   |       |
|   |                                       |   |       |
|   |                                       |   |       |
|   |                                       |   |       |
|   | t/ <sup>0</sup> C Mole fra            | ction solubility (x 10 <sup>4</sup> )               |       |
|   | 25                                    | 4.71  |       |
|   | 30                                    | 5.63  |       |
|   | 37                                    | 7.79  |       |
|   | . <u></u>                             |   |       |
|   |                                       |   |       |
|   |                                       |   |       |
|   |                                       |   |       |
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|   |                                       |   |       |
| · · · · · · · · · · · · · · · · · · ·                                   | AUXILIARY                             | INFORMATION   |       |
| METHOD/APPARATUS/PROCEDUR   | E:                                    | SOURCE AND PURITY OF MATERIALS:                     |       |
| A const temp bath contg   | screw-capped bottles                  | Sulfadimethoxine: lot 203057, Hoffm                 | ann - |
| with sulfadimethoxine in  | excess and 1-propa-                   | La Roche, Inc.                                      |       |
| nol was rotated for 24 h  | . Samples were with                   | - 1-Propanol: Baker Analyzed Reagent,               | J. T. |
| drawn through a pledget   | of glass wool into a                  | Baker Chemical Co.                                  |       |
| pipet, which was wiped c  | lean and allowed to                   |   |       |
| drain into a volumetric   | flask. Solute                         |   |       |
| concns were detd by spec  | trophotometric assay                  |   |       |
| at predetd wavelengths u  | sing a Cary model 16                  |   |       |
| spectrophotometer (1).  |                                       | ESTIMATED ERROR:                                    |       |
|   |                                       | Soly: av values of 3 detns are give                 | n     |
|   |                                       | (authors).  |       |
|   |                                       | Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES: |       |
|   |                                       |   |       |
|   |                                       | 1. Paruta, A. N.; Mauger, J. W.                     |       |
|   |                                       | J. Pharm. Sci. <u>1971,</u> 60,                     | 432.  |
|   |                                       |   |       |
|   |                                       |   |       |
|   |                                       |   |       |

|  |  |                   |                        |   | 4   |
|--|--|-------------------|------------------------|---|---|
| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2]<br/>(2) 1-Propanol; C<sub>3</sub>H<sub>8</sub>O; [71-23-8]</pre> |  |                   | )- (sulfad<br>[122-11- | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),<br>163-83. |   |
|  | • • • •                                      | 30,               |                        |   |   |
| VARIA  | BLES:  |                   |                        |   | PREPARED BY:  |
|  | Temperatu                                    | ure               |                        |   | R. Piekos   |
| EXPERI   | IMENTAL VALUES                               | 5:                |                        |   | L.,   |
|  |  |                   |                        |   |   |
|  |  | <b>10</b> -       |                        | Solu  | bility  |
|  |  | t/ <sup>0</sup> C | mg/m1                  | 10 <sup>4</sup> x   | a $10^2 \text{ mol } dm^{-3} b$   |
|  |  | 25                | 1.95                   | 4.71  | 0.63  |
|  |  | 30                | 2.32                   | 5.63  | 0.75  |
|  |  | 37                | 3.20                   | 7.79  | 1.03  |
|  |  | a                 | X = mole               | fraction  | n   |
|  |  |                   | Calculated             |   |   |
|  |  |                   |                        |   |   |
|  |  |                   | A                      | JXILIARY  | INFORMATION   |
|  | D/APPARATUS/Pinst temp bath                  |                   |                        | bottles   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203027 Hoffmann- |
| with   | sulfadimethor                                | xine in e         | xcess and              | 1-propa-  | La Roche, Inc. Its mp agreed with the                                     |
|  | was rotated fo                               |                   | -                      |   |   |
|  | n through a pi                               | -                 | -                      |   | Analyzed Reagent ( J. T. Baker Chemical Co                                |
|  | pet, which was<br>rain into a vo             |                   |                        |   | Its refractive index value and density agreed with literature values.     |
|  | from absorba                                 |                   |                        | -   |   |
| tain   | tained Beer's law plots detd on a Cary model |                   |                        |   |   |
| 16 sı  | pectrophotome                                | ter (1).          |                        |   | ESTIMATED ERROR:  |
|  |  |                   |                        |   | Soly: av of at least 3 detns is reported                                  |
|  |  |                   |                        |   | (authors).<br>Temp: ±0.1 <sup>0</sup> C (authors).                        |
|  |  |                   |                        |   | REFERENCES:   |
|  |  |                   |                        |   | 1. Mauger, J. W.; Paruta, A. N.   |
|  |  |                   |                        |   | Gerraughty, R. J. J. Pharm. Sci.  |
|  |  |                   |                        |   | <u>1972,</u> 61(1), 94.   |
|  |  |                   |                        |   | l   |

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|  | NENTS:  |  | ORIGINAL MEASUREMENTS:  |  |  |
|--|---|--|---|--|--|
| (1)  | (1) Benzenesulfonamide, 4-amino-N-(2,6-di-  |  | Mauger, J. W.; Paruta, A. N.;   |  |  |
|  | methoxy-4-pyrimidi  | nyl)- (sulfadimeth-  | Gerraughty, R. J. J. Pharm. Sci.  |  |  |
|  | oxine); $C_{12}H_{14}N_{4}O$  | 4 <b>S; [122-11-2]</b>   | <u>1972,</u> 61(1), 94-7.   |  |  |
| (2) 1-Butanol; C <sub>4</sub> H <sub>10</sub> 0; [71-36-3] |   | 0; [71-36-3]   |   |  |  |
| VARIA  | ABLES:  |  | PREPARED BY:  |  |  |
|  | Temperatu   | re   | R. Piekos   |  |  |
| EXPER  | RIMENTAL VALUES:  |  | I   |  |  |
|  |   |  |   |  |  |
|  |   |  |   |  |  |
|  |   | t/ <sup>0</sup> C Mole fract   | ion solubility (x 10 <sup>4</sup> )   |  |  |
|  |   | 25   | 3.89  |  |  |
|  |   | 30   | 5.26  |  |  |
|  |   | 37   | 6.70  |  |  |
|  |   | <u></u>  |   |  |  |
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|  |   |  |   |  |  |
|  |   |  | INFORMATION   |  |  |
|  | OD/APPARATUS/PROCEDU<br>onst temp bath contg  |  | SOURCE AND PURITY OF MATERIALS:   |  |  |
| A co<br>with   | onst temp bath contg<br>h sulfadimethoxine i  | RE:<br>; screw-capped bottle:<br>.n excess and 1-buta-   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.   |  |  |
| A co<br>with<br>nol  | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24  | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>drav                                | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget  | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe                        | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped   | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>drat                | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric   | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-                        | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns         | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr                        | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-                        | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr                        | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>S<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).  |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:                                    |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1 <sup>0</sup> C (authors).   |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W. |  |  |
| A co<br>with<br>nol<br>draw<br>pipe<br>dram<br>cns<br>at p | onst temp bath contg<br>h sulfadimethoxine i<br>was rotated for 24<br>wn through a pledget<br>et, which was wiped<br>in into a volumetric<br>were detd by spectr<br>predetd wavelengths | RE:<br>screw-capped bottles<br>n excess and 1-buta-<br>h. Samples were with<br>of glass wool into a<br>clean and allowed to<br>flask. Solute con-<br>cophotometric assay | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffma<br>La Roche, Inc.<br>1-Butanol was from Mallinckrodt Chem W<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).<br>REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W. |  |  |

| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2] (2) 1-Butanol; C<sub>4</sub>H<sub>10</sub>O; [71-36-3]</pre> | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),<br>163-83. |
|--|---|
| VARIABLES:<br>Temperature  | PREPARED BY:<br>R. Piekos   |
| EXPERIMENTAL VALUES:   | <b>.</b>  |

| t/ <sup>o</sup> C | Solubility |                                |  |  |  |
|-------------------|------------|--------------------------------|--|--|--|
| L/ U              | mg/ml      | 10 <sup>4</sup> x <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3 b</sup> |  |  |
| 25                | 1.31       | 3.89                           | 4.22                                   |  |  |
| 30                | 1.77       | 5.26                           | 5.70                                   |  |  |
| 37                | 2.25       | 6.70                           | 7.25                                   |  |  |

 $a_{X}$  = mole fraction

<sup>b</sup> Calculated by compiler

# AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:                              |
|--|--|
| A const temp bath contg screw-capped bottles | Sulfadimethoxine: lot 203027, Hoffmann-                      |
| with sulfadimethoxine in excess and 1-buta-  | La Roche Inc. Its mp agreed with the li-                     |
| nol was rotated for 24 h. Samples were       | terature value. 1-Butanol was from the                       |
| withdrawn through a pledget of glass wool    | Mallinckrodt Chemical Works. Its refract-                    |
| into a pipet, which was wiped clean and      | ive index value and density agreed with                      |
| allowed to drain into a volumetric flask.    | literature values.   |
| Soly was detd from absorbance and previously |  |
| ascertained Beer's law plots detd on a Cary  |  |
| model 16 spectrophotometer (1).              | ESTIMATED ERROR:<br>Soly: av of at least 3 detns is reported |
|  | (authors).   |
|  | Temp: ±0.1 <sup>0</sup> C (authors).                         |
|  | REFERENCES:  |
|  | 1. Mauger, J. W.; Paruta, A. N.;                             |
|  | Gerraughty, R. J. J. Pharm. Sci.                             |
|  | <u>1972,</u> 61(1), 94.                                      |
|  |  |
|  |  |

| COMPONENTS:  |  | ORIGINAL MEASUREMENTS:  |
|--|--|---|
| (1) Benzenesulfonamide,  |  | Mauger, J. W.; Paruta, A. N.;   |
| methoxy-4-pyrimidiny   |  | Gerraughty, R. J. J. Pharm. Sci.  |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub>  | s; [122-11-2]  | <u>1972,</u> 61(1), 94-7.   |
| (2) 1-Pentanol; C <sub>5</sub> H <sub>12</sub> 0; [71-41-0]  |  |   |
| VARIABLES:   | <u></u>  | PREPARED BY:  |
| Temperature  |  | R. Piekos   |
| EXPERIMENTAL VALUES:   |  |   |
|  |  |   |
|  |  |   |
|  |  |   |
|  | t/ <sup>0</sup> C Mole fract   | ion solubility ( x 10 <sup>4</sup> )  |
|  | 25   | 3.41  |
|  | 30   | 4.41  |
|  | 37   | 5.65  |
| -  |  |   |
|  |  |   |
|  |  |   |
|  |  |   |
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|  |  |   |
|  |  |   |
|  | AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDU   |  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS;  |
| METHOD/APPARATUS/PROCEDUM<br>A const temp bath contg   | RE:  | SOURCE AND PURITY OF MATERIALS:   |
|  | RE:<br>screw-capped bottles  | SOURCE AND PURITY OF MATERIALS:   |
| A const temp bath contg  | RE:<br>screw-capped bottles<br>n excess and 1-pen-   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-  |
| A const temp bath contg<br>with sulfadimethoxine in  | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.  |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24  | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool  | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.  |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea  | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.  |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was   | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>dget of glass wool<br>wiped clean and al-<br>plumetric flask. So-   | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.  |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo   | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>dget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric                       | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.  |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plec<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by                             | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1 <sup>o</sup> C (authors).   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | <pre>SOURCE AND PURITY OF MATERIALS:<br/>Sulfadimethoxine: lot 203057, Hoffmann-<br/>La Roche, Inc.<br/>1-Pentanol was from Fisher Scientific Co.<br/>ESTIMATED ERROR:<br/>Soly: av values of 3 detns are given<br/>(authors).<br/>Temp: ±0.1<sup>o</sup>C (authors).<br/>REFERENCES:<br/>1. Paruta, A. N.; Mauger, J. W.</pre> |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203057, Hoffmann-<br>La Roche, Inc.<br>1-Pentanol was from Fisher Scientific Co.<br>ESTIMATED ERROR:<br>Soly: av values of 3 detns are given<br>(authors).<br>Temp: ±0.1°C (authors).<br>REFERENCES:   |
| A const temp bath contg<br>with sulfadimethoxine in<br>tanol was rotated for 24<br>withdrawn through a plea<br>into a pipet, which was<br>lowed to drain into a vo<br>lute concns were detd by<br>assay at predetd waveler | RE:<br>screw-capped bottles<br>n excess and 1-pen-<br>h. Samples were<br>lget of glass wool<br>wiped clean and al-<br>plumetric flask. So-<br>y spectrophotometric<br>ngths using a Cary | <pre>SOURCE AND PURITY OF MATERIALS:<br/>Sulfadimethoxine: lot 203057, Hoffmann-<br/>La Roche, Inc.<br/>1-Pentanol was from Fisher Scientific Co.<br/>ESTIMATED ERROR:<br/>Soly: av values of 3 detns are given<br/>(authors).<br/>Temp: ±0.1<sup>o</sup>C (authors).<br/>REFERENCES:<br/>1. Paruta, A. N.; Mauger, J. W.</pre> |

|   | ORIGINAL MEASUREMENTS:   |
|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-methoxy-4-pyrimidinyl)- (sulfadimeth-oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S; [122-11-2]</li> <li>1-Pentanol; C<sub>5</sub>H<sub>12</sub>0; [71-41-0]</li> </ol> | Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977</u> 3(2),<br>163-83. |
| VARIABLES:  | PREPARED BY:   |
| Temperature   | R. Piekos  |

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EXPERIMENTAL VALUES:

| t/°C |       | Solubilit                      | 9                             |
|------|-------|--------------------------------|-------------------------------|
| t/ C | mg/ml | 10 <sup>4</sup> x <sup>a</sup> | $10^3 \text{ mol } dm^{-3} b$ |
| 25   | 0.98  | 3.41                           | 3.16                          |
| 30   | 1.26  | 4.41                           | 4.06                          |
| 37   | 1.60  | 5.65                           | 5.16                          |

 $a_{X}$  = mole fraction

<sup>b</sup> Calculated by compiler

# AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:            |
|--|--|
| A const temp bath contg screw-capped bottles | Sulfadimethoxine: lot 203027, Hoffmann-    |
| with sulfadimethoxine in excess and 1-penta- | La Roche, Inc. Its mp agreed with the li-  |
| nol was rotated for 24 h. Samples were with  | terature value. 1-Pentanol was from Fisher |
| drawn through a pledget of glass wool into a | Scientific Co. Its refractive index value  |
| pipet, which was wiped clean and allowed to  | and density agreed with literature values. |
| drain into a volumetric flask. Soly was      |  |
| detd from absorbance and previously ascer-   |  |
| tained Beer's law plots detd on a Cary model |  |
| 16 spectrophotometer (1).                    | ESTIMATED ERROR:                           |
|  | Soly: av of at least 3 detns is reported   |
|  | (authors).                                 |
|  | Temp: ±0.1 <sup>0</sup> C (authors).       |
|  | REFERENCES:                                |
|  | 1. Mauger, J. W.; Paruta, A. N.;           |
|  | Gerraughty, R. J. J. Pharm. Sci.           |
|  | <u>1972</u> , <i>61(1)</i> , 94.           |
|  |  |
|  |  |

| +22  |  |                               |  |
|--|--|-------------------------------|--|
|  |  | 1 and n = 11 (0 ( 11          | ORIGINAL MEASUREMENTS:   |
| (1)  | (1) Benzenesulfonamide, 4-amino-N-(2,6-di-   |                               | Mauger, J. W.; Paruta, A. N.;  |
|  | methoxy-4-pyrimidinyl)- (sulfadimeth-<br>oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [122-11-2] |                               | Gerraughty, R. J. J. Pharm. Sci.   |
|  |  |                               | <u>1972</u> , <i>61(1)</i> , 94-7.                                       |
| (2) 1-Octanol; C <sub>8</sub> H <sub>18</sub> 0; [111-87-5]                  |  | 30; [111-87-5]                |  |
| VARIABLES:   |  |                               | PREPARED BY:   |
|  | Temperature  |                               | R. Piekos  |
|  |  |                               |  |
| EXPE   | RIMENTAL VALUES:   |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  | t/ <sup>0</sup> C Mole fracti | con solubility ( x 10 <sup>4</sup> )                                     |
|  |  | 25                            | 2.04   |
|  |  |                               |  |
|  |  | 30                            | 2.78   |
|  | 37 3   |                               | 3.59   |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |
| 10000  |  |                               |  |
|  | HOD/APPARATUS/PROCEI   |                               | SOURCE AND PURITY OF MATERIALS:  |
|  | •  | tg screw-capped bottles       |  |
| with sulfadimethoxine in excess and 1-octa-                                  |  |                               |  |
|  |  | 4 h. Samples were with        |  |
| drawn through a pledget of glass wool into a                                 |  | -                             |  |
| pipet, which was wiped clean and allowed to                                  |  |                               |  |
| drain into a volumetric flask. Solute  |  |                               |  |
| concns were detd by spectrophotometric                                       |  |                               |  |
| assay at predetd wavelengths using a Cary<br>model 16 spectrophotometer (1). |  |                               | ESTIMATED ERROR:   |
|  |  | meter (1).                    | Soly: av of 3 detns are given (authors).                                 |
|  |  |                               | Temp: ±0.1°C (authors).  |
|  |  |                               |  |
|  |  |                               | REFERENCES:<br>1. Paruta, A. N.; Mauger, J. W.                           |
| l  |  | /                             | 1. Paruta, A. N.; Mauger, J. W.<br>J. Pharm. Sci. <u>1971</u> , 60, 432. |
|  |  |                               | $0. \ F(41)(1. \ 300. \ 19/1, \ 00, \ 432.$                              |
|  |  |                               |  |
|  |  |                               |  |
|  |  |                               |  |

| <ul> <li>COMPONENTS:         <ul> <li>Benzenesulfonamide, 4-amino-N-(2,6-di-methoxy-4-pyrimidinyl)- (sulfadimethoxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>0<sub>4</sub>S; [122-11-2]</li> <li>1-Octanol; C<sub>8</sub>H<sub>18</sub>0; [111-87-5]</li> </ul> </li> </ul> | ORIGINAL MEASUREMENTS:<br>Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977</u> , 3(2),<br>163-83. |
|---|--|
| VARIABLES:<br>Temperature   | PREPARED BY:<br>R. Piekos  |
| EXPERIMENTAL VALUES:  | l  |

| t/ <sup>o</sup> C | Solubility |                                |  |  |  |
|-------------------|------------|--------------------------------|--|--|--|
|                   | mg/ml      | 10 <sup>4</sup> x <sup>a</sup> | 10 <sup>3</sup> mol dm <sup>-3</sup> b |  |  |
| 25                | 0.40       | 2.04                           | 1.29                                   |  |  |
| 30                | 0.54       | 2.78                           | 1.74                                   |  |  |
| 37                | 0.70       | 3.59                           | 2.26                                   |  |  |

 $a_X = mole fraction$ 

<sup>b</sup> Calculated by compiler

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                  | SOURCE AND PURITY OF MATERIALS:  |
|--|--|
| A const temp bath contg screw-capped bottles | Sulfadimethoxine: lot 203027; Hoffmann-                                    |
| with sulfadimethoxine in excess and 1-octa-  | La Roche, Inc. Its mp agreed with the li-                                  |
| nol was rotated for 24 h. Samples were with  | terature value. 1-Octanol was from the                                     |
| drawn through a pledget of glass wool into a | Fisher Scientific Co. Its refractive index                                 |
| pipet, which was wiped clean and allowed to  | value and density agreed with literature                                   |
| drain into a volumetric flask. Soly was      | values.  |
| detd from absorbance and previously ascer-   |  |
| tained Beer's law plots detd on a Cary model |  |
| 16 spectrophotometer (1).                    | ESTIMATED ERROR:<br>Soly: av of at least 3 detns is reported<br>(authors). |
|  | Temp: $\pm 0.1^{\circ}C$ (authors).  |
|  | REFERENCES:  |
|  | 1. Mauger, J. W.; Paruta, A. N.;   |
|  | Gerraughty, R. J. J. Pharm. Sci.   |
|  | <u>1972,</u> 61(1), 94.  |
|  |  |
|  |  |

| 767 | 4 | 2 | 4 |
|-----|---|---|---|
|-----|---|---|---|

| COMPONENTS :   | · · ·          |           |   | ORTGINAL MEASUREMENTS .   |  |
|--|----------------|-----------|---|---|--|
| <pre>COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-di-<br/>methoxy-4-pyrimidinyl)- (sulfadimeth-<br/>oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2] (2) 1-Decanol; C<sub>10</sub>H<sub>22</sub>O; [112-30-1]</pre>   |                |           | adimeth-<br>L1-2]   | ORIGINAL MEASUREMENTS:<br>Mauger, J.W.; Paruta, A.N.;<br>Gerraughty, R.J. <i>J. Pharm. Sci.</i><br><u>1972,</u> 61(1), 94-7.  |  |
| VARIABLES:   |                |           |   | PREPARED BY:  |  |
| Temperatu  | re             |           |   | R. Piekos   |  |
| EXPERIMENTAL VALUES  | :              |           |   |   |  |
|  |                |           |   |   |  |
|  | t/°C           |           | Solubi  | llity   |  |
|  |                | mg/ml     | 10 <sup>4</sup> X <sup>4</sup>  | a $10^3 \text{ mol } dm^{-3} b$   |  |
|  | 25             | 0.36      | 2.24  | 1.16  |  |
|  | 30             | 0.44      | 2.69  | 1.42  |  |
|  | 37             | 0.54      | 3.37  | 1.74  |  |
|  | a x            | = mole    | fraction  |   |  |
|  | <sup>b</sup> c | alculated | by compil   | ler   |  |
|  |                |           | AUXILIARY   | INFORMATION   |  |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>A const temp bath contg screw-capped bottles<br>with sulfadimethoxine in excess and 1-decanol<br>was rotated for 24 h. Samples were with-<br>drawn through a pledget of glass wool into a<br>pipet, which was wiped clean and allowed to<br>drain into a volumetric flask. Solute concres<br>were detd by spectrophotometric assay at pre-<br>determined wavelengths using a Cary model 16<br>spectrophotometer (1). |                |           | d bottles<br>1-decano<br>with-<br>ol into a<br>lowed to<br>ute concha | SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203027, Hoffmann-<br>La Roche, Inc. M.p. agreed with the liter-<br>ature value. 1-Decanol was purchased from<br>Matheson, Coleman and Bell. Refractive in-<br>dex value and density agreed with those re-<br>ported in the literature. |  |

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| Components :  |                   |   |                   | ORIGINAL MEASUREMENTS:   |
|---|-------------------|---|-------------------|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(2,6 -di-methoxy-4-pyrimidinyl)- (sulfadimeth-oxine); C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; [122-11-2]</li> <li>1-Decanol; C<sub>10</sub>H<sub>22</sub>O; [112-30-1]</li> </ol> |                   | Mauger, J. W.; Petersen, H., Jr.;<br>Alexander, K. S.; Paruta, A. N.<br>Drug Dev. Ind. Pharm. <u>1977,</u> 3(2),<br>163-83. |                   |  |
| VARIABLES:  |                   |   |                   | PREPARED BY:   |
| Tempera   | ature             |   |                   | R. Piekos  |
| EXPERIMENTAL VAL  | LUES:             |   |                   | L  |
|   |                   |   |                   |  |
|   |                   |   |                   |  |
|   | t/ <sup>o</sup> C |   | Solubi            | ility  |
|   |                   | mg/ml   | 10 <sup>4</sup> X | $10^3 \text{ mol } \text{dm}^{-3} \text{ b}$   |
|   | 25                | 0.36  | 2.24              | 1.16   |
|   | 30                | 0.44  | 2.69              | 1.42   |
|   | 37                | 0.54  | 3.37              | 1.74   |
|   | a <sub>X</sub>    | <b>≠</b> mole f:  | raction           |  |
|   | <sup>ь</sup> с    | alucalted by  | y compil          | ler  |
|   |                   |   |                   |  |
|   |                   |   |                   |  |
|   |                   |   |                   |  |
|   |                   | AU  | KILIARY           | INFORMATION  |
| METHOD/APPARATU<br>The soly was do  |                   | <u></u>   |                   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfadimethoxine: lot 203027, Hoffma |

dimethoxine in excess and 1-decanol were rotated in a const temp bath for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Soly was detd from absorbance and previously ascertained Beer's law plots detd on a Cary model 16 spectrophotometer.

# dex value and density agreed with those reported in the literature. ESTIMATED ERROR:

terature. 1-Decanol was purchased from

Matheson, Coleman and Bell. Refractive in-

Temp: ±0.1°C (authors). Soly: not specified.

### **REFERENCES:**

1. Paruta, A. N.; Mauger, J. W.; Gerraughty, R. J. J. Pharm. Sci. <u>1972,</u> *61*, 94.

| COMPONENTS:   | ORIGINAL MEASUREMENTS:                 |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(2,6-di-  | Riess, W.                              |
| methoxy-4-pyrimidinyl)- (sulfadimeth-   | Intern. Congr. Chemotherapy, Proc.,    |
| oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [122-11-2] |  |
|   | 3rd, Stuttgart <u>1963,</u> 1, 627-32. |
| (2) Methane, trichloro- (chloroform);   |  |
| CHC1 <sub>3</sub> ; [67-66-3]   |  |
| VARIABLES:  | PREPARED BY:                           |
| One temperature: 20 <sup>0</sup> C  | R. Piekos                              |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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|   |  |
| Solubility of sulfadimethoxine in chlor   | coform at 20°C is 134 mg%              |
|   | _                                      |
| $(4.32 \times 10^{-3} \text{ mol dm}^{-3} \text{ solution, compile})$               | Ler).                                  |
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|   | INFORMATION                            |
|   |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:        |
| Nothing specified.  | Nothing specified.                     |
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|   | ESTIMATED ERROR:                       |
|   |  |
|   | Nothing specified.                     |
|   |  |
|   | REFERENCES:                            |
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|      | ONENTS:   | ORIGINAL MEASUREMENTS:                    |
|------|---|---|
| (1)  | Benzenesulfonamide, 4-amino-N-(2,6-di-  | Yamazaki, M.; Aoki, M; Kamada, A.;        |
|      | methoxy-4-pyrimidinyl)- (sulfadimeth-   | Yata, N. Yakuzaigaku <u>1967</u> , 27(1), |
|      | oxine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S; [122-11-2] | 37-40.                                    |
| (2)  | Methane, trichloro- (chloroform);   |   |
|      | CHC1 <sub>3</sub> ; [67-66-3]   |   |
| VARI | ABLES :   | PREPARED BY:                              |
|      | One temperature: 30 <sup>0</sup> C  | R. Piekos                                 |
|      |   |   |
| EXPE | RIMENTAL VALUES:  |   |
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|      |   |   |
|      | Solubility of sulfadimethoxine in chloro  | form at $30^{\circ}$ C is 7.30 mmo1/t     |
|      |   |   |
|      | $(2.26 \text{ g dm}^{-3}, \text{ compiler }).$                                      |   |
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|      | AUXILIARY   | INFORMATION                               |
|      | HOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:           |
|      | fadimethoxine (0.5 g) was placed in an L-   | Nothing specified                         |
| sha  | ped tube together with 20 ml of chloro-   |   |
| for  | m. The mixt was shaken in a thermostat  |   |
| unt  | il equilibrium was attained. The sulfa-   |   |
| dím  | ethoxine was assayed in the supernatant   |   |
| spe  | ctrophotometrically at 545 nm on a Beck-  |   |
| man  | n DU spectrophotometer. The results were  |   |
| tak  | en from a calibration graph.  |   |
|      |   | ESTIMATED ERROR:                          |
|      |   | Soly: not specified.                      |
|      |   | Temp: ±1°C (authors).                     |
|      |   |   |
|      |   | REFERENCES :                              |
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|   | ORIGINAL MEASUREMENTS:  |
|---|---|
| COMPONENTS:<br>(1) Copper, bis[4-amino- <u>N</u> -(2,6-dimethoxy-4-                           |   |
| pyrimidinyl)benzenesulfonamidato]-,   | Tskitishvili, M. G.; Mikadze, I. I.                                   |
| hydrate; $C_{24}H_{26}CuN_80_8S_2 \cdot nH_20;$   | Soobshch. Akad. Nauk Gruz. SSR  |
| [86729-19-3]  | <u>1978,</u> 89(3), 589-92.   |
| (2) Hydrochloric acid; HC1; [7647-01-0]   |   |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:  | PREPARED BY:  |
| pH  | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
| K <sub>so</sub> over the HCl concentration range 2.<br>at 25°C, is 1.63 x 10 <sup>-14</sup> . | .5 x 10 <sup>-2</sup> - 2.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , |
|   |   |
| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                                       |
| In a glass vessel, a mixt of 100 ml of HC1  | Nothing specified.  |
| of appropriate concn and the solute was   |   |
| placed and shaken for 6 h in a water ther-  |   |
| mostat at 25°C. After attaining equilibrium,  |   |
| the pH of the soln was measured and the   |   |
| $Cu^{2+}$ and S content was detd to calculate   |   |
| K <sub>so</sub> .   |   |
| 80  |   |
|   | ESTIMATED ERROR:  |
|   | Nothing specified.  |
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|   | REFERENCES:   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:   |
|--|--|
| (1) Cobalt; bis[4-amino-N-(2,6-dimethoxy-4-  | Tskitishvili, M. G.; Mikadze, I. I.                                    |
| pyrimidinyl)benzenesulfonamidato]- hy-   | Soobshch. Akad. Nauk Gruz. SSR <u>1978,</u>                            |
| drate; $C_{24}H_{26}CoN_80_8S_2 \cdot nH_20;$  | 89(3), 589-92.   |
| [ 86729-20-6]  |  |
| (2) Hydrochloric acid; HC1; [7647-01-0]  |  |
| (3) Water; H <sub>2</sub> O; [7732-18-5]<br>VARIABLES:                                       | PREPARED BY:   |
|  |  |
| рН   | R. Piekos  |
|  | L  |
| EXPERIMENTAL VALUES:   |  |
| K <sub>so</sub> over the HCl concentration range 2<br>at 25°C, is 2.28 x 10 <sup>-11</sup> . | 2.5 x 10 <sup>-2</sup> - 2.5 x 10 <sup>-5</sup> mol dm <sup>-3</sup> , |
|  |  |
| AUXILIARY  | INFORMATION .  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |
| In a glass vessel, a mixt of 100 ml of HCl   | Nothing specified.   |
| of appropriate concn and the solute was pla-   |  |
| ced and shaken for 6 h in a water thermostat   |  |
| at 25°C. After attaining equilibrium, the  |  |
| pH of the soln was measured and the $Co^{2+}$  |  |
| and S content was detd to calculate K <sub>so</sub>  |  |
|  |  |
|  |  |
|  | POTIMATED EDDAD.   |
|  | ESTIMATED ERROR:   |
|  | Nothing specified.   |
|  |  |
|  | REFERENCES:  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| <ol> <li>Copper, bis[4-amino-N-(2,6-dimethoxy-<br/>4-pyrimidiny1)benzenesulfonamidato]-,<br/>hydrate; C<sub>24</sub>H<sub>26</sub>CuN<sub>8</sub>O<sub>8</sub>S<sub>2</sub>•nH<sub>2</sub>O;<br/>[86729-19-3]</li> <li>Hydrochloric acid; HC1; [7647-01-0]</li> </ol>       | Tskitishvili, M.G.; Mikadze, I.I.<br>Soobshch. Akad. Nauk Gruz. SSR<br><u>1978,</u> 89(3), 589-92. |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:   |
| pH  | R. Piekos  |
| EXPERIMENTAL VALUES:  | • L  |
| K <sub>so</sub> over the HCl concentration range 2.5<br>at 25 <sup>0</sup> C, is 1.63 x 10 <sup>-14</sup> .   | $\times 10^{-2} - 2.5 \times 10^{-5} \text{ mol dm}^{-3}$ ,  |
|   |  |
| AUXTLIAR  | Y INFORMATION  |
| AUXILIAR<br>METHOD/APPARATUS/PROCEDURE:   | Y INFORMATION<br>SOURCE AND PURITY OF MATERIALS:   |
|   | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.  |
| METHOD/APPARATUS/PROCEDURE:<br>In a glass vessel, a mixt of 100 ml of HCl<br>of appropriate concn and the solute was<br>placed and shaken for 6 h in a water thermo<br>stat at 25°C. After attaining equilibrium<br>the pH of the soln was measured and the Cu <sup>2</sup> | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.<br>-<br>+<br>ESTIMATED ERROR:                |
| METHOD/APPARATUS/PROCEDURE:<br>In a glass vessel, a mixt of 100 ml of HCl<br>of appropriate concn and the solute was<br>placed and shaken for 6 h in a water thermo<br>stat at 25°C. After attaining equilibrium<br>the pH of the soln was measured and the Cu <sup>2</sup> | SOURCE AND PURITY OF MATERIALS:<br>Nothing specified.  |

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| <ul> <li>COMPONENTS:         <ol> <li>Magnesium, (<u>T</u>-4)-bis[4-amino-<u>N</u>-(2,6-di-methoxy-4-pyrimidiny1)benzenesulfonami-dato]-hydrate; C<sub>24</sub>H<sub>26</sub>MgN<sub>8</sub>O<sub>8</sub>S<sub>2</sub>•nH<sub>2</sub>O; [84812-81-7]</li> <li>Hydrochloric acid; HCl; [7647-01-0]</li> <li>Water; H<sub>2</sub>O; [7732-18-5]</li> </ol> </li> </ul> | ORIGINAL MEASUREMENTS:<br>Tskitishvili, M. G. Shvelashvili, A. E.;<br>Mikadze, I. I.; Zhorzholiani, N. B.;<br>Chrelashvili, M. V. <i>Izv. Akad. Nauk</i><br><i>Gruz. SSR, Ser. Khim.</i> <u>1981</u> , 7(4),<br>300-4. |
|--|--|
| VARIABLES:   | PREPARED BY:   |
| pH   | R. Piekos  |

EXPERIMENTAL VALUES:

 $K_{so}$  over the HCl concentration range 5.0 x  $10^{-3}$  to 1.5 x  $10^{-5}$  mol dm<sup>-3</sup>, at 25°C, is 6.33 x  $10^{-5}$ .

### AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: The earlier described apparatus and method was used (1): in a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute were placed and shaken for 6 h in a water thermostat at  $25^{\circ}$ C. After attaining equilibrium, the pH of the soln was measured and the Mg<sup>2+</sup> and S content was determined to calculate K<sub>so</sub>. The pH was measured on a pH-673 pH meter.

| • |  |
|---|--|
|   | SOURCE AND PURITY OF MATERIALS:                        |
|   | 0.1M solns of chem pure Mg(0Ac) <sub>2</sub> , monoso- |
|   | dium salt of sulfadimethoxine and HCl as               |
|   | well as doubly distd water were used. The              |
|   | source of the materials was not specified.             |

# ESTIMATED ERROR:

Nothing specified.

# **REFERENCES:**

 Tskitishvili, M. G.; Mikadze, I. I. Soobshch. Akad. Nauk Gruz. SSR <u>1978</u>, 89(3), 589.

| 432  |  |  |  |
|--|--|--|--|
| <pre>COMPONENTS:<br/>(1) Manganese, bis[4-amino-N-(2,6-dimethoxy-<br/>4-pyrimidinyl)benzenesulfonamidato]-<br/>hydrate; C<sub>24</sub>H<sub>26</sub>MnN<sub>8</sub>O<sub>8</sub>S<sub>2</sub>·nH<sub>2</sub>O;<br/>[84812-80-6]<br/>(2) Hydrochloric acid; HC1; [7647-01-0]<br/>(3) Water; H<sub>2</sub>O; [7732-18-5]</pre> | ORIGINAL MEASUREMENTS:<br>Tskitishvili, M. G.; Shvelashvili, A. E.;<br>Mikadze, I. I.; Zhorzholiani, N. B.;<br>Chrelashvili, M. V. Izv. Akad. Nauk<br>'Gruz. SSR, Ser. Khim. <u>1981</u> 7(4),<br>300-4. |  |  |
| VARIABLES:   | PREPARED BY:   |  |  |
| рН   | R. Piekos  |  |  |
| EXPERIMENTAL VALUES:   |  |  |  |
| Concentration of HC1<br>(mol/1)  | pH 10 <sup>9</sup> K <sub>so</sub> at 25 <sup>0</sup> C  |  |  |
| $5.0 \times 10^{-3}$ 6   | .54 7.45   |  |  |
| $2.5 \times 10^{-3}$ 7   | .02 7.40   |  |  |
| $1.0 \times 10^{-3}$ 7.  | .09 7.41   |  |  |
| $5.0 \times 10^{-4}$ 7   | .16 7.39   |  |  |
| $2.5 \times 10^{-4}$ 7.  | .21 7.43   |  |  |
| $1.0 \times 10^{-4}$ 7.  | .26 7.39   |  |  |
| $5.0 \times 10^{-5}$ 7   | .27 7.43   |  |  |
| $1.5 \times 10^{-5}$ 7   | .30 7.38   |  |  |
|  | Mean 7.41  |  |  |
|  |  |  |  |
|  | INFORMATION  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |  |  |
| The earlier described apparatus and method   | 0.1M solns of chem. pure Mn(OAc) <sub>2</sub> , monoso-  |  |  |
| was used (1): in a glass vessel, a mixt of   | dium salt of sulfadimethoxine, and HCl as  |  |  |
| 100 ml of HCl of appropriate concn and the solute were placed and shaken for 6 h in a  | well as doubly distd water were used. The source of the materials was not specified.   |  |  |
| water thermostat at 25°C. After attaining  |  |  |  |
| equilibrium, the pH of the soln was measured   |  |  |  |
| and the $Mn^{2+}$ and S content was determined to  |  |  |  |
| calculate K <sub>so</sub> The pH was measured on a pH-   |  |  |  |
| 673 pH meter.  | ESTIMATED ERROR:<br>K <sub>so</sub> : std deviation 2x10 <sup>-11</sup> (compiler).  |  |  |
|  | Temp and pH: not specified.  |  |  |
|  | REFERENCES:  |  |  |
| · ·  | 1. Tskitishvili, M. G.; Mikadze, I. I.   |  |  |
|  | Soobshch. Akad. Nauk Gruz. SSR   |  |  |
|  | <u>1978,</u> 89(3), 589.   |  |  |

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|---|---|--|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |  |  |
| (1) Nickel, bis[4-amino-N-(2,6,-dimethoxy-  | Tskitishvili, M. G.; Shvelashvili, A. E.;                                       |  |  |
| 4-pyrimidinyl)benzenesulfonamidato]-<br>hydrate; C <sub>24</sub> H <sub>26</sub> N <sub>8</sub> NiO <sub>8</sub> S <sub>2</sub> •nH <sub>2</sub> O; | Mikadze, I. I.; Zhorzholiani, N. B.;  |  |  |
| [84812-79-3]  | Chrelashvili, M. V. Izv. Akad. Nauk   |  |  |
| (2) Hydrochloric acid; HCl; [7647-01-0]   | Gruz. SSR. Ser. Khim. <u>1981</u> , 7(4),                                       |  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  | 300~4.<br>PREPARED BY:  |  |  |
| VARIABLES:  |   |  |  |
| pH  | R. Piekos   |  |  |
| [   |   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
|   |   |  |  |
| Concentration of HCl  | pH 10 <sup>9</sup> K <sub>so</sub> at 25 <sup>o</sup> C                         |  |  |
| (mo1/1)   |   |  |  |
|   |   |  |  |
| $2.5 \times 10^{-2}$  | 6.37 3.17   |  |  |
| $1.0 \times 10^{-2}$  | 6.66 3.20   |  |  |
| $5.0 \times 10^{-3}$  | 6.85 3.16   |  |  |
| $2.5 \times 10^{-3}$  | 6.96 3.17   |  |  |
| $1.0 \times 10^{-3}$  | 7.05 3.13   |  |  |
| $5.0 \times 10^{-4}$  | 7.10 3.18   |  |  |
| $2.5 \times 10^{-4}$  | 7.16 3.16   |  |  |
| $1.0 \times 10^{-4}$  | 7.63 3.16   |  |  |
| $5.0 \times 10^{-5}$  | 7.80 3.11   |  |  |
| $2.5 \times 10^{-5}$  | 7.82  |  |  |
|   | Mean 3.16   |  |  |
|   |   |  |  |
| ······  |   |  |  |
|   | INFORMATION   |  |  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |  |  |
| The earlier described apparatus and method  | 0.1M solns of chem pure Ni(OAc) <sub>2</sub> , monoso-                          |  |  |
| was used (1): in a glass vessel, a mixt of  | dium salt of sulfadimethoxine, HCl as well                                      |  |  |
| 100 ml of HCl of appropriate concn and the  | as doubly distd water were used. The source of the materials was not specified. |  |  |
| solute were placed and shaken for 6 h in a water thermostat at 25°C. After attaining  | source of the materials was not specified.                                      |  |  |
| equilibrium, the pH of the soln was measured  |   |  |  |
| and the Ni <sup>2+</sup> and S content was determined   | 1   |  |  |
| to calculate K <sub>so</sub> The pH was measured on a   |   |  |  |
| pH-673 pH meter.  | ESTIMATED ERROR:  |  |  |
|   | $K_{so}$ : std deviation 2.5 x 10 <sup>-11</sup> (compiler).                    |  |  |
|   | Temp and pH: not specified.   |  |  |
|   | REFERENCES:   |  |  |
|   | 1. Tskitishvili, M. G.; Mikadze, I. I.  |  |  |
|   | Soobshch. Akad. Nauk Gruz. SSR  |  |  |
|   | <u>1978</u> , <i>89(3)</i> , 589.   |  |  |
| 1   |   |  |  |
| L   | <u> </u>  |  |  |

|      | ONENTS:   |                                |               | ORIGINAL MEASUREMENTS:  |  |
|------|---|--------------------------------|---------------|---|--|
| (1)  | Benzenesulfonamide, 4-amino-N-(5,6-di-<br>methoxy-4-pyrimidinyl)- (sulfadoxine);<br>$C_{12}H_{14}N_4O_4S$ ; [2447-57-6]<br>Phosphoric acid, disodium salt;<br>$Na_2HPO_4$ ; [7558-94-4] |                                |               | Hekster, Ch. A.; Vree, T. B.<br>Antibiotics Chemother. <u>1982</u> , 31,<br>22-118.       |  |
| (2)  |   |                                |               |   |  |
| (3)  | Phosphoric a<br>KH <sub>2</sub> PO <sub>4</sub> ; [   | cid, monopotassi<br>7778-77-0] | um salt;      |   |  |
| (4)  | Water; H <sub>2</sub> 0   | ; [7732-18-5]                  |               | PREPARED BY:  |  |
| VARI | ABLES:  | РН                             |               | R. Piekos   |  |
|      |   |                                |               |   |  |
|      |   |                                |               |   |  |
|      |   | ٩V                             | Solub         | ility at 25 <sup>0</sup> C  |  |
|      |   | рН                             | Solub<br>mg/l | $\frac{11 \text{ ty at } 25^{\circ}\text{C}}{10^4 \text{ mol } \text{dm}^{-3} \text{ a}}$ |  |
|      |   | рН<br><br>5.5                  | <u></u>       |   |  |

<sup>a</sup> Calculated by compiler.

| AUXILIARY INFORMATION  |   |  |  |  |  |
|--|---|--|--|--|--|
| METHOD/APPARATUS/PROCEDURE:<br>The earlier developed method (1) was used<br>(personal communication). Satd solns of sul-<br>fadoxine were prepd in phosphate buffers of<br>pH 5.5 and 7.5 at 25°C. The concn of the<br>solute was measured by means of a Spectra<br>Physics 3500B high-performance liquid chro-<br>matograph equipped with a Model 748 column<br>oven and a Pye-Unicam LC-UV spectrophotome- | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor the purity of the mate-<br>rials was specified.   |  |  |  |  |
| tric detector.   | <pre>ESTIMATED ERROR:<br/>Soly: the detection limit of the solute<br/>by HPLC was 0.5 mg/l (authors).<br/>The errors in temp and pH were not specified<br/>REFERENCES:<br/>1. Hekster, Y. A.; Vree, T. B.;<br/>Damsma, J. E.; Friesen, W. T.<br/>J. Antimicrob. Chemother. <u>1981</u>, 8,<br/>133.</pre> |  |  |  |  |

|                                |   |                            |                         |  |                 | 430              |
|--------------------------------|---|----------------------------|-------------------------|--|-----------------|------------------|
| COMP                           | ONENTS:   |                            |                         | ORIGINAL MEASUREMEN                    | TS:             |                  |
| (1)                            | Acetamide, N-[4-[[(5,6-dimethoxy-4-pyri-<br>midinyl)amino]sulfonyl]phenyl]-   |                            |                         |  |                 |                  |
|                                | <ul> <li>(N<sup>4</sup>-acetylsulfadoxine); C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>O<sub>5</sub>S;<br/>[5018-54-2]</li> <li>(2) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> <li>(3) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul> |                            | N405S;                  | Antibiotics Chemother. 1982, 31,       |                 |                  |
| 1                              |   |                            | 22-118.                 |  |                 |                  |
| [                              |   |                            |                         |  |                 |                  |
| (3)                            |   |                            | PREPARED BY:            | <u> </u>                               |                 |                  |
| (4) Water; $H_20;$ [7732-18-5] |   |                            | R. Piek                 |  |                 |                  |
|                                | IABLES:   | рН                         |                         | K. Flek                                | .08             |                  |
| EXPE                           | RIMENTAL VALUES   |                            |                         | I                                      |                 |                  |
|                                |   |                            |                         |  |                 |                  |
| 1                              |   |                            |                         |  |                 |                  |
|                                |   |                            |                         |  |                 |                  |
| {                              |   |                            |                         |  |                 |                  |
|                                |   | рН                         | Solu                    | bility at 25 <sup>0</sup> C            |                 |                  |
|                                |   |                            | mg/1                    | 10 <sup>4</sup> mol dm <sup>-3</sup> a |                 |                  |
|                                |   | 5.5                        | 221                     | 6.27                                   |                 |                  |
|                                |   | 7.5 <sup>b</sup>           | 3,420                   | 97.06                                  |                 |                  |
|                                |   |                            | -                       |  |                 |                  |
|                                |   | a cal                      | culated by              | compiler                               |                 |                  |
|                                |   |                            |                         | -                                      |                 | •                |
|                                |   | <sup>D</sup> Erro          | oneous pH               | value of 7.0 is give                   | n               |                  |
|                                |   | in t                       | the articl              | e.                                     |                 |                  |
|                                |   |                            |                         |  |                 |                  |
|                                |   |                            |                         |  |                 |                  |
| <b> </b>                       |   |                            | AUXILIARY               | INFORMATION                            |                 |                  |
| MET                            | HOD/APPARATUS/PR  | OCEDURE:                   |                         | SOURCE AND PURITY O                    | OF MATERIALS :  |                  |
| 1                              |   | ped method (1) wa          | as used                 | Neither source no                      |                 | the mate-        |
| (pe                            | ersonal communica   | ation). Satd sol           | lns of N <sup>4</sup> - | rials was specifi                      | .ed.            |                  |
| ace                            | etylsulfadoxine v   | vere prepd in pho          | osphate                 |  |                 |                  |
| buf                            | fers of pH 5.5 a  | and 7.5 at $25^{\circ}$ C. | The conc                | n                                      |                 |                  |
| of                             | the solute was a  | neasured by means          | s of a                  | 1                                      |                 |                  |
| Spe                            | ectra Physics 350   | 00B high-performa          | ance liq-               |  |                 |                  |
| uid                            | l chromatograph   | equipped with a N          | 1odel 748               |  |                 |                  |
| c01                            | lumn oven and a l   | Pye-Unicam LC-UV           | spectro-                |  |                 |                  |
| pho                            | tometric detect   | or.                        |                         | ESTIMATED ERROR:                       |                 |                  |
|                                |   |                            |                         | Soly: the detect                       | ion limit of th | e solute by      |
|                                |   |                            |                         | HPLC was C                             | .5 mg/l (author | s).              |
|                                |   |                            |                         | The errors in tem                      | p and pH were n | ot specified     |
| 1                              |   |                            |                         | REFERENCES:                            |                 |                  |
|                                |   |                            |                         | 1. Hekster, Y.                         |                 |                  |
| 1                              |   |                            |                         | ſ                                      | .; Friesen, W   |                  |
|                                |   |                            |                         | J. Antimicro                           | b. Chemother.   | <u>1981</u> , 8, |
|                                |   |                            |                         | 133.                                   |                 |                  |
|                                |   |                            |                         |  |                 |                  |

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| <pre>COMPONENTS:<br/>(1) Benzoic acid, 5-[[4-[[(2,4-dimethoxy-6-<br/>pyrimidinyl)amino]sulfonyl] phenyl]azo]-<br/>2-hydroxy- (salazodimethoxine);<br/>C<sub>19</sub>H<sub>17</sub>N<sub>5</sub>O<sub>7</sub>S; [40016-88-4]<br/>(2) Water; H<sub>2</sub>O; [7732-18-5]<br/>VARIABLES:</pre>                              | ORIGINAL MEASUREMENTS:<br>Ezerskii, M. L; Per'kova, N. N.<br>KhimFarm. Zh. <u>1979</u> , 13(11), 87-91.<br>PREPARED BY:                              |
|--|--|
| Grinding regime  | R. Piekos  |
| EXPERIMENTAL VALUES:   |  |
| EAFENIAL VALUES.   | Solubility at room temperature   |
| Specimen of salazodimethoxine  | $\frac{\text{solubility at room competitive}}{\text{g/cm}^3 \qquad 10^4 \text{ mol dm}^{-3} \text{ a}}$  |
| Commercial   | 0.000075 1.6   |
| Commercial<br>Commercial, ground in a ball mill  |  |
|  | 0.000100 2.2   |
|  |  |
| <sup>a</sup> Calculated by compiler  |  |
|  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by prolonged agitation<br>of an excess of salazodimethoxine in water<br>at room temp. The solns were then allowed<br>to stand for 12 and h and filtered. The concr<br>of the solute in the filtrate was detd spec-<br>trophotometrically at 462 nm in a 1-cm cuvet. | used (source not specified). It was ground<br>in a Pulverisette-5 lab mill or in a C-1266-<br>00 jet mill. Purity of the water was not<br>specified. |
|  | ESTIMATED ERROR:<br>Nothing specified.<br>REFERENCES:  |

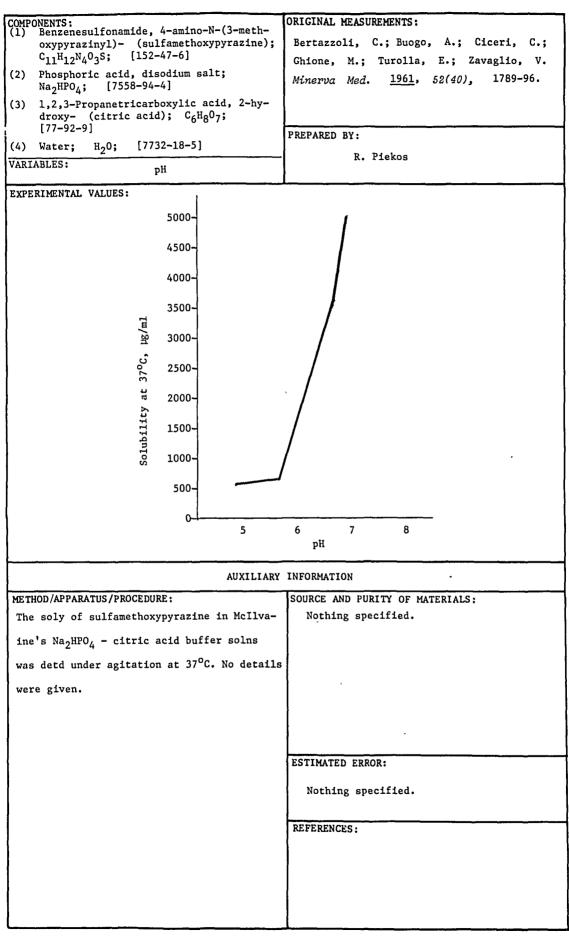
| I | COMPONENTS:   | ORIGINAL MEASUREMENTS:                            |
|---|---|---|
|   | <ol> <li>Pyrimidine, 2,5-bis[[(4-aminophenyl)sul-</li> </ol>                                  | Roblin, R. O., Jr.; Winnek, P. S.;                |
|   | fonyl]amino]-; C <sub>16</sub> H <sub>16</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub> ; | English, J. P. J. Am. Chem. Soc.                  |
| İ | [71119-39-6]  | <u>1942</u> , <i>64</i> , 567-70.                 |
|   | (2) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
|   | VARIABLES:  | PREPARED BY:                                      |
|   | One temperature: 37 <sup>0</sup> C  | R. Piekos   |
|   |   |   |
|   | EXPERIMENTAL VALUES:  |   |
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|   |   |   |
|   | Solubility of 2,5-bis[[(4-aminopheny1)s   | ulfonyl]amino]pyrimidine in water                 |
|   | at $37^{\circ}$ C is 2.2 mg/100 cm <sup>3</sup> solution ( 5.                                 | $2 \times 10^{-5}$ mol dm <sup>-3</sup> compiler) |
|   |   | Z X IO MOI UM , COMPILEI ).                       |
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|   | AUXILIARY   | INFORMATION                                       |
|   | METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                   |
|   | Excess sulfonamide in water was heated and  | The sulfonamide, mp 231-2°C (cor), was prepd      |
|   | stirred on a steam bath for 30 min. The sus   | by the authors. Anal: %C 45.4 (calcd 45.6);       |
|   | pension was then agitated for 24 h in a ther  | ZH 4.0 (3.8); ZN 20.1 (20.1)                      |
|   | mostat at 37 <sup>0</sup> C. A sample of the satd soln  | Purity of the water was not specified.            |
|   | was withdrawn through a glass filter, dild,   |   |
|   | and analyzed by the Marshall method (1)   |   |
|   | using a General Electric recording spectro-   |   |
|   | photometer for comparing the colors develop-  |   |
|   | ed with those of the standards.   | ESTIMATED ERROR:                                  |
|   |   | Nothing specified.                                |
|   |   |   |
|   |   |   |
|   |   | REFERENCES ;                                      |
|   |   | 1. Bratton, A. C.; Marshall, E. K., Jr.           |
|   |   | J. Pharmacol. 1939, 66, 4.                        |
|   |   |   |
|   |   |   |
|   |   |   |

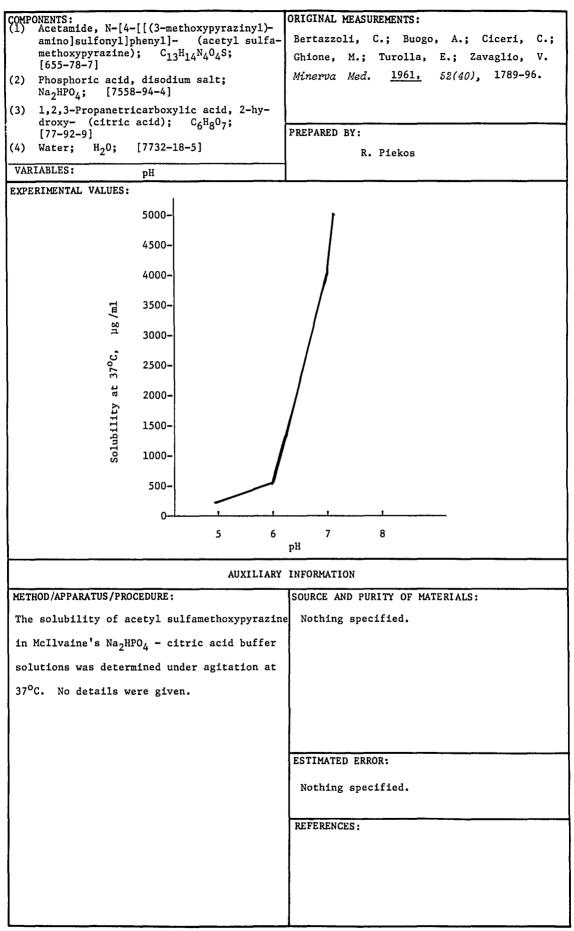
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438
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                     |  |
|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-5-[2,4(   | Roblin, R. O., Jr.; Williams, J. H.;       |  |
| 1H,3H)-pyrimidinedionyl]-;  | Winnek, P. S.; English, J. P.              |  |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub> S; [6912-98-7]  |  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  | J. Am. Chem. Soc. <u>1940,</u> 62, 2002-5. |  |
| (2) water, n <sub>2</sub> 0, [//52-10-5]  |  |  |
| VARIABLES:  | PREPARED BY:                               |  |
| One temperature: 37°C   | R. Piekos                                  |  |
|   |  |  |
|   |  |  |
| EXPERIMENTAL VALUES:  |  |  |
| Solubility of 4-amino-N-5-[2,4(1H,3H)<br>in water at 37 <sup>0</sup> C is 48.6 mg/100 cm <sup>3</sup> so<br>compiler ).           |  |  |
|   |  |  |
|   | RY INFORMATION                             |  |
| METHOD/APPARATUS/PROCEDURE:<br>Excess sulfonamide in water was heated and<br>The sulfonamide, mp 277-9 <sup>O</sup> C (dec, cor), |  |  |
| stirred on a steam bath for 30 min. The s   |  |  |
| pension was then agitated for 24 h in a th  |  |  |
| mostat at 37°C. A sample of the satd soln   |  |  |
| was withdrawn through a glass filter, dild  |  |  |
| and analyzed by the Marshall method (1) us  |  |  |
| a General Electric recording spectrophotom  |  |  |
| ter for comparing the colors developed wit  |  |  |
| those of the standards.   |  |  |
|   | ESTIMATED ERROR:                           |  |
|   | Nothing specified.                         |  |
|   |  |  |
|   | REFERENCES :                               |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.    |  |
|   | J. Pharmacol. <u>1939</u> , 66, 4.         |  |
|   |  |  |
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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                       |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-pyrazinyl-                                      | Bunland H M                                  |
| (sulfapyrazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; | Burlage, H. M.                               |
| [116-44-9]  | J. Am. Pharm. Assoc., Sci. Ed.               |
|   | <u>1948</u> , <i>37</i> , 345.               |
| (2) 2-Propanol; C <sub>3</sub> H <sub>8</sub> 0; [67-63-0]                        |  |
|   |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 25 <sup>0</sup> C  | R. Piekos                                    |
|   |  |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of sulfapyrazine in 2-prop   | anol at 25°C is 0.0290 g/100 cm <sup>3</sup> |
| solution $(1.16 \times 10^{-3} \text{ mol } \text{dm}^{-3}, \text{ comp})$        | iler).                                       |
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|   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| Satd solns of sulfapyrazine in 2-propanol   | The sulfapyrazine N.N.R. was manufd by       |
| were prepd at 25 <sup>o</sup> C and definite vols of the                          | Mead Johnson. The source and purity of       |
| solns were measured into tared dishes by  | 2-propanol were not reported.                |
| means of standard pipets. The alcohol was   |  |
|   |  |
| allowed to evap at room temp and the residue                                      |  |
| was dried at 105 <sup>0</sup> C. In the case of losses                            |  |
| due to apparent decompn, the residue was  |  |
| dried in a dessicator (1).  |  |
|   | ESTIMATED ERROR:                             |
|   | Nothing specified.                           |
|   |  |
|   |  |
|   | REFERENCES :                                 |
|   |  |
|   | 1. Burlage, H. M.                            |
| 1   | J. Am. Pharm. Assoc., Sci. Ed.               |
|   | <u>1947</u> , <i>36(1)</i> , 16.             |
|   | 1  |
|   |  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:  |
|---|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-pyrazinyl-,</li> </ol>               |   |
| monosodium salt (sodium sulfapyrazine);                                     | Burlage, H. M.  |
| $C_{10}H_{10}N_4O_2S\cdot Na;$ [547-31-9]                                   | J. Am. Pharm. Assoc., Sci. Ed.  |
|   | <u>1948,</u> 37, 345.   |
| (2) 2-Propanol; C <sub>3</sub> H <sub>8</sub> 0; [67-63-0]                  |   |
|   |   |
| VARIABLES:  | PREPARED BY:  |
| One temperature: 25 <sup>0</sup> C  | R. Piekos   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
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| Solubility of sodium sulfapyrazine in 2-p                                   | propanol at $25^{\circ}$ C is 0.7080 g/100 cm <sup>3</sup>                  |
|   |   |
| solution ( 2.600 x $10^{-2}$ mol dm <sup>-3</sup> , compile                 | er ).   |
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| AUXILIARY   | INFORMATION   |
|   |   |
| METHOD/APPARATUS/PROCEDURE:<br>Satd solns of sodium sulfapyrazine in 2-pro- | SOURCE AND PURITY OF MATERIALS:<br>The sodium pyrazine N.N.R. was manufd by |
| panol were prepd at $25^{\circ}$ C and definite vols                        | Mead Johnson. The source and purity of                                      |
|   |   |
| of the solns were measured into tared dishes                                | 2-propanol were not specified.  |
| by means of standard pipets. The alcohol was                                | 1 1   |
| allowed to evap at room temp and the residue,                               |   |
| was dried at 105 <sup>0</sup> C. In the case of losses                      |   |
| due to apparent decompn, the residue was                                    |   |
| dried in a desiccator (1).  |   |
|   | ESTIMATED ERROR:  |
|   | Nothing specified.  |
|   |   |
|   |   |
|   | REFERENCES:   |
|   | 1. Burlage, H. M.   |
|   | J. Am. Pharm. Assoc., Sci. Ed.  |
|   | <u>1947,</u> 36(1), 16.   |
|   |   |
|   |   |





| COMPONENTS :   | ORIGINAL MEASUREMENTS:                              |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-                                      | Anderson, G. W.; Faith, H. E.; Marson,              |
| diamino-1,3,5-triazin-2-y1)-;  | H. W.; Winnek, P. S.; Roblin, R. O., Jr.            |
| C <sub>9</sub> H <sub>11</sub> N <sub>7</sub> O <sub>2</sub> S; [51249-11-7] | J. Am. Chem. Soc. 1942, 64, 2902-5.                 |
| (2) Water; H <sub>2</sub> O; [7732-18-5]                                     |   |
|  |   |
| VARIABLES:   | PREPARED BY:  |
| One temperature: 37°C  | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of 4-amino-N-(4,6-diamino-1,                                      | ,3,5-triazin-2-yl)benzenesulfonamide                |
| in water at 37°C is 728 mg/100 cm <sup>3</sup> solu                          |   |
| in water at 3/°C is /28 mg/100 cm <sup>-</sup> solt                          | ution ( $2.59 \times 10^{-1} \text{ mol dm}^{-1}$ , |
| compiler ).  |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                     |
| Excess sulfonamide in water was heated and                                   | The sulfonamide, mp 290-5°C (cor), was              |
| stirred on a steam bath for 30 min. The                                      | prepd by the authors. Anal: %C 38.9                 |
| suspension was then agitated for 24 h in a                                   | (calcd 38.4); %H 4.3 (3.9); %N 34.7                 |
| thermostat. A sample of the satd soln was                                    | (34.9).   |
| withdrawn through a glass filter, dild, and                                  | Purity of the water was not specified.              |
| analyzed by the Marshall method (1) using a                                  |   |
| General Electric recording spectrophotometer                                 |   |
| for comparing the colors developed with                                      |   |
| those of the standards.  | ESTIMATED ERROR:                                    |
|  |   |
|  | Nothing specified.                                  |
|  |   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.             |
|  | J. Pharmacol. <u>1939</u> , 66, 4.                  |
|  |   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |  |
|--|---|--|
| (1) Benzenesulfonamide, 4-amino-N-2-quin-  | Paál, T.; Regüsz, P.  |  |
| oxalinyl- (sulfaquinoxaline);  | <i>Gyógyszerészet</i> <u>1973</u> , <i>17</i> , 59–63.  |  |
| C <sub>14</sub> H <sub>12</sub> N <sub>3</sub> O <sub>2</sub> S; [59-40-5]<br>(2) Hydrochloric acid; HCl; [7647-01-0]  | <i>Gyogyozereozet</i> <u>1975,</u> 17, 59-05.   |  |
|  |   |  |
| (3) Water; H <sub>2</sub> O; [7732-18-5]   |   |  |
| VARIABLES:   | PREPARED BY:  |  |
| Concentration of HCl   | R. Piekos   |  |
| EXPERIMENTAL VALUES:   |   |  |
| Concentration Concentratio<br>of HC1 real solutio  | n of the most concentrated<br>n of sulfaquinoxaline at 26 <sup>0</sup> C<br>ol dm <sup>-3</sup> solvent |  |
| <u> </u>   | ol dm <sup>-3</sup> solvent   |  |
| 5 3 x 10 <sup>-</sup>  | $(9 \times 10^{-2})^a$  |  |
| 1 < 2 × 10   | 3   |  |
| 0.1 < 2 x 10 <sup>-</sup>  | 3   |  |
|  |   |  |
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| AUXILIARY  | INFORMATION   |  |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:   |  |
| Satd solns were prepd by addn of increasing  | Sulfaquinoxaline was a product of Chinoin   |  |
| quantities of aq HCl to weighed quantities   | Pharm and Chem Works. Its purity was 99.6%  |  |
| of sulfaquinoxaline. After the dissoln had   | as detd by diazotization. The source and  |  |
| been completed, the soln was stirred with a  | purity of the remaining materials were not  |  |
| magnetic stirrer and allowed to stand for 24   | specified.  |  |
| h. The soln was considered stable, if it re-   |   |  |
| mained clear during a 24-h period. If the  |   |  |
| solute pptd out from the clear soln, the solution of the solut |   |  |
| was considered metastable.   | ESTIMATED ERROR:  |  |
|  | Soly: accuracy ±10% (authors).  |  |
|  | Temp: ±3 <sup>0</sup> C (authors).  |  |
|  | REFERENCES:   |  |
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| COMPONENTS :   | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-quin-  | Paál, T.; Regüsz, P.  |
| oxalinyl- (sulfaquinoxaline);  | <i>Gyógyszerészet</i> <u>1973,</u> <i>17</i> , 59–63.   |
| C <sub>14</sub> H <sub>12</sub> N <sub>3</sub> O <sub>2</sub> S; [59-40-5]   |   |
| (2) Perchloric acid; HC10 <sub>4</sub> ; [7601-90-3]   |   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | PREPARED BY:  |
| Concentration of HCl0 <sub>4</sub>   | R. Piekos   |
| EXPERIMENTAL VALUES:   | L   |
| Concentration Concentra  | tion of the most concentrated   |
| of HClO <sub>4</sub> real solu   | tion of sulfaquinoxaline at 26 <sup>0</sup> C   |
| N  | mol dm <sup>→3</sup> solvent  |
| 5 2  | $\times 10^{-2}$ ( 0.67 ) <sup>a</sup>  |
| 1 < 2  | x 10 <sup>-3</sup>  |
| 0.1 < 2  | x 10 <sup>-3</sup>  |
|  |   |
|  |   |
| <sup>a</sup> Concentration of the most conc  | entrated metastable solution  |
|  |   |
| that could be prepared without   | precipitation of the solute   |
| that could be prepared without   | precipitation of the solute   |
| that could be prepared without   | precipitation of the solute   |
| that could be prepared without   | precipitation of the solute   |
| that could be prepared without   | precipitation of the solute .   |
| that could be prepared without   | precipitation of the solute   |
| that could be prepared without   | precipitation of the solute .   |
| that could be prepared without   | precipitation of the solute .   |
|  | precipitation of the solute<br>INFORMATION  |
|  |   |
| AUXILIARY  | INFORMATION   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and<br>purity of the remaining materials were not   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and<br>purity of the remaining materials were not   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-  | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and<br>purity of the remaining materials were not   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and<br>purity of the remaining materials were not   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).                                       |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.67<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:   |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).                                       |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).<br>Temp: ±3 <sup>O</sup> C (authors). |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).<br>Temp: ±3°C (authors).              |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).<br>Temp: ±3 <sup>O</sup> C (authors). |
| AUXILIARY<br>METHOD/APPARATUS/PROCEDURE:<br>Satd solns were prepd by addn of increasing<br>amts of aq HClO <sub>4</sub> to weighed quantities of<br>sulfaquinoxaline. After the dissoln had been<br>completed, the soln was stirred with a magne<br>tic stirrer and allowed to stand for 24 h.<br>The soln was considered stable, if it re-<br>mained clear during a 24-h period. If the<br>solute pptd out from the clear soln, the | INFORMATION<br>SOURCE AND PURITY OF MATERIALS:<br>Sulfaquinoxaline was a product of Chinoin<br>Pharm and Chem Works. Its purity was 99.6%<br>as detd by diazotization. The source and<br>purity of the remaining materials were not<br>specified.<br>ESTIMATED ERROR:<br>Soly: accuracy ±10% (authors).<br>Temp: ±3°C (authors).              |

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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                         |
|--|--|
| (1) Benzenesulfonamide, 4-amino-N-2-quin-                                  | ORIGINAL MEASUREMENTS:                         |
| oxalinyl- (sulfaquinoxaline);  | Paál, T.; Regösz, P.                           |
| -  | Gyógyszerészet <u>1973</u> , 17, 59–63.        |
| C <sub>14</sub> H <sub>12</sub> N <sub>3</sub> O <sub>2</sub> S; [59-40-5] |  |
| (2) Nitric acid; HNO <sub>3</sub> ; [7697-37-2]                            |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]                                   |  |
| VARIABLES:   | PREPARED BY:                                   |
| Concentration of HNO3  | R. Piekos                                      |
|  |  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
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|  |  |
| Concentration Concetra   | tion of the most concentrated                  |
| of HNO <sub>3</sub> real solu  | ution of sulfaquinoxaline at 26 <sup>0</sup> C |
| N  | mol dm <sup>-3</sup> solvent                   |
| •••••••••••••••••••••••••••••••••••••••                                    |  |
| 5  | $2 \times 10^{-2} (0.2)^{a}$                   |
| 1  | $< 2 \times 10^{-3}$                           |
| +  |  |
| 0.1  | $< 2 \times 10^{-3}$                           |
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| <sup>a</sup> Concentration of the mo                                       | st concentrated metastable solution            |
| that could be prepared   | without precipitation of the solute            |
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| AUXILIARY  | INFORMATION                                    |
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| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                |
| Satd solns were prepd by addn of increasing                                | Sulfaquinoxaline was a product of Chinoin      |
| amts of aq HNO <sub>3</sub> to weighed quantities of                       | Pharm and Chem Works. Its purity was 99.6%     |
| sulfaquinoxaline. After the dissoln had                                    | as detd by diazotization.                      |
| been completed, the soln was stirred with a                                | The source and purity of the remaining mate-   |
| magnetic stirrer and allowed to stand for                                  | rials were not specified.                      |
|  |  |
| 24 h. The soln was considered stable, if                                   |  |
| it remained clear during a 24-h period. If                                 |  |
| the solute pptd out from the clear soln,                                   |  |
| the soln was considered metastable.  | ESTIMATED ERROR:                               |
|  | Soly: accuracy ±10% (authors).                 |
|  |  |
|  | Temp: ±3 <sup>0</sup> C (authors).             |
|  | REFERENCES:                                    |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-[5,6,7,8-<br>tetrahydro-5-methyl-8-(2-propyl)-2-<br>quinozalinyl]-; C <sub>18</sub> H <sub>24</sub> N <sub>4</sub> O <sub>2</sub> S;<br>[71119-36-3]<br>(2) Water; H <sub>2</sub> O; [7732-18-5] | ORIGINAL MEASUREMENTS:<br>Caldwell, W. T.; Kornfeld, E. C.;<br>Donnell, E. K. J. Am. Chem. Soc.<br><u>1941</u> , 63, 2188-90. |
|---|---|
| VARIABLES:<br>One temperature: 29°C<br>EXPERIMENTAL VALUES:   | PREPARED BY:<br>R. Piekos   |

| Solubility of 4-amino-N-[5,6,7,8-tetrahydro-5-methyl-8-(2-propyl)-2-        |
|---|
| quinozalinyl]benzenesulfonamide in water at $29^{\circ}$ C is 2.4 mg/100 ml |
| solution ( $6.6 \times 10^{-5} \text{ mol dm}^{-3}$ , compiler ).           |

| AUXILIARY | INFORMATION  |
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| METHOD/APPARATUS/PROCEDURE:               | SOURCE AND PURITY OF MATERIALS:              |
|---|--|
| Soly was detd by weighing the residue ob- | The sulfonamide, mp 185-7°C (cor, recrystd   |
| tained by evapg to dryness a known volume | from aq EtOH), was prepd by condensing 2-    |
| of soln satd at 29 <sup>0</sup> C.        | amino-5,6,7,8-tetrahydro-5-methy1-8-(2-      |
|   | propyl)-quinazoline with acetylsulfanilyl    |
|   | chloride followed by hydrolysis with aq NaOH |
|   | and pptn at pH 6. Anal: %N 15.58 (calcd      |
|   | 15.55). Purity of the water was not spe-     |
|   | cified.                                      |
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|   | ESTIMATED ERROR:                             |
|   | Nothing specified.                           |
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|   | REFERENCES:                                  |
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| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-(5,6,7,8-                    | ORIGINAL MEASUREMENTS:                       |
|---|--|
|   | Caldwell, W. T.; Kornfeld, E. C.;            |
| tetrahydro-2-quinazolinyl)-;  | Donnell, C. K. J. Am. Chem. Soc.             |
| C <sub>14</sub> H <sub>16</sub> N <sub>4</sub> O <sub>2</sub> S; [71119-34-1] | <u>1941,</u> 63, 2188-90.                    |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]                                      | ·  |
| -   |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 29 <sup>0</sup> C  | R. Piekos                                    |
| One cemperature. 25 G   |  |
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| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(5,6,7,8-tetr   |  |
| sulfonamide in water at 29 <sup>0</sup> C is 6.8 m                            | g/100 ml solution ( 2.2 x $10^{-4}$          |
| mol $dm^{-3}$ - compiler ).   |  |
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| AUXILIARY   | INFORMATION                                  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| Soly was detd by weighing the residue ob-                                     | The sulfonamide, mp 255-6°C (cor, recrystd   |
| tained by evapg to dryness a known volume                                     | from aq dioxane) was pred by condensing 2-   |
| of soln satd at 29 <sup>0</sup> C.  | amino-5,6,7,8-tetrahydroquinazoline with     |
|   | acetylsulfanilyl chloride followed by hydro- |
|   | lysis with aq NaOH and pptn at pH 6. Anal:   |
|   | %N 18.40 (calcd 18.41). Purity of the water  |
|   | was not specified.                           |
|   |  |
|   |  |
|   | ESTIMATED ERROR:                             |
|   | Nothing specified.                           |
|   |  |
|   | REFERENCES :                                 |
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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                       |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(5,6,7,8-   | Caldwell, W. T.; Kornfeld, E. C.;            |
| tetrahydro-8,9,9-trimethy1-5,8-methano-   | Donnell, C. K. J. Am. Chem. Soc.             |
| quinazolin - 2-yl)-; C <sub>18</sub> H <sub>22</sub> N <sub>4</sub> O <sub>2</sub> S; | <u>1941</u> , <i>63</i> , 2188-90.           |
| [71720-66-6]  |  |
| (2) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:  | PREPARED BY:                                 |
| One temperature: 29 <sup>0</sup> C  | R. Piekos                                    |
|   |  |
| EXPERIMENTAL VALUES:  |  |
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| Solubility of 4-amino-N-(5,6,7,8-tetra  | hydro-8,9,9-trimethy1-5,8-methano-           |
| quinazolin-2-yl)benzenesulfonamide in   | water at $29^{\circ}$ C is 3.0 mg/100 ml     |
|   |  |
| solution ( $8.4 \times 10^{-5} \text{ mol dm}^{-3}$ - compi                           | ler ).                                       |
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| AUXILIAR  | Y INFORMATION                                |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:              |
| Soly was detd by weighing the residue ob-   | The sulfonamide, mp 276-7°C (cor, recrystd   |
| tained by evapg to dryness a known volume c   | f from aq dioxane), was prepd by condensing  |
|   | 2-amino-5,6,7,8-tetrahydro-8,9,9-trimethy1-  |
| soln satd at 29 <sup>0</sup> C.   | 5,8-methanoquinazoline with acetylsulfanilyl |
|   | chloride followed by hydrolysis with aq NaOH |
|   | and pptn at pH 6. Anal: %N 15.39 (calcd      |
|   | 15.63). Purity of the water was not speci-   |
|   | fied.  |
|   | ESTIMATED ERROR:                             |
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|   | Nothing specified.                           |
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| 1   | REFERENCES:                                  |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                                      |  |
|--|---|--|
| <ol> <li>Benzenesulfonamide, 4-amino- (sulfanil-<br/>amide); C<sub>6</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>S; [63-74-1]</li> </ol>   | Langecker, H.   |  |
| (2) Acetamide, N-[(4-aminosulfonyl)phenyl]-<br>(acetyl sulfanilamide); [121-61-9]  | Arch. Exptl. Path. Pharmakol. <u>1948,</u><br>205, 291-301. |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]   | 2003  |  |
| VARIABLES:   | PREPARED BY:  |  |
| One temperature: 37 <sup>0</sup> C   | R. Piekos   |  |
| EXPERIMENTAL VALUES:   |   |  |
| Solubility of sulfanilamide and acetyl sulfanilamide in a saturated solution<br>of both compounds in water at $37^{\circ}$ C is 1620 mg% (9.4 x $10^{-2}$ mol dm <sup>-3</sup> ,<br>compiler ) and 375 mg% (1.75 x $10^{-2}$ mol dm <sup>-3</sup> , compiler), respectively. |   |  |
|  | INFORMATION   |  |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:                             |  |
| A mixt of sulfanilamide and acetyl sulfanil-   |   |  |
| amide was boiled with water and the compo-   | Nothing specifieu.  |  |
|  |   |  |
| nents were detd colorimetrically by the me-<br>thod of Bratton and Marshall (1) using a Ha-  |   |  |
|  |   |  |
| vemann colorimeter (2)   |   |  |
|  |   |  |
|  |   |  |
|  |   |  |
|  | ESTIMATED ERROR:  |  |
|  | Nothing specified.  |  |
|  |   |  |
|  | REFERENCES :  |  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                     |  |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.                      |  |
|  | 2. Havemann, R. Klin. Wochenschr.                           |  |
|  | <u>1940,</u> p. 503.  |  |
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| <pre>COMPONENTS:<br/>(1) Benzenesulfonamide, 4-amino-N-2-thia-<br/>zolyl- (sulfathiazole); C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>;<br/>[72-14-0]<br/>(2) Acetamide, N-[4-[(2-thiazolylamino)sul-<br/>fonyl]phenyl]- (acetyl sulfathiazole);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S<sub>2</sub>; [127-76-4]<br/>(3) Water; H<sub>2</sub>O; [7732-18-5]<br/>VARIABLES:</pre> | ORIGINAL MEASUREMENTS:<br>Langecker, H.<br>Arch. Exptl. Path. Pharmakol. <u>1948</u> ,<br>205, 291-301.<br>PREPARED BY:                                     |
|--|---|
| One temperature: 37°C  | R. Piekos   |
| EXPERIMENTAL VALUES:   | <u>I</u>  |
| Solubility of sulfathiazole and acetyl<br>of both compounds in water at $37^{\circ}$ C is 11<br>and 14 mg% ( 5.5 x $10^{-4}$ mol dm <sup>-3</sup> , comp   | 0 mg% ( 4.3 x $10^{-3}$ mol dm <sup>-3</sup> , compiler )   |
| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| A mixt of sulfathiazole and acetyl sulfa-<br>thiazole was boiled with water and the com-<br>ponents were detd colorimetrically by the<br>method of Bratton and Marshall (1) using a<br>Havemann colorimeter (2).   | Nothing specified.  |
|  | ESTIMATED ERROR:  |
|  | Nothing specified.  |
|  | <pre>REFERENCES: 1. Bratton, A. C.; Marshall, E. K., Jr. J. Biol. Chem. <u>1939</u>, 128, 537. 2. Havemann, R. Klin. Wochenschr. <u>1940</u>, p. 503.</pre> |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:  |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-(5-ethyl-  | Tenne alterna II  |
| 1,3,4-thiadiazol-2-y1)- (sulfaethyl-<br>thiadiazole); C <sub>10</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub> ; [94-19-9] | Langecker, H.   |
| (2) Acetamide, N-[4-[[(5-ethyl-1,3,4-thiadi-   | Arch. Exptl. Path. Pharmakol. <u>1948</u> ,   |
| azo1-2-y1)amino]sulfony1]pheny1]-  | 205, 291-301.   |
| (acetyl sulfaethylthiadiazole);<br>C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S <sub>2</sub> ; [1037-51-0]                  |   |
| (3) Water; $H_20$ ; [7732-18-5]  | PREPARED BY:  |
| VARIABLES:   | R. Piekos   |
| One temperature: 37°C  | R. Flekos   |
| EXPERIMENTAL VALUES:   | · · · · · · · · · · · · · · · · · · ·   |
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| Solubility of sulfaethylthiadiazole and  | acetyl sulfaethylthiadiazole in a   |
|  |   |
| saturated solution of both compounds in  | water at 37°C is 117 mg% ( 4.1 x  |
| $10^{-3}$ mol dm <sup>-3</sup> , compiler ) and 40 mg% (   | $1.2 \times 10^{-3}$ mol dm <sup>-3</sup> , compiler ),   |
| respectively.  |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:   |
| A mixt of sulfaethylthiadiazole and acetyl   | Nothing specified.  |
| sulfaethylthiadiazole was boiled with water  |   |
| and the components were detd colorimetri-  |   |
|  |   |
| cally by the method of Bratton and Marshall  |   |
| cally by the method of Bratton and Marshall<br>(1) using a Havemann colorimeter (2).   |   |
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|  |   |
|  | ESTIMATED ERROR:  |
|  | ESTIMATED ERROR:<br>Nothing specified.  |
|  |   |
|  | Nothing specified.  |
|  | Nothing specified.  |
|  | Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.  |
|  | Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.                                      |
|  | Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.<br>2. Havemann, R. Klin. Wochenschr. |
|  | Nothing specified.<br>REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.                                      |

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|   |   | 453  |  |
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| COMPONENTS:   |   | ORIGINAL MEASUREMENTS:   |  |
| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-2-pyri-<br/>midinyl- (sulfadiazine, SD);</li> </ul>  |   | Garcia Onandia, A.; Holz, E.; Holz, S.   |  |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]  |   | Acta Cient. Venezolana <u>1955,</u> 6(4),  |  |
| <pre>(2) Benzenesulfonamide, 4-amino-N-2-thiazo-<br/>lyl- (sulfathiazole, ST);<br/>C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>; [72-14-0]</pre> |   | 157-63.  |  |
| (3) Sodium hydroxide; NaOH; [1310-73-2]   |   |  |  |
| (4) Water;  | H <sub>2</sub> 0; [7732-18-5]               | PREPARED BY:   |  |
| VARIABLES:  | SD/ST ratio                                 | R. Piekos  |  |
| EXPERIMENTAL  | EXPERIMENTAL VALUES:                        |  |  |
|   |   |  |  |
|   | of sulfonamide required to<br>mixt SD/ST at | 5N NaOH solution<br>dissolve the mixture<br>: 25 <sup>0</sup> C  |  |
|   | g/g cm <sup>2</sup>                         | }  |  |
|   | 0.1/0.1 0.55                                | 5  |  |
|   | 0.1/0.2 0.85                                | 5  |  |
|   | 0.1/0.3 1.12                                | 5  |  |
|   | 0.1/0.4 1.37                                | 5  |  |
|   | 0.1/0.5 1.67                                |  |  |
|   | 0.2/0.1 0.85                                |  |  |
|   | 0.3/0.1 1.12                                |  |  |
| 0.4/0.1 1.35  |   |  |  |
|   | 0.5/0.1 1.67                                | 2  |  |
|   | AUXILIARY                                   | INFORMATION  |  |
| METHOD/APPARA   | ATUS/PROCEDURE:                             | SOURCE AND PURITY OF MATERIALS:  |  |
| Nothing spe   | ecified.                                    | Nothing specified.   |  |
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|   |   | ESTIMATED ERROR:   |  |
|   |   | Nothing specified.   |  |
|   |   | REFERENCES:  |  |
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| 154  |                               |  |  |
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| COMPONENTS :   |                               | ORIGINAL MEASUREMENTS:   |  |
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-pyrimidiny1- (sulfadiazine, SD);<br/>C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S; [68-35-9]</li> <li>Benzenesulfonamide, 4-amino-N-2-thiazo-ly1- (sulfathiazole, ST);<br/>C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>; [72-14-0]</li> </ol> |                               | - Holz, E.; Garcia Onandia, A.; Holz, S.                                     |  |
|  |                               | Acta Cient. Venezolana 1955, 6(2),   |  |
|  |                               | 68-73.   |  |
|  |                               |  |  |
| (3) Sodium h   | ydroxide; NaOH; [1310-73-2    | 2]   |  |
| (4) Water;   | H <sub>2</sub> 0; [7732-18-5] | PREPARED BY:   |  |
| VARIABLES:<br>SD/ST ratio  |                               | R. Piekos  |  |
| EXPERIMENTAL   | VALUES:                       |  |  |
|  | of sulfonamide rec            | lume of 1N NaOH soln<br>quired to dissolve the<br>kture at 26 <sup>0</sup> C |  |
|  | g/g                           | cm <sup>3</sup>  |  |
|  | 0.1/0.1                       | 0.825  |  |
|  | 0.1/0.2                       | 1.225  |  |
|  | 0.1/0.3                       | 1.625  |  |
|  | 0.1/0.4                       | 2.025  |  |
|  | 0.1/0.5                       | 2.425  |  |
|  | 0.2/0.1                       | 1.25   |  |
|  | 0.3/0.1                       | 1.675  |  |
|  | 0.4/0.1                       | 2.075  |  |
| 0.5/0.1  |                               | 2.5  |  |
|  | AUXILI                        | ARY INFORMATION  |  |
| METHOD/APPARA  | TUS/PROCEDURE:                | SOURCE AND PURITY OF MATERIALS:  |  |
| Nothing spec   |                               | Not specified. Distd water was used.   |  |
|  |                               |  |  |
|  |                               | ESTIMATED ERROR:   |  |
|  |                               | Not specified.   |  |
|  |                               | REFERENCES :   |  |
|  |                               |  |  |
|  |                               |  |  |
|  |                               |  |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-thiazo-   | ORIGINAL MEASUREMENTS:                     |
|--|--|
| <pre>lyl- (sulfathiazole);</pre>   | Frisk, A. R.; Hagerman, G.;                |
| $C_9 H_9 N_{302} S_2;$ [72-14-0]   | Helander, S.; Sjögren, B. Hygiea           |
| (2) Benzenesulfonamide, 4-amino-N-2-pyri-  | <u>1946,</u> 108(12), 639-51.              |
| midinyl- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9] |  |
| <ul><li>(3) Phosphoric acid, disodium salt;</li></ul>  |  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | DAEDADED DV.                               |
| (4) Phosphoric acid, monopotassium salt;   | PREPARED BY:                               |
| $KH_2PO_4$ ; [7778-77-0]   | R. Piekos                                  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]<br>VARIABLES:   |  |
| One temperature: 37°C; one pH: 6.1   |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of a mixture of sulfathiazo   | $1_{0}$ and sulfadiaging in $Y/30$         |
|  |  |
| phosphate buffer of pH 6.1 at 37°C is  | 113 mg/100 ml solvent.                     |
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| AUXILIARY  | INFORMATION                                |
|  |  |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of sulfathiazole and sulfadiazine                             | SOURCE AND PURITY OF MATERIALS:            |
| -  | Neither source nor purity of the materials |
| in the phosphate buffer was shaken at 37°C   | was specified.                             |
| for 24 h. The concn of the sulfonamides was  |  |
| detd by the Bratton and Marshall method (1)  |  |
| using a photoelec colorimeter.   |  |
|  |  |
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|  | ESTIMATED ERROR:                           |
| 1  | Soly: precision ±11 mg/100 ml (authors).   |
|  |  |
|  | Temp and pH: not specified.                |
|  | REFERENCES:                                |
|  |  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.     |
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|  | 1  |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |  |
|---|--|--|
| (1) Benzenesulfonamide, 4-amino-N-(4-methyl-  |  |  |
| 2-pyrimidinyl)- (sulfamerazine, SM);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | Garcia Onandia, A.; Holz, E.; Holz, S.<br>Acta Cient. Venezolana 1955, 6(4), |  |
| (2) Benzenesulfonamide, 4-amino-N-2-thiazo-   | Acta Cient. Venezolana <u>1955,</u> 6(4),<br>157-63.                         |  |
| lyl- (sulfathiazole, ST);<br>C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S <sub>2</sub> ; [72-14-0] | 1,-01.   |  |
| (3) Sodium Hydroxide; NaOH; [1310-73-2]   |  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]  | PREPARED BY:   |  |
| VARIABLES:  | R. Piekos  |  |
| SM/ST ratio   |  |  |
| EXPERIMENTAL VALUES:  |  |  |
| Composition Volum   | e of 1.5N NaOH soultion  |  |
| of sulfonamide requi  | red to dissolve the  |  |
| mixt SM/ST mi   | xture at 26 <sup>0</sup> C   |  |
| g/g   | cm <sup>3</sup>  |  |
| 0.1/0.1   | 0.54   |  |
| 0.1/0.2   | 0.8  |  |
| 0.1/0.3   | 1.1  |  |
| 0.1/0.4   | 1.375  |  |
| 0.1/0.5   | 1.625  |  |
| 0.2/0.1   | 0.8  |  |
| 0.3/0.1   | 1.1  |  |
| 0.4/0.1   | 1.325  |  |
| 0.5/0.1   | 1.6  |  |
|   |  |  |
|   |  |  |
| METHOD /APPARATUS / PROCEDURE :   | INFORMATION<br>SOURCE AND PURITY OF MATERIALS;                               |  |
|   |  |  |
| Nothing specified.  | Nothing specified.   |  |
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|   | ESTIMATED ERROR:   |  |
|   | Nothing specified.   |  |
|   |  |  |
|   | REFERENCES:  |  |
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|   |  |                  |  | 457                       |
|---|--|------------------|--|---------------------------|
| COMPONENTS :  |  |                  | ORIGINAL MEASUREME   | NTS •                     |
| (1) Benzenesulf   | onamide, 4-amino-N-(4-<br>yl)- (sulfamerazine,<br>; [127-79-7] | -methyl-<br>SM); |  | La Onandia, A.; Holz, S.  |
| <ul> <li>Benzenesulfonamide, 4-amino-N-2-thiazo-<br/>lyl- (sulfathiazole, ST);<br/>C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>0<sub>2</sub>S<sub>2</sub>; [72-14-0]</li> <li>Sodium hydroxide; NaOH; ]1310-73-2]</li> </ul> |  | 68-73.           | 1955, 0127 <b>,</b>  |                           |
|   |  |                  |  |                           |
| (4) Water; H <sub>2</sub>   | 0; [7732-18-5]   |                  | PREPARED BY:   |                           |
| VARIABLES:<br>SM/ST ratio   |  | R. Piekos        | Piekos   |                           |
| EXPERIMENTAL VALU   | JES:   |                  | • • · · · · · · · · · · · · · · · · · ·                                | <u> </u>                  |
|   | Composition<br>of sulfonamide<br>mixture SM/ST                 | requ             | me of 1N NaOH soln<br>ired to dissolve<br>mixture at 26 <sup>0</sup> C | _                         |
|   | g/g  |                  | cm <sup>3</sup>  | -                         |
|   | 0.1/0.1  |                  | 0.8  | -                         |
|   | 0.1/0.2  |                  | 1.2  |                           |
|   | 0.1/0.3  |                  | 1.6  |                           |
|   | 0.1/0.4  |                  | 2.0  |                           |
|   | 0.1/0.5  |                  | 2.5  |                           |
|   | 0.2/0.1  |                  | 1.2  |                           |
|   | 0.3/0.1  |                  | 1.6  |                           |
|   | 0.4/0.1  |                  | 2.0  |                           |
|   | 0.5/0.1  |                  | 2.4  | _                         |
|   | AU   | XILIARY          | INFORMATION  |                           |
| METHOD/APPARATUS  | /PROCEDURE:  |                  | SOURCE AND PURITY  | OF MATERIALS;             |
| Nothing specific  | ed.  |                  | Nothing specifie   | ed. Distd water was used. |
|   |  |                  |  |                           |
|   |  |                  | ESTIMATED ERROR:   |                           |
|   |  |                  | Nothing specifie   | ed.                       |
|   |  |                  | REFERENCES:  |                           |
|   |  |                  |  |                           |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                     |
|--|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-thiazo-<br/>lyl- (sulfathiazole); C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>;</li> </ol> | Frisk, A. R.; Hagerman, G.;                |
| [72-14-0]  | Nolandor S. Silleron P. Huging             |
| (2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl)- (sulfamethylpyrimidine)  |  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]  | <u> </u>                                   |
| (3) Phosphoric acid, disodium salt;  |  |
| $Na_2HPO_4$ ; [7558-94-4]  | PREPARED BY:                               |
| (4) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  | R. Piekos                                  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:   |  |
| One temperature: 37°C; one pH: 6.1   |  |
| EXPERIMENTAL VALUES:   |  |
|  |  |
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|  |  |
| Solubility of a mixture of sulfathiazol  |  |
| phosphate buffer of pH 6.1 at 37 <sup>0</sup> C is 1   | 35 mg/100 ml solvent.                      |
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| AUXILIARY  | INFORMATION                                |
| METHOD /APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:            |
| An excess of sulfathiazole and sulfamethyl-  | Neither source nor purity of the materials |
| pyrimidine in the phosphate buffer was sha-  | was specified.                             |
| ken at 37°C for 24 h. The concn of the sul-  | -  |
| fonamides was detd by the Bratton and Mar-   |  |
| shall method (1) using a photoelec colori-   |  |
| meter.   |  |
| meter.   |  |
|  |  |
| ]  | ESTIMATED ERROR:                           |
|  | Soly: precision ±14 mg/100 ml (authors).   |
|  |  |
|  | Temp and pH: not specified.                |
|  | REFERENCES:                                |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.     |
|  |  |
|  |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-pyri-                             | ORIGINAL MEASUREMENTS:                             |
|--|--|
| midinyl- (sulfadiazine, SD);   | Garcia Onandia, A.; Holz, E.; Holz, S.             |
| $C_{10}H_{10}N_4O_2S;$ [68-35-9]   | Acta Cient. Venezolana <u>1955</u> , 6(4),         |
| (2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl)- (sulfamerazine, SM); | 157-63.  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]          |  |
| (3) Sodium hydroxide; NaOH; [1310-73-2]  |  |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | PREPARED BY:                                       |
| VARIABLES:<br>SD/SM ratio  | R. Piekos  |
|  |  |
| EXPERIMENTAL VALUES:   |  |
|  | ume of 1.5N NaOH solution                          |
|  | uired to dissolve the<br>ture at 26 <sup>0</sup> C |
|  |  |
| g/g  |  |
| 0.1/0.1  | 0.55   |
| 0.1/0.2  | 0.825  |
| 0.1/0.3  | 1.075  |
| 0.1/0.4  | 1.35   |
| 0.1/0.5  | 1.6  |
| 0.2/0.1  | 0.825  |
| 0.3/0.1  | 1.1  |
| 0.4/0.1  | 1.375  |
| 0.5/0.1  | 1.675  |
|  |  |
|  |  |
| AUXILIARY  | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                    |
| Nothing specified.   | Nothing specified.                                 |
| Nothing specified.   | Nothing Specificu.                                 |
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|  | ESTIMATED ERROR:                                   |
|  | Nothing specified.                                 |
|  |  |
|  | REFERENCES:  |
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| midiny1-<br>$C_{10}H_{10}N_4O_{25}$<br>(2) Benzenesuli<br>2-pyrimidin<br>$C_{11}H_{12}N_4O_{25}$<br>(3) Sodium hydr<br>(4) Water; H.<br>VARIABLES: | fonamide, 4-amino-N-(4-mu<br>nyl)- (sulfamerazine, SN<br>S; [127-79-7]<br>roxide; NaOH; [1310-73-<br>2 <sup>0</sup> ; [7732-18-5]<br>SM ratio | ethyl-<br>4);<br>-2] | ORIGINAL MEASUREMENTS:<br>Holz, E.; Garcia Onandia, A.; Holz, S.<br>Acta Cient. Venezolana 1955, 6(2),<br>68-73.<br>PREPARED BY:<br>R. Piekos<br>e of 1N NaOH soln |
|--|---|----------------------|--|
|  | Composition<br>of sulfonamide   | requi                | red to dissolve  |
|  | mixt SD/SM  | the m                | ixture at 26 <sup>°</sup> C  |
|  | 0.1/0.1   |                      | 0.825  |
|  | 0.1/0.2   |                      | 1.2  |
|  | 0.1/0.3   |                      | 1.6  |
|  | 0.1/0.4   |                      | 2.0  |
|  | 0.1/0.5   |                      | 2.4  |
|  | 0.2/0.1   |                      | 1.225  |
|  | 0.3/0.1   |                      | 1.65   |
|  | 0.4/0.1   |                      | 2.075  |
|  | 0.5/0.1   |                      | 2.5  |
|  | AUXI  | LIARY                | INFORMATION  |
| METHOD/APPARATUS   | •   |                      | SOURCE AND PURITY OF MATERIALS:  |
| Nothing spec:  | ltled.  |                      | Nothing specified. Distd water was used.   |
|  |   |                      | ESTIMATED ERROR:   |
|  |   |                      | Nothing specified.   |
|  |   |                      | REFERENCES:  |
|  |   |                      |  |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-pyri-<br>midiny1- (sulfadiazine);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]                   | ORIGINAL MEASUREMENTS:<br>Frisk, A. R.; Hagerman, G.;                         |
|--|---|
| <ul> <li>(2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br/>2-pyrimidinyl)- (sulfamethylpyrimidine)<br/>C11<sup>H</sup>12<sup>N</sup>4<sup>0</sup>2<sup>S</sup>; [127-79-7]</li> </ul> | Helander, S.; Sjögren, B.   |
| <ul> <li>(3) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>   | PREPARED BY:  |
| <ul> <li>(4) Phosphoric acid, monopotassium salt;</li> <li>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul>  | R. Piekos   |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:<br>One temperature: 37 <sup>o</sup> C; one pH: 6.1  |   |
| EXPERIMENTAL VALUES:   |   |
| Solubility of a mixture of sulfadiazin   | e in sulfamethylpyrimidine in M/30  |
| phosphate buffer of pH 6.1 at 37 <sup>0</sup> C is   | 56 mg/100 ml solvent.   |
|  |   |
|  |   |
|  |   |
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|  |   |
| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:<br>An excess of sulfadiazine and sulfamethyl-  | SOURCE AND PURITY OF MATERIALS:<br>Neither source nor purity of the materials |
| pyrimidine in the phosphate buffer was sha-  | was specified.  |
| ken at 37°C for 24 h. The concn of the sul-  |   |
| fonamides was detd by the Bratton and Mar-   |   |
| shall method (1) using a photoelec colori-   |   |
| meter.   |   |
|  |   |
|  |   |
|  | ESTIMATED ERROR:  |
|  | Soly: precision ±6 mg/100 ml (authors).                                       |
|  | Temp and pH: not specified.   |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.                                       |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|  |   |

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| COMPONENTS :  | ORIGINAL MEASUREMENTS:                              |  |  |
|---|---|--|--|
| <pre>(1) Benzenesulfonamide, 4-amino-N-2-pyri-<br/>dinyl- (sulfapyridine);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>S; [144-83-2]</pre>  | Langecker, H.                                       |  |  |
| <ul><li>(2) Acetamide, N-[4](2-pyridinylamino)sul-</li></ul>  | Arch. Exptl. Path. Pharmakol. <u>1948</u> ,         |  |  |
| fony1]pheny1]- (acety1 sulfapyridine);<br>C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S; [19077-98-6]                                   | 205, 291-301.                                       |  |  |
| (3) Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |  |
| VARIABLES:  | PREPARED BY:  |  |  |
| One temperature: 37°C   | R. Piekos   |  |  |
| EXPERIMENTAL VALUES:  |   |  |  |
| Solubility of sulfapyridine and acetyl<br>solution of both compounds in water at<br>mol dm <sup>-3</sup> , compiler ) and 48 mg% ( 1.6 ;<br>respectively. | $37^{\circ}$ C is 131 mg% ( 5.25 x 10 <sup>-3</sup> |  |  |
| AUXILIARY INFORMATION   |   |  |  |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:                     |  |  |
| A mixt of sulfapyridine and acetyl sulfa-   | Nothing specified.                                  |  |  |
|   | Nothing specifica.                                  |  |  |
| pyridine was boiled with water and the com-   |   |  |  |
| ponents were detd colorimetrically by the<br>method of Bratton and Marshall (1) using a   |   |  |  |
| _   |   |  |  |
| Havemann colorimeter (2).   |   |  |  |
|   |   |  |  |
|   | ESTIMATED ERROR:                                    |  |  |
|   | Nothing specified.                                  |  |  |
|   | REFERENCES :  |  |  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.             |  |  |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.              |  |  |
|   | 2. Havemann, R. Klin. Wochenschr.                   |  |  |
|   | <u>1940,</u> p. 503.                                |  |  |
|   |   |  |  |

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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                     |
| (1) Acetamide, N-[4-[[(2-thiazolylamino)-  | Frisk, A. R.; Hagerman, G.;                |
| <pre>sulfonyl]phenyl]- (acetyl sulfathi-<br/>azole); C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S<sub>2</sub>; [127-76-4]</pre>   | Helander, S.; Sjögren, B.                  |
| <ul> <li>Acetamide , N-[4-[(2-pyrimidinylamino)-<br/>sulfonyl] phenyl]- (acetyl sulfapyri-<br/>midine); C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>S; [127-74-2]</li> </ul> | Hygiea, <u>1946,</u> 108(12), 639–51.      |
| (3) Phosphoric acid, disodium salt;  |  |
| Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | PREPARED BY:                               |
| (4) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  | R. Piekos                                  |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   |  |
| VARIABLES:<br>One temperature: 37 <sup>o</sup> C; one pH: 6.1  |  |
| EXPERIMENTAL VALUES:   | -  |
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|  |  |
| Solubility of a mixture of acetyl sulfa  | thiazole and acetyl sulfapyrimidine        |
|  |  |
| in M/30 phosphate buffer of pH 6.1 at 3  | 3/°C is 44 mg/100 ml solvent.              |
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| AUXILIARY  | INFORMATION                                |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:            |
| An excess of acetyl sulfathiazole and acetyl   | Neither source nor purity of the materials |
| sulfapyrimidine in the phosphate buffer was  | was specified.                             |
| shaken at $37^{\circ}$ C for 24 h. The concn of the  |  |
| f  |  |
| acetyl sulfonamides was detd by the Bratton  |  |
| and Marshall method (1) using a photoelec  |  |
| colorimeter.   |  |
|  |  |
|  |  |
|  | ESTIMATED ERROR:                           |
| }  | Soly: precision ±4 mg/100 ml (authors).    |
|  | · · ·                                      |
|  | Temp and pH: not specified.                |
|  | REFERENCES:                                |
|  |  |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.    |
| 1  | J. Biol. Chem. <u>1939</u> , 128, 537.     |
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| COMPONENTS:<br>(1) Acetamide, N-[4-[(2-thiazolylamino)sul-<br>fonyl]phenyl]- (acetyl sulfathiazole);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub> S <sub>2</sub> ; [127-76-4] | ORIGINAL MEASUREMENTS:<br>Frisk, A. R.; Hagerman, G.;<br>Helander, S; Sjögren, B. |
|---|---|
| <ul> <li>Acetamide, N-[4-[[(4-methyl-2-pyrimi-dinyl)amino]sulfonyl]phenyl]- (acetyl sulfamethylpyrimidine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub>S; [127-73-1]</li> </ul>        | Hygiea <u>1946,</u> 108(12), 639-51.  |
| (3) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | PREPARED BY:  |
| <ul> <li>(4) Phosphoric acid, monopotassium salt;</li> <li>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul>   | R. Piekos   |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C; one pH: 6.1   |   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of a mixture of acetyl sulfa   | thiazole and acetyl sulfamethyl-  |
| pyrimidine in M/30 phosphate buffer of $r$  | pH 6.1 at 37 <sup>o</sup> C is 62 mg/100 ml                                       |
| solvent.  |   |
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| AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:   |
| An excess of acetyl sulfathiazole and acetyl  | 1   |
| sulfamethylpyrimidine in the phosphate buf-<br>fer was shaken at 37°C for 24 h. The concn   | was specified.  |
| of the acetylated sulfonamides was detd by  |   |
| the Bratton and Marshall method (1) using a   |   |
| photoelec colorimeter.  |   |
|   |   |
|   |   |
|   | ESTIMATED ERROR:<br>Soly: precision ±6 mg/100 ml solvent                          |
|   | (authors).<br>Temp and pH: not specified.   |
|   | REFERENCES:   |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.  |
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| <pre>COMPONENTS:<br/>(1) Acetamide, N-[4-[(2-pyrimidinylamino)-<br/>sulfonyl]phenyl]- (acetyl sulfapyrimi-<br/>dine); C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>S; [127-74-2]<br/>(2) Acetamide, N-[4-[[(4-methyl-2-pyrimi-<br/>dinyl)amino]sulfonyl]phenyl]- (acetyl<br/>sulfamethylpyrimidine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub>S;<br/>[127-73-1]<br/>(3) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]<br/>(4) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]<br/>(5) Water; H<sub>2</sub>O; [7732-18-5]<br/>VARIABLES:<br/>One temperature: 37<sup>o</sup>C; one pH: 6.1<br/>EXPERIMENTAL VALUES:</pre> | ORIGINAL MEASUREMENTS:<br>Frisk, A. R.; Hagerman, G.;<br>Helander, S.; Sjögren, B.<br>Hygiea 1946, 108(12), 639-51.<br>PREPARED BY:<br>R. Piekos |  |  |  |
| Solubility of a mixture of acetyl sulfapyrimidine and acetyl sulfamethyl-<br>pyrimidine in M/30 phosphate buffer of pH 6.1 at 37 <sup>0</sup> C is 80 mg/100 ml<br>solvent.  |  |  |  |  |
| AUXILIARY  | INFORMATION  |  |  |  |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:  |  |  |  |
| An excess of acetyl sulfapyrimidine and ace-<br>tyl sulfamethylpyrimidine in the phosphate<br>buffer was shaken at 37°C for 24 h. The concr<br>of the acetylated sulfonamides was detd by<br>the Bratton and Marshall method (1) using a<br>photoelec colorimeter.   | Neither source nor purity of the materials<br>was specified.   |  |  |  |
|  | ESTIMATED ERROR:<br>Soly: precision ±8 mg/100 ml (authors).<br>Temp and pH: not specified.   |  |  |  |
|  | REFERENCES:<br>1. Bratton, A. C.; Marshall, E. K., Jr.<br>J. Biol. Chem. <u>1939</u> , 128, 537.   |  |  |  |

|     | ONENTS:  | ORIGINAL MEASUREMENTS:          |             |
|-----|--|---------------------------------|-------------|
| (1) | Benzamide, N-[(4-aminophenyl)sulfonyl]-<br>(sulfabenzamide); C <sub>13</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> S;      | Bhattacharyya, R.;              | Basu, U. P. |
|     | [127-71-9]   | Indian Pharmacist               |             |
| (2) | Benzenesulfonamide, 4-amino-N-2-pyrimi-<br>dinyl- (sulfadiazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S; | 86.                             | <u></u> ,,, |
| (3) | [68-35-9]<br>Benzenesulfonamide, 4-amino-N-(4-methyl-  |                                 |             |
|     | 2-pyrimidinyl)- (sulfamerazine);   |                                 |             |
|     | $C_{11}H_{12}N_4O_2S;$ [127-79-7]  | PREPARED BY:                    |             |
| (4) | Water; H <sub>2</sub> 0; [7732-18-5]   | R. Piekos                       |             |
|     | IABLES:  |                                 |             |
|     | oosition of the sulfonamide mixture  |                                 |             |
|     |  |                                 |             |
|     | Composition of the sulfonamide   | Solubility at 30 <sup>0</sup> C | Final pH    |
|     | mixture  | mg/ml solution                  | [           |
|     |  | mermi corderon                  |             |
|     | (1) : (2) : (3)  |                                 |             |
|     | 7 : 8 : 5  | 30.8                            | 3.8         |
|     | 5 : 8 : 7  | 94.6                            | 5.54        |
|     |  |                                 |             |
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|     | AUXILIARY  | INFORMATION                     |             |
|     | HOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF I          |             |
|     | weighed sample of the sulfonamides was   | Neither source nor p            |             |
| p1  | aced in a clean reagent bottle and a known   | amides was specified            | •           |
| vo  | l of water was added. The mixt was shaken  | Doubly distd water w            | as used.    |
| in  | a mech shaker at 80-100 strokes/min. Af-   | •                               |             |
| te  | r at least 24 h the mixt was filtered  |                                 |             |
| th  | rough a clean, dried and weighed sintered-   |                                 |             |
|     | ass crucible. At the end of the filtra-  |                                 |             |
|     | on the crucible was washed with about 1  |                                 |             |
|     | of water, dried at 105°C for 2-3 h, cool-  |                                 |             |
| 1   |  | LOTTINIED ENKON.                |             |
| 1   | , and weighed to const wt. The pH was  | Soly: not specified             |             |
| 1   | td with a Cambridge bench type pH meter  | Temp: ±0.2°C (auth              |             |
| us  | ing a glass electrode.   | pH : ±0.01 unit (               | authors).   |
|     |  | REFERENCES :                    |             |
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| OMD   | סאר | NTC                |                         |                |          |  | ORIGINAL MEASUREMENTS:                                 |                 |
|---|-----|--------------------|-------------------------|----------------|----------|--|--|-----------------|
| <ol> <li>Benzamide, N-[(4-aminophenyl)sulfonyl]-</li> </ol> |     |                    |                         |                |          |  |  |                 |
|   |     |                    | abe<br>71-              |                | mide);   | <sup>C</sup> 13 <sup>H</sup> 12 <sup>N</sup> 2 <sup>0</sup> 3 <sup>S</sup> ; | Bhattacharyya, R.; Basu,                               | U. P.           |
| 2)  | Be  | nze                | nes                     | ulf            | onamide  | e, 4-amino-N-2-pyrimi-   | Indian Pharmacist <u>1950,</u>                         | 6(3), 77-8,     |
|   |     |                    | <br>5-9                 |                | lfadia   | zine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;      | 86.  |                 |
| 3)  | Be  | nze                | nes                     | ulf            | onamide  | e, 4-amino-N-(4-methyl-  | ]  |                 |
|   | 2-  | руr<br>.н.         | imi<br>2 <sup>N</sup> 4 | din<br>0.S     | y1)- (1) | (sulfamerazine);<br>27-79-7]   |  |                 |
| 4)  |     |                    |                         |                |          | nonopotassium salt;  | PREPARED BY:   |                 |
|   |     |                    | 4;                      |                | 7778-7   |  | R. Piekos  |                 |
| 5)  | So  | diu                | m h                     | ydr            | oxide;   | NaOH; [1310-73-2]  |  |                 |
| 5)  | Wa  | ter                | ;                       | <sup>H</sup> 2 | 0; []    | 732-18-5]  |  |                 |
| /ARI  | AB  | LES                | :                       |                | pН       |  | ]  |                 |
| EXPE  | RI  | MEN                | TAL                     | VA             | LUES:    |  | -  |                 |
|   |     |                    |                         |                |          |  |  |                 |
| Con   | ipo | sit                | ion                     | of             | the      | Solut  | oility at 30°C in M/20 KH <sub>2</sub> PO <sub>4</sub> |                 |
| sul   | fo  | nar                | ide                     | mi             | xture    | Initial pH solut   | ion of pH corrected with                               | Final pH        |
| (parts)   |     | M/20 NaOH solution |                         |                |          |  |  |                 |
| (1)   |     | :                  | (2)                     | :              | (3)      |  | (mg/ml solution)                                       |                 |
|   |     |                    |                         |                |          | <u></u>  |  |                 |
|   | 7   | :                  | 8                       | :              | 5        | 6.18   | 134.5  | 5.50            |
|   | 7   | :                  | 8                       | :              | 5        | 7.05   | 482.8  | 6.45            |
|   | 7   | :                  | 8                       | :              | 5        | 7.45   | 486.6  | 6.7             |
|   | 5   | :                  | 8                       | :              | 7        | 6.18   | 111  | 5.75            |
|   | 5   | :                  | 8                       | :              | 7        | 7.05   | 353.6  | 6.71            |
|   | 5   | :                  | 8                       | :              | 7        | 7.45   | 382.8  | 6.9             |
|   |     |                    |                         |                |          |  |  |                 |
|   |     |                    |                         |                |          |  | ,  |                 |
|   |     |                    |                         |                |          |  |  |                 |
|   |     |                    |                         |                |          |  | <u></u>  |                 |
|   |     |                    |                         |                |          | AUXILIARY  | INFORMATION  |                 |
|   |     |                    |                         |                | S/PROCE  |  | SOURCE AND PURITY OF MATERIA                           |                 |
| A weighed sample of the mixture of sulfon-                  |     |                    |                         | mp1            | e of th  | e mixture of sulfon-   | Neither source nor purity o                            | f the materials |
| amides was placed in a clean reagent bottle                 |     |                    |                         |                | ed in a  | clean reagent bottle   | with the exception of water                            | , was specified |
| nd  | a l | kno                | wn '                    | vo1            | of the   | buffer soln was added.   | The water was doubly distil                            | led.            |

The mixt was shaken in a mech shaker at 80-100 strokes/min. After at least 24 h the mixt was filtered through a clean, dried and weighed sintered-glass crucible. At the end of the filtration the crucible was washed with about 1 ml of water, dried at 105°C for ESTIMATED ERROR: 2-3 h, cooled, and weighed to const wt. The pH was detd with a Cambridge bench type pH meter using a glass electrode.

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Soly: not specified. Temp: ±0.2°C (authors). pH : ±0.01 unit (authors).

**REFERENCES:** 

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| COMPONENTS:   | ORIGINAL MEASUREMENTS:                      |
|---|---|
| (1) Benzamide, N-[(4-aminophenyl)sulfonyl]-<br>(sulfabenzamide); C <sub>13</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> S;                 | Bhattacharyya, R.; Basu, U. P.              |
| [127-71-9]  | Indian Pharmacist <u>1950</u> , 6(3), 77-8, |
| (2) Benzenesulfonamide, 4-amino-N-2-thiazo-<br>lyl- (sulfathiazole); C <sub>g</sub> H <sub>g</sub> N <sub>3</sub> 0 <sub>2</sub> S <sub>2</sub> ; | 86.   |
| [72-14-0]   |   |
| (3) Benzenesulfonamide, 4-amino-N-2-pyrimi-   |   |
| dinyl- (sulfadiazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;<br>[68-35-9]  |   |
| (4) Benzenesulfonamide, 4-amino-N-(4-methyl-  | PREPARED BY:                                |
| 2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]                                   | R. Piekos                                   |
| (5) Water; $H_20$ ; [7732-18-5]   |   |
| (J) water; n <sub>2</sub> 0; [7732-18-3]  |   |
| VARIABLES:<br>One temperature: 30 <sup>0</sup> C  |   |
|   |   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of a mixture containing 3 pa   | rte of sulfabenzamide. 4 marts of           |
|   |   |
| sulfathiazole, 8 parts of sulfadiazine,   |   |
| water <sup>°</sup> at 30 <sup>°</sup> C is 93.4 mg per ml solutio   | n <sup>a</sup> .                            |
|   |   |
| <sup>a</sup> The final pH was 3.5   |   |
| The final ph was 5.5  |   |
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| AUXILIARY   | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| A weighed sample of the sulfonamides was  | Neither source nor purity of the sulfon-    |
| placed in a clean reagent bottle and a known  | amides was specified.                       |
| vol of water was added. The mixt was shaken   | Doubly distd water was used.                |
| in a mech shaker at 80-100 strokes/min. Af-   |   |
| ter at least 24 h the mixt was filtered   |   |
| through a clean, dried and weighed sintered-  |   |
| glass crucible. At the end of the filtration  |   |
| the crucible was washed with about 1 ml of  |   |
| water, dried at 105°C for 2-3 h, cooled, and  |   |
|   | ESTIMATED ERROR:<br>Soly: not specified.    |
| weighed to const wt. The pH was detd with a   | Temp: $\pm 0.2^{\circ}$ C (authors).        |
| Cambridge bench type pH meter using a glass   | -   |
| electrode.  | pH : ±0.01 unit (authors).                  |
|   | REFERENCES :                                |
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|   |   |

| (2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl- (sulfamerazine, SM); 157-63.  | Holz, S. |
|--|----------|
| dinyl- (sulfadiazine, SD);<br>C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]<br>(2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl- (sulfamerazine, SM);<br>Garcia Onandia, A.; Holz, E.;<br>Acta Cient. Venezolana 1955<br>157-63. |          |
| C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; [68-35-9]<br>(2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl- (sulfamerazine, SM);<br>Acta Cient. Venezolana <u>1955</u><br>157-63.   |          |
| (2) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl- (sulfamerazine, SM); 157-63.  |          |
| 2-pyrimidinyi- (Sullamerazine, Sh),  | •        |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]  |          |
| (3) Benzenesulfonamide, 4-amino-N-2-thiazo-  |          |
| lyl- (sulfathiazole, ST); PREPARED BY:   |          |
| C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S <sub>2</sub> ; [72-14-0]<br>(4) Sodium hydroxide; NaOH; [1310-73-2] R. Piekos  |          |
| (4) Sodium nydroxide; Naon, [1510-75-2]  |          |
| (5) Water; H <sub>2</sub> 0; [7732-18-5]   |          |
| SD/SM/ST ratio   |          |
| EXPERIMENTAL VALUES:   |          |
| Compostion of Volume of 1.5N NaOH soln Composition of Volume of 1  |          |
| sulfonamide mixt required to dissolve the sulfonamide soln requir<br>SD/SM/ST mixture at 26°C mixt SD/SM/ST solve the m  |          |
|  |          |
| g/g/g cm <sup>3</sup> g/g/g cm <sup>3</sup>  |          |
| 0.1/0.1/0.1 0.825 0.1/0.1/0.2 1.1  |          |
| 0.1/0.2/0.2 1.375 0.1/0.1/0.3 1.375  |          |
| 0.1/0.3/0.3 1.9 0.1/0.1/0.4 1.675  |          |
| 0.1/0.4/0.4 2.425 0.1/0.1/0.5 1.925  |          |
| 0.1/0.5/0.5 2.975 0.1/0.2/0.1 1.075  |          |
| 0.2/0.1/0.2 1.375 0.1/0.3/0.1 1.35   |          |
| 0.3/0.1/0.3 1.925 0.1/0.4/0.1 1.6  |          |
| 0.4/0.1/0.4 2.45 0.1/0.5/0.1 1.875   |          |
| 0.5/0.1/0.5 3.025 0.2/0.1/0.1 1.1  |          |
| 0.2/0.2/0.1 1.375 0.3/0.1/0.1 1.375  |          |
| 0.3/0.3/0.1 1.9 0.4/0.1/0.1 1.675  |          |
| 0.4/0.4/0.1 2.475 0.5/0.1/0.1 1.95   |          |
| 0.5/0.5/0.1 3.025  |          |
|  |          |
| AUXILIARY INFORMATION  |          |
| METHOD/APPARATUS/PROCEDURE: SOURCE AND PURITY OF MATERIALS:  |          |
| Nothing specified. Nothing specified.  |          |
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|  |          |
|  |          |
| ESTIMATED ERROR:   |          |
| Nothing specified.   |          |
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| REFERENCES:  |          |
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| COMPONENTS:  |   |   | ORIGINAL MEASUREMENTS:                 |                          |  |
|--|---|---|--|--------------------------|--|
| <ul> <li>Benzenesulfonamide, 4-amino-N-2-pyrimi-<br/>dinyl- (sulfadiazine, DS);</li> <li>C10H10N602S; [68-35-9]</li> </ul> |   |   | Holz, E.; Garcia Onandia, A.; Holz, S. |                          |  |
|  | 10 10 4 2                                       |   | Acta Cient. Venez                      | olana <u>1955,</u> 6(2), |  |
| (2)  | 2-pyrimidiny1)-                                 | e, 4-amino-N-(4-methyl-<br>(sulfamerazine, SM); | 68-73.                                 |                          |  |
|  | II IC 7 C                                       | 27-79-7]  |  |                          |  |
| (3)  |   | e, 4-amino-N-2-thiazo-                          |  |                          |  |
| {  | lyl- (sulfathiaz                                | ole, ST);<br>2-14-0]                            | PREPARED BY:                           |                          |  |
|  | 99522   | -   | R. Pie                                 | ekos                     |  |
| (4)<br>(5)   | Sodium hydroxide;<br>Water; H <sub>2</sub> O; [ | NaOH; [1310-73-2]<br>7732-18-5]                 |  |                          |  |
|  | IABLES:   |   |  |                          |  |
| . · · · ·  |   | ST ratio  |  |                          |  |
| EXP  | ERIMENTAL VALUES:                               |   | 4                                      |                          |  |
|  | omposition of                                   | Volume of 1N NaOH soln                          | Composition of                         | Volume of 1N NaOH        |  |
|  | ulfonamide mixt                                 | required to dissolve                            | sulfonamide                            | soln required to         |  |
| 1  | SD/SM/ST  | the mixt at 26°C                                | mixt SD/SM/ST                          | dissolve the mixt        |  |
|  |   | cm <sup>3</sup>                                 | g/g/g                                  | cm <sup>3</sup>          |  |
|  | g/g/g   | Cill  | 6/6/6                                  | Сш                       |  |
| 1  | 0.1/0.1/0.1                                     | 1.25  | 0.4/0.1/0.4                            | 3.725                    |  |
|  | 0.1/0.1/0.2                                     | 1.625   | 0.5/0.1/0.5                            | 4.5                      |  |
| 1  | 0.1/0.1/0.3                                     | 2.025   | 0.2/0.1/0.1                            | 1.65                     |  |
|  | 0.1/0.1/0.4                                     | 2.425   | 0.3/0.1/0.1                            | 2.075                    |  |
|  | 0.1/0.1/0.5                                     | 2.85  | 0.4/0.1/0.1                            | 2.5                      |  |
| 1  | 0.1/0.2/0.2                                     | 2.05  | 0.5/0.1/0.1                            | 2.9                      |  |
|  | 0.1/0.3/0.3                                     | 2.825   | 0.2/0.2/0.1                            | 2.05                     |  |
|  | 0.1/0.4/0.4                                     |   | 0.3/0.3/0.1                            | 2.85                     |  |
|  | • •   | 3.65  | 0.4/0.4/0.1                            | 3.7                      |  |
|  | 0.1/0.5/0.5                                     | 4.425   |  | 4.45                     |  |
|  | 0.1/0.2/0.1                                     | 1.625   | 0.5/0.5/0.1                            | 4.45                     |  |
|  | 0.1/0.3/0.1                                     | 2.025   |  |                          |  |
|  | 0.1/0.4/0.1                                     | 2.425   |  |                          |  |
|  | 0.1/0.5/0.1                                     | 2.825   |  |                          |  |
| 1  | 0.2/0.1/0.2                                     | 2.05  |  |                          |  |
| ł  | 0.3/0.1/0.3                                     | 2.975   |  |                          |  |
|  |   |   |  |                          |  |
|  |   | AUXILIARY                                       | INFORMATION                            |                          |  |
| MET  | HOD/APPARATUS/PROCI                             | EDURE:  | SOURCE AND PURITY OF                   | MATERIALS:               |  |
|  | thing specified.                                |   | Not specified. Div                     | std water was used.      |  |
|  | ching specified.                                |   |  |                          |  |
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| 1  |   |   |  |                          |  |
|  |   |   | ESTIMATED ERROR:                       |                          |  |
| 1  |   |   | Nothing specified.                     |                          |  |
|  |   |   |  |                          |  |
|  |   |   |  |                          |  |
|  |   |   | REFERENCES:                            |                          |  |
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| (1) Benzenesulfonamide, 4-amino-N-2-thiazo-<br>ly1- (sulfathiazole); $C_9H_9N_3O_2S_2$ ;<br>[72-14-0]<br>(2) Benzenesulfonamide, 4-amino-N-2-pyrimi-<br>diny1- (sulfadiazine); $C_{10}H_{10}N_4O_2S$ ;<br>[68-35-9]<br>(3) Benzenesulfonamide, 4-amino-N-(4-methy1-<br>2-pyrimidiny1)- (sulfamerazine);<br>$C_{11}H_{12}N_4O_2S$ ; [127-79-7]<br>(4) Phosphoric acid, monopotassium salt;<br>$KH_2PO_4$ ; [7778-77-0]<br>(5) Sodium hydroxide; NaOH; [1310-73-2]<br>(6) Water; $H_2O$ ; [7732-18-5]<br>VARIABLES:<br>PH<br>EXPERIMENTAL VALUES:  | lazine, and sulfamera- |  |  |  |
|--|------------------------|--|--|--|
|  | lazine, and sulfamera- |  |  |  |
| Initial pH Solubility at 30°C of a mixture of 1 part each Final pH<br>of sulfathiazole, sulfadiazine, and sulfamera-<br>zine in M/20 KH <sub>2</sub> PO <sub>4</sub> solution of pH corrected<br>with M/20 NaOH solution   |                        |  |  |  |
| mg/ml solu   | Lution                 |  |  |  |
| 6.18 114.8   | 8 6.24                 |  |  |  |
| 7.05 212   | 7.49                   |  |  |  |
|  |                        |  |  |  |
| AUXILIARY IN   | FORMATION              |  |  |  |
| AUXILIARY INFORMATION<br>METHOD/APPARATUS/PROCEDURE:<br>A weighed sample of the sulfonamides was pla-<br>ced in a clean reagent bottle and a known vol<br>of the M/20 KH <sub>2</sub> PO <sub>4</sub> soln was added, and the pH<br>was adjusted to the desired value with M/20<br>NaOH soln. The mixt was shaken in a mech<br>shaker at 80-100 strokes/min. After at least<br>24 h the mixt was filtered through a clean,<br>dried and weighed sintered-glass crucible.<br>At the end of the filtration the crucible was<br>washed with about 1 ml of water, dried at<br>105°C for 2-3 h, cooled, and weighed to const<br>wt. The pH was detd with a Cambridge bench<br>type pH meter using a glass electrode.<br>BUXILIARY INFORMATION<br>METHOD/APPARATUS/PROCEDURE:<br>Solurce AND PURITY OF MATERIALS:<br>Neither source nor purity of the materi<br>with the exception of water, was specif<br>The water was doubly distilled.<br>Solurce AND PURITY OF MATERIALS:<br>Neither source nor purity of the materi<br>with the exception of water, was specif<br>The water was doubly distilled.<br>ESTIMATED ERROR:<br>Soly: not specified.<br>Temp: ±0.2°C<br>pH : ±0.01 unit (authors).<br>REFERENCES: |                        |  |  |  |

|  | ONENTS:   | ORIGINAL MEASUREMENTS:                      |  |  |  |
|--|---|---|--|--|--|
| (1)  | Benzenesulfonamide, 4-amino-N-2-thiazo-<br>lyl- (sulfathiazole); C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S <sub>2</sub> ; | Frisk, A. R.; Hagerman, G.;                 |  |  |  |
|  | [72-14-0]   | Helander, S.; Sjögren, B.                   |  |  |  |
| (2)  | Benzenesulfonamide, 4-amino-N-2-pyrimi-   | Hygiea 1946, 108(12), 639-51.               |  |  |  |
|  | diny1- (sulfapyrimidine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;<br>[68-35-9]                                       | <i>nyyteu</i> <u>1940,</u> 100(12), 039-51. |  |  |  |
| (3)  | Benzenesulfonamide, 4-amino-N-(4-methyl-  |   |  |  |  |
|  | 2-pyrimidinyl)- (sulfamethylpyrimidine);  |   |  |  |  |
|  | $C_{11}H_{12}N_4O_2S;$ [127-79-7]   | PREPARED BY:                                |  |  |  |
| (4)  | Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]   | R. Piekos                                   |  |  |  |
| (5)  | Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   |   |  |  |  |
| (6)  | Water; H <sub>2</sub> 0; [7732-18-5]  |   |  |  |  |
| VAR  | IABLES:   |   |  |  |  |
| <b>]</b> 0:  | ne temperature: 37 <sup>0</sup> C; one pH: 6.1  |   |  |  |  |
| EXP  | ERIMENTAL VALUES:   |   |  |  |  |
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|  | Solubility of a mixtrue of sulfathiazol   | le, sulfapyrimidine and sulfamethyl-        |  |  |  |
|  |   |   |  |  |  |
| pyrimidine in M/30 phosphate buffer of pH 6.1 at $37^{\circ}$ C is 160 mg/100 ml |   |   |  |  |  |
| 1  | solvent.  |   |  |  |  |
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|  | AUXILIARY INFORMATION   |   |  |  |  |
| METH   | HOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:             |  |  |  |
| An   | excess of sulfathiazole, sulfapyrimidine  | Neither source nor the purity of the mate-  |  |  |  |
| and  | sulfamethylpyrimidine in the phosphate  | rials was specified.                        |  |  |  |
|  | fer was shaken at 37°C for 24 h. The  |   |  |  |  |
|  | cn of the sulfonamides was detd by the  |   |  |  |  |
|  | -   |   |  |  |  |
|  | tton and Marshall method (1) using a pho-   |   |  |  |  |
| toe  | lec colorimeter.  |   |  |  |  |
| 1  |   |   |  |  |  |
|  |   |   |  |  |  |
| l  |   | ESTIMATED ERROR:                            |  |  |  |
|  |   | Soly: precision ±0.7 mg/100 ml (authors).   |  |  |  |
|  |   | Temp and pH: not specified.                 |  |  |  |
| 1  |   |   |  |  |  |
| 1  |   | L   |  |  |  |

REFERENCES:

 Bratton, A. C.; Marshall, E. K., Jr. J. Biol. Chem. <u>1939</u>, 128, 537.

|   | 473  |
|---|--|
| COMPONENTS:   | ORIGINAL MEASUREMENTS:                                   |
| <pre>(1) Acetamide, N-[4-[(2-thiazolylamino)sul-<br/>fonyl]phenyl]- (acetyl sulfathiazole);<br/>C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>S<sub>2</sub>; [127-76-4]</pre> | Frisk, A. R.; Hagerman, G.;<br>Helander, S.; Sjögren, B. |
| (2) Acetamide, N-[4-[(2-pyrimidinylamino)-<br>sulfonyl]phenyl]- (acetyl sulfapyrimi-<br>dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]            | ·Hygiea <u>1946</u> , 108(12), 639-51.                   |
| (3) Acetamide, N-[4-[[(4-methyl(2-pyrimidinyl)<br>amino]sulfonyl]phenyl]- (acetyl sulfa-<br>methylpyrimidine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S;       | PREPARED BY:   |
| <pre>[127-73-1] (4) Phosphoric acid, disodium salt; Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</pre>  | R. Piekos  |
| (5) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   |  |
| (6) Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C; one pH 6.1  |  |
| EXPERIMENTAL VALUES:  |  |
|   |  |
|   |  |
| Solubility of a mixture of acetyl sulfat  | hiazole, acetyl sulfapyrimidine, and                     |
| acetyl sulfamethylpyrimidine in M/30 pho  | sphate buffer of pH 6.1 at 37 <sup>0</sup> C is          |
| 89 mg/100 ml solvent.   |  |
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| AUXILIARY INFORMATION   |  |
| METHOD /APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:                          |
| An excess of acetyl sulfathiazole, acetyl   | Neither source nor purity of the materials               |
| sulfapyrimidine and acetyl sulfamethylpyri-   | was specified.   |
| midine in the phosphate buffer was shaken at  |  |
| 37 <sup>0</sup> C for 24 h. The concn of the acetylated   |  |
| sulfonamides was detd by the Bratton and Mar-   |  |
| shall method (1) using a photoelec colorime-  |  |
| ter.  |  |
|   | ESTIMATED ERROR:   |
|   | Soly: precision ±9 mg/100 ml (authors).                  |
|   | Temp and pH: not specified.                              |
|   | REFERENCES:  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.                  |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.                   |
|   |  |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                    |
|--|---|
| <ol> <li>Benzenesulfonamide, 4-amino-N-(4,6-di-<br/>methyl-2-pyrimidinyl)- (sulfamethazine)</li> </ol>                                 |   |
| $C_{12}H_{14}N_4O_2S;$ [57-68-1]   | Danderin, r. J., Haresh, w.               |
| (2) Benzenesulfonamide, 4-amino-N-(4-meth-   |   |
| yl-2-pyrimidinyl)- (sulfamerazine);  | <u>1959,</u> 48, 177-81.                  |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]  |   |
| (3) Benzenesulfonamide, 4-amino-N-2-pyrimi-<br>dinyl- (sulfadiazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> 0 <sub>2</sub> S; |   |
| [68-35-9]  | PREPARED BY:                              |
| (4) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | R. Piekos                                 |
| (5) Phosphoric acid, monopotassium salt;   |   |
| KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]  |   |
| (6) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:   | 1   |
| pH at 37°C   | j   |
| EXPERIMENTAL VALUES:   |   |
| Solubility of a 1:1:1 (by wt.) mixture   | of the three sulfonamides (triple         |
| sulfonamide) in buffers of varying mixtures of the following solutions:  |   |
| $Na_2HPO_4 \cdot 7H_2O$ 71.6 g/l of distilled water (0.27 mol dm <sup>-3</sup> , compiler );   |   |
| $KH_2PO_2$ 36.3 g/l of distilled water (0.27 mol dm <sup>-3</sup> , compiler ) at 37°C   |   |
| Initial pH Sc  | lubility in mg/100 ml buffer              |
| 4.5  | 96  |
| 5.0  | 98  |
| 5.5  | 102                                       |
| 6.0  | 109                                       |
| 6.5  | 130; 139 <sup>a</sup>                     |
| 7.0  | 192                                       |
| 7.5  | 209                                       |
|  |   |
| <sup>a</sup> obtained by extrapolation of the solubility curve.  |   |
| AUXILIARY INFORMATION  |   |
| METHOD / APPARATUS / PROCEDURE :   | SOURCE AND PURITY OF MATERIALS:           |
| Solns were prepd by adding an excess of the  | Neither source nor the purity of the rea- |
| sulfonamides to 10 ml of buffer soln at each   |   |
| pH level in 18 x 150-mm test tubes, stopper-   |   |
| ing the tubes, placing in a water bath at 37   |   |
| C with gentle agitation for 24 h. The mixt   |   |
| was then filtered and a 1-ml aliquot was ac-   |   |
| curately pipetted into a volumetric flask fo   |   |
| diln and analysis. The balance was retained  |   |
| for pH detn to ascertain any change in pH va   |   |
| lue. The sulfonamides were assayed colorime  |   |
| trically at 545 nm by the method of Bratton  | lysis (authors).                          |
| and Marshall as described in detail by Bia-  | Temp: nothing specified.                  |
|  | pH : nothing specified.<br>REFERENCES:    |
| mente and Schneller (1). Standard curves   | 1 Birmonto A P : Schnollor C F            |
| were prepd for individual sulfonamides using   | ,,,,,                                     |

 J. Am. Pharm. Assoc., Sci. Ed., <u>1952</u>, 41, 341.

accurately prepd std solns.

| COMPONENTS:  | ORIGINAL MEASUREMENTS:                              |
|--|---|
| (1) Benzenesulfonamide, 4-amino-N-2-pyri-  | Langaskan H   |
| midinyl- (sulfapyrimidine);<br>CloHloN/02S; [68-35-9]                              | Langecker, H.                                       |
| 10 10 4 2 *  | Arch. Exptl. Path. Pharmakol. 1948,                 |
| (2) Acetamide, N-[4-[(2-pyrimidinylamino)-<br>sulfonyl]phenyl]- (acetyl sulfapyri- | 205, 291-301.                                       |
| midine); $C_{12}H_{12}N_4O_3S$ ; [127-74-2]  |   |
| (3) Water; $H_20$ ; [7732-18-5]  |   |
|  | PREPARED BY:  |
| VARIABLES:   |   |
| One temperature: 37°C  | R. Piekos   |
|  |   |
| EXPERIMENTAL VALUES:   |   |
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| Solubility of sulfapyrimidine and acet   | al cultonuminiding in a coturated                   |
| Solubility of sulfapyrimidine and acet   | yr sullapyrimidine in a saturated                   |
| solution of both compounds in water at   | $37^{\circ}$ C is 176 mg% (7.0 x 10 <sup>-3</sup>   |
|  |   |
| mol $dm^{-3}$ , compiler) at 47 mg% ( 1.6 x  | 10 <sup>-5</sup> mol dm <sup>-5</sup> , compiler ), |
| respectively.  |   |
| respectively.  |   |
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| AUXILIARY  | INFORMATION   |
| METHOD/APPARATUS/PROCEDURE:  | COURCE AND DUDING OF MAREDIALC.                     |
|  | SOURCE AND PURITY OF MATERIALS:                     |
| A mixt of sulfapyrimidine and acetyl sulfa-  | Nothing specified.                                  |
| pyrimidine was boiled with water and the   |   |
| components were detd colorimetrically by   |   |
| the method of Bratton and Marshall (1) using                                       |   |
|  |   |
| a Havemann colorimeter (2).  |   |
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|  | ESTIMATED ERROR:                                    |
|  | Nothing specified.                                  |
|  |   |
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|  | REFERENCES :  |
|  |   |
| }  | 1. Bratton, A. C.; Marshall, E. K., Jr.             |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.              |
|  | 2. Havemann, R. Klin. Wochenschr.                   |
| }  | 1940, p. 503.                                       |
|  | <u></u> p. 505.                                     |
|  |   |

| COMPONENTS:  | ORIGINAL MEASUREMENTS:            |  |
|--|-----------------------------------|--|
| <ol> <li>Benzenesulfonamide, 4-amino-N-2-pyrimi-<br/>dinyl- (sulfadiazine); C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>0<sub>2</sub>S;<br/>[68-35-9]</li> <li>Benzenesulfonamide, 4-amino-N-(4-methyl-<br/>2-pyrimidinyl)- (sulfamerazine);<br/>C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>0<sub>2</sub>S; [127-79-7]</li> </ol> | Biamonte, A. R.; Schneller, G. H. |  |
| (3) Benzenesulfonamide, 4-amino-N-(4,6-di-<br>methyl-2-pyrimidinyl)- (sulfamethazine);<br>C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> 0 <sub>2</sub> S; [57-68-1]   | PREPARED BY:                      |  |
| (4) Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  | R. Piekos                         |  |
| <pre>(5) 1,2,3-Propanetricarboxylic acid, 2-hy-<br/>droxy- (citric acid); C<sub>6</sub>H<sub>8</sub>O<sub>7</sub>;<br/>[77-92-9]<br/>(6) Water; H<sub>2</sub>O; [7732-18-5]</pre>  |                                   |  |
| VARIABLES:   |                                   |  |
| pH   |                                   |  |
| EXPERIMENTAL VALUES:   |                                   |  |
| Solubility of a mixture of equal portion   |                                   |  |
| and sulfamethazine in McIlvaine's disodium phosphate - citric acid buffer  |                                   |  |

## solutions at 37°C

| Initial pH<br>of buffer | Solubility<br>(mg/100 ml solution) | Final pH |
|-------------------------|------------------------------------|----------|
| 4.5                     | 95.9                               | 4.5      |
| 5.0                     | 98.4                               | 5.0      |
| 6.0                     | 108.9                              | 5.8      |
| 7.0                     | 186.0                              | 6.9      |
| 8.0                     | 476.0                              | 7.5      |
|                         |                                    |          |

## AUXILIARY INFORMATION

| METHOD/APPARATUS/PROCEDURE:                             | SOURCE AND PURITY OF MATERIALS:  |
|---|--|
| A sample large enough to supply an excess o             | f The source and purity of the materials was   |
| each constituent was equilibrated in buffer             | not specified. The mp of sulfadiazine,   |
| solns at 37 <sup>0</sup> C for 18 h with agitation. The | sulfamerazine and sulfamethazine was 253.5-  |
| suspension was then immediately filtered                | 4.5°C, 235.5-6.5°C, and 197.7-8.6°C, resp.   |
| through a Whatman No. 1 paper. The filtra-              |  |
| tion time was approx 2 min. The sulfonami-              |  |
| des in the filtrate were assayed spectropho-            | -  |
| tometrically by the method of Bratton and               |  |
| Marshall (1) using a Beckmann DU spectropho             |  |
| tometer.  | pH and temp: not specified. Accuracy of the  |
|   | anal method was illustrated by the following values: expected 2.003, 3.004, 4.006, 5.007 |
|   | mg/100 ml; found: 2.08, 3.06, 4.12, 5.10.  |
|   | REFERENCES:  |
|   | 1. Bratton, A. C.; Marshall, E. K., Jr.  |
|   | J. Biol. Chem. <u>1939</u> , 128, 537.   |
|   |  |
|   |  |
|   |  |

| COMPONENTS:<br>(1) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimi-  | ORIGINAL MEASUREMENTS:                                    |
|---|---|
| dinyl)amino]sulfonyl]phenyl]- (acetyl   | Bandelin, F. J.; Malesh, W.                               |
| sulfamethazine); $C_{14}H_{16}N_4O_3S$ ; [100-90-3]   | J. Am. Pharm. Assoc., Sci. Ed.                            |
| (2) Acetamide, N-4-[[(4-methyl-2-pyrimidinyl)<br>amino]sulfonyl]phenyl]- (acetyl sulfa-<br>merazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> 0 <sub>3</sub> S; [127-73-1] | <u>1959,</u> 48, 177-81.                                  |
| (3) Acetamide, N-[4-[(2-pyrimidinylamino)sul-<br>fonyl]phenyl]- (acetyl sulfadiazine);<br>C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]             | PREPARED BY:  |
| <ul> <li>(4) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</li> </ul>  | R. Piekos   |
| (5) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   |   |
| (6) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES:<br>pH at 37°C  |   |
| ·   |   |
| EXPERIMENTAL VALUES:  |   |
| Solubility of acetylated 1:1:1 (by wt.)   |   |
| of varying mixtures of the following sol  |   |
| distilled water (0.27 mol $dm^{-3}$ , compiler  | ), KH <sub>2</sub> PO <sub>4</sub> 36.3 g/1 of distilled  |
| water (0.27 mol dm <sup>-3</sup> , compiler ) at 37°C   |   |
| Equilibrium pH mg/100 ml of bu  | ffer based on free sulfonamides                           |
| 4.5   | 116   |
| 5.0   | 121   |
| 5.5   | 132   |
| 6.0   | 158   |
| 6.4   | 216   |
| 6.5   | 230 <sup>a</sup>  |
| 7.0   | 420 <sup>a</sup>  |
| 7.1   | 490   |
| <sup>a</sup> obtained by extrapolation of the solub   | ility curve.  |
| AUXILIARY   | INFORMATION   |
| METHOD / APPARATUS / PROCEDURE :  | SOURCE AND PURITY OF MATERIALS:                           |
| Solns were prepd by adding an excess of the   | Neither source nor the purity of the rea-                 |
| acetyl derivs to 10 ml of buffer soln at  | gents were specified.                                     |
| each pH level in 18 x 150-mm test tubes,  | Distilled water was used.                                 |
| stoppering the tubes, placing in a water bath   |   |
| at 37°C with gentle agitation for 24 h. The   |   |
| mixt was then hydrolyzed with 5% $H_2SO_4$ for 1  |   |
| h to liberate the free sulfonamides. One-ml   |   |
| aliquot was accurately pipetted into a volu-  |   |
| metric flask for diln and analysis. The sul-  |   |
| fonamides were assayed colorimetrically at  | Soly: duplicate samples were used for analysis (authors). |
| 545 nm by the method of Bratton and Marshall  | Temp: Nothing specified.                                  |
| as described in detail by Biamonte and  | pH : Nothing specified.                                   |
| Schneller (1). Standard curves were prepd   | REFERENCES:   |
| for individual sulfonamides using accurately  |   |
| prepd std solns.  | J. Am. Pharm. Assoc., Sci. Ed.,                           |
|   | <u>1952,</u> 41, 341.                                     |
|   |   |

| COMPONENTS:   | ORIGINAL MEASUREMENTS:   |
|---|--|
| (1) Benzenesulfonamide, 4-amino-N-(4,6-di-  |  |
| methyl-2-pyrimidinyl)-, (sulfameth-   | Bandelin, F. J.; Malesh, W.,                                   |
| azine); C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S; [57-68-1]                    | J. Am. Pharm. Assoc., Sci. Ed.                                 |
| (2) Benzenesulfonamide, 4-amino-N-(4-methyl-  | <u>1959,</u> 48, 178-81.                                       |
| 2-pyrimidinyl)-, (sulfamerazine);   |  |
| C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]                           |  |
| (3) Benzenesulfonamide, 4-amino-N-2-pyrimi-   | PREPARED BY:   |
| diny1-, (sulfadiazine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;<br>[68-35-9] | R. Piekos  |
| (4) Calcium chloride; CaCl <sub>2</sub> ; [10043-52-4]  |  |
| (5) Magnesium chloride; MgCl <sub>2</sub> ; [7786-30-3]   |  |
| (6) Phosphoric acid, monoammonium salt;   |  |
| NH <sub>4</sub> H <sub>2</sub> PO <sub>4</sub> ; [7722-76-1]  |  |
| (7) Potassium chloride; KC1; [7447-40-7]  |  |
| (8) Sodium chloride; NaCl; [7647-14-5]  |  |
| (9) Urea; CH <sub>4</sub> N <sub>2</sub> O; [57-13-6]   |  |
| (10) Water; H <sub>2</sub> O; [7732-18-5]   |  |
|   |  |
| VARIABLES:  |  |
| pH at 37 <sup>0</sup> C   |  |
| EXPERIMENTAL VALUES:  |  |
|   |  |
| Continued on the next page.   |  |
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| AUXILIARY   | INFORMATION  |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:                                |
| Excess sulfonamides was added to aliquots of  | Nothing specified.   |
| synthetic urine solutions and 1% $H_3PO_4$ or 1%  |  |
| NaOH solns were used to adjust the pH to the  |  |
| required value. The solns were agitated for   |  |
| 24 h with addn of acid or base to keep them   |  |
| at the desired pH level until equilibrium   |  |
| in pH and concn was attained. The solns were  | e  |
| filtered and in aliquots the sulfonamides   |  |
| were assayed spectrophotometrically by a me-  |  |
| thod described by Biamonte and Schneller (1)  | ESTIMATED ERROR:<br>Soly: average values of 2 detns are given. |
| and described by blamonice and Schneiter (1)  |  |
|   | Temp: not specified.   |
|   | pH : not specified.<br>REFERENCES:                             |
|   |  |
|   | 1. Biamonte, A. R.; Schneller, G. E.,                          |
|   | J. Am. Pharm. Assoc., Sci. Ed.                                 |
|   | 1952, 41, 341.   |
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| COMPONENTS:                                 | ORIGINAL MEASUREMENTS: (CONTINUED)      |
|---|---|
| (1) Sulfamethazine; $C_{12}H_{14}N_4O_2S$ ; | Bandelin, F.; Malesh, W.,               |
| [57-68-1]                                   | J. Am. Pharm. Assoc., Sci. Ed.          |
| (2) Sulfamerazine; $C_{11}H_{12}N_4O_2S;$   | <u>1959</u> , <i>48</i> , 177-81.       |
| [127-79-7]                                  |   |
| (3) Sulfadiazine; $C_{10}H_{10}N_4O_2S;$    |   |
| [68-35-9]                                   | PREPARED BY:                            |
| (4) - (10) Synthetic urine                  | R. Piekos                               |
| see previous page for details               |   |
| EXPERIMENTAL VALUES:                        |   |
| Solubility of a 1:1:1 (by wt.) mixture      | e of the three sulfonamides (triple     |
| sulfonamide) in a solution containing       |   |
| 0.300, KCl 1.660, NaCl 2.950 and urea       |   |
| Vehicle) at 37 <sup>o</sup> C               |   |
|   |   |
| Equilibrium pH                              | Solubility<br>3/100 ml synthetic urine) |
|   | -                                       |
| 4.5   | 100                                     |
| 5.0   | 108                                     |
| 5.5   | 118                                     |
| 6.0   | 136                                     |
| 6.4   | 182                                     |
| 7.1   | 275 .                                   |
|   |   |
| AUXILIA                                     | RY INFORMATION                          |
| METHOD/APPARATUS/PROCEDURE:                 | SOURCE AND PURITY OF MATERIALS:         |
| HE THOD/AFFARATOS/FROCEDORE.                | SOURCE AND FURITI OF MATERIALS;         |
|   |   |
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|   | ESTIMATED ERROR:                        |
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|   | REFERENCES :                            |
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| COMPC<br>(1)<br>(2)<br>(3) | DNENTS:<br>Acetamide, N-[4-[(2-pyrimidinylamino)-<br>sulfonyl]phenyl]- (acetyl sulfadiazine<br>C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]<br>Acetamide, N-[4-[(4-methyl-2-pyrimidin-<br>ylamino)sulfonyl]phenyl]- (acetyl sul-<br>famerazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S; [127-73-1]<br>Acetamide, N-[4-[[(4,6-dimethyl-2-pyri- | J. Am. Pharm. Assoc., Sci. Ed.<br><u>1952,</u> 41, 341-5.   |
| (4)                        | midinyl)amino]sulfonyl]phenyl]- (acety<br>sulfamethazine); $C_{14}H_{16}N_4O_3S$ ; [100-90-3<br>Phosphoric acid, disodium salt;<br>Na <sub>2</sub> HPO <sub>4</sub> ; [7558-94-4]  |   |
| (5)                        | 1,2,3-Propanetricarboxylic acid, 2-hy-<br>droxy- (citric acid); C <sub>6</sub> H <sub>8</sub> 0 <sub>7</sub> ; [77-92-9]   |   |
|                            | Water; H <sub>2</sub> O; [7732-18-5]<br>ABLES:<br>pH<br>RIMENTAL VALUES:   |   |
|                            | •  |   |
|                            | 4.5  | 119.0 4.5   |
|                            | 5.0  | 119.0 5.0   |
|                            | 6.0  | 152.7 6.0   |
|                            | 7.0  | 390.2 6.8   |
|                            | AUXILIAR   | Y INFORMATION   |
|                            | IOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS;   |
|                            | ample large enough to supply an excess of  |   |
|                            | h constituent was equilibrated in buffer<br>ns at 37 <sup>0</sup> C for 18 h with agitation. The   |   |
|                            | pension was then immediately filtered  | and were supplied by the American Cyanamid  |
|                            | ough a Whatman No. 1 paper. The filtra-  |   |
|                            | on time was approx. 2 min. The compds  | The source and purity of the remaining mate-  |
| wer                        | e assayed in the filtrate spectrophotome   | - rials were not specified.   |
| tri                        | cally by the Bratton and Marshall method   | 1   |
| The                        | after deacetylation with concd HCl <sub>aq</sub> .<br>e instrument used was a Beckmann DU spec-<br>photometer.   | ESTIMATED ERROR: pH and temp: not specified.<br>Accuracy of the anal method was illustrated<br>by the following values: expected 2.003,<br>3.004, 4.006, 5.007 mg/100 ml; found 2.08,<br>3.06, 4.12, 5.10, resp.<br>REFERENCES: |
|                            |  | <ol> <li>Bratton, A. C.; Marshall, E. K., Jr.</li> <li>J. Biol. Chem. <u>1939</u>, 128, 537.</li> </ol>   |

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| COMP<br>(1) | ONENTS:<br>Acetamide, N-[4-[[(4,6-dimethy1-2-pyrimi-  | ORIGINAL MEASUREMENTS:                     |
|-------------|---|--|
|             | dinyl)amino]sulfonyl]phenyl]- (acetyl<br>sulfamethazine); C <sub>14</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S; [100-90-3]                             | Bandelin, F. J.; Malesh, W.                |
| (2)         | Acetamide, N-[4-[[(4-methyl-2-pyrimidin-  | J. Am. Pharm. Assoc., Sci. Ed.             |
|             | yl)amino]sulfonyl]phenyl]- (acetyl sul-<br>famerazine); C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub> S; [127-73-1]                               | <u>1959</u> , <i>48</i> , 177-81.          |
| (3)         | Acetamide, N-[4-[(2-pyrimidinylamino)sul-<br>fonyl]phenyl]- (acetyl sulfadiazine);<br>C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2] | PREPARED BY:                               |
| (4)         | Calcium chloride; CaCl <sub>2</sub> ; [10043-52-4]  | R. Piekos                                  |
|             | Magnesium chloride; MgCl <sub>2</sub> ; [7786-30-3]   |  |
| (6)         | Phosphoric acid, monoammonium salt;   |  |
|             | NH <sub>4</sub> H <sub>2</sub> PO <sub>4</sub> ; [7722-76-1]  |  |
|             | Potassium chloride; KC1; [7447-40-7]  |  |
| (8)         | Sodium chloride; NaCl; [7647-14-5]  |  |
|             | Urea; $CH_4N_20$ ; [57-13-6]  |  |
| (10)        | Water; H <sub>2</sub> 0; [7732-18-5]  |  |
| VAI         | RIABLES:  |  |
|             | pH at 37°C  |  |
| EXI         | PERIMENTAL VALUES:  |  |
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| <u> </u>    |   |  |
|             |   | INFORMATION                                |
|             | HOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:            |
|             | cess acetyl sulfonamides was added to ali-  | Nothing specified.                         |
|             | ots of synthetic urine solns and $1\%$ H <sub>3</sub> PO <sub>4</sub>   |  |
|             | 1% NaOH solns were used to adjust the pH  |  |
|             | the required value. The solns were agi-   |  |
|             | ted for 24 h with addn of acid or base to   |  |
|             | ep them at the desired pH level until equi  | 1  |
|             | brium in pH and concn was attained. Then  |  |
|             | e solns were filtered and in aliquots the   |  |
| 1           | lfonamides were assayed spectrophotometri-  | LOTIMIED ERROR.                            |
|             | lly by the method described by Biamonte   | Soly: average values of 2 detns are given. |
|             | d Schneller (1). Before detn the soln was   |  |
| 1           | fluxed with $5\%$ $H_2SO_4$ for 1 h to liberate   | pH : not specified.                        |
| the         | e free amino compounds.   | REFERENCES:                                |
| 1           |   | 1. Biamonte, A. R.; Schneller, G. E.,      |
| 1           |   | J. Am. Pharm. Assoc., Sci. Ed.             |
|             |   | <u>1952,</u> <i>41</i> , 341.              |
|             |   |  |
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|---|---|---|
| COMPONENTS :  |   | ORIGINAL MEASUREMENTS: (CONTINUED)  |
| midinyl)amino]sulf  | [(4,6-dimethyl-2-pyri-<br>conyl]phenyl]- (acetyl<br>C <sub>14</sub> H <sub>16</sub> N <sub>4</sub> 0 <sub>3</sub> S; [100-90-3] | Bandelin, F. J.; Malesh, W.,  |
| (2) Acetamide, N-[[(4-  |   | J. Ат. Pharm. Аввос., Sci. Ed.  |
| merazine); C <sub>13</sub> H <sub>14</sub>                          | N <sub>4</sub> 0 <sub>3</sub> S; [127-73-1]   | <u>1959,</u> 48, 177-81.  |
| <pre>sulfony1]pheny1]-</pre>  | (2-pyrimidinylamino)-<br>(acetyl sulfadiazine);   | PREPARED BY:  |
| 12 <sup>n</sup> 12 <sup>N</sup> 4 <sup>0</sup> 3 <sup>5</sup> , [12 | 2/~/4-2]  | R. Piekos   |
| (4) - (10) Synthetic u<br>EXPERIMENTAL VALUES:                      | irine   |   |
| EXFERIMENTAL VALUES:  |   |   |
| (acetyl triple sul  | fonamide) in a solution<br>.300, KCl 1.660, NaCl  | of the three acetyl sulfonamides<br>n containing CaCl <sub>2</sub> 0.143, MgCl <sub>2</sub><br>2.950 and urea 20 g/dm <sup>3</sup> (synthetic |
|   | Equilibrium pH  | Solubility<br>(mg/100 ml synthetic urine)   |
|   | 4.5   | 218   |
|   | 5.0   | 223   |
|   | 5.5   | 231   |
|   | 6.0   | 254   |
|   | 6.5   | 163   |
|   | 7.0   | 630   |
|   | AUXILIARY   | INFORMATION   |
| METHOD/APPARATUS/PROCEI   | DURE:   | SOURCE AND PURITY OF MATERIALS:   |
|   |   |   |
|   |   | ESTIMATED ERROR:  |
|   |   |   |
|   |   | REFERENCES:   |
|   |   |   |
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| COMPONENTS:  | ORIGINAL MEASUREMENTS:                         |
|--|--|
| <ul> <li>(1) Benzenesulfonamide, 4-amino-N-2-thia</li> <li>ly1- (sulfathiazole); C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>;</li> </ul> | .zo-<br>Bhattacharyya, R.; Basu, U. P.         |
| [72-14-0]  |  |
| <ul> <li>Benzenesulfonamide, 4-amino-N-2-pyri<br/>dinyl- (sulfadiazine); C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S</li> </ul>                    |  |
| [68-35-9]<br>(3) Benzenesulfonamide, 4-amino-N-(4-met  | hy1-   |
| 2-pyrimidiny1)- (sulfamerazine);   |  |
| $C_{11}H_{12}N_4O_2S;$ [127-79-7]  | PREPARED BY:                                   |
| (4) Water; H <sub>2</sub> 0; [7732-18-5]   | R. Piekos                                      |
| VARIABLES:<br>One temperature: 30°C  |  |
| EXPERIMENTAL VALUES:   |  |
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| Solubility of a mixture of 1 part  | each of sulfathiazole, sulfadiazine,           |
| and culfamerazine in water at 30 <sup>0</sup>  | C is 98.3 mg per ml of solution <sup>2</sup> . |
| and Sullamelazine in water at 50   | o is so,s mg per mi of solution .              |
|  |  |
| <sup>a</sup> The final pH was 4.4  |  |
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| AUXII  | LIARY INFORMATION                              |
| METHOD/APPARATUS/PROCEDURE:  | SOURCE AND PURITY OF MATERIALS:                |
| A weighed sample of the sulfonamides was   | pla- Neither source nor purity of the sulfon-  |
| ced in a clean reagent bottle and a know   | m vol amides was specified.                    |
| of water was added. The mixt was shaken  |  |
| mech shaker at 80-100 strokes/min. Afte  | -  |
| least 24 h the mixt was filtered through   |  |
| clean, dried, and weighed sintered-glass   |  |
| crucible. At the end of the filtration   |  |
| crucible was washed with about 1 ml of w   |  |
| dried at $105^{\circ}$ C for 2-3 h, cooled and wei   |  |
|  | -  |
| to const wt. The pH was detd with a Cam  |  |
| bridge bench type pH meter using a glass   |  |
| electrode.   | pH : ±0.01 unit (authors).<br>REFERENCES:      |
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|---|---|
| COMPONENTS:<br>(1) Benzamide, N-[(4-aminophenyl)sulfonyl]-  | ORIGINAL MEASUREMENTS:                      |
| (sulfabenzamide); C <sub>13</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> S;  | Bhattacharyya, R.; Basu, U. P.              |
| <pre>[127-71-9] (2) Benzenesulfonamide, 4-amino-N-2-thiazo-</pre>   | Indian Pharmacist <u>1950,</u> 6(3), 77-8,  |
| $[y]- (sulfathiazole); C_{g}H_{g}N_{3}O_{2}S_{2};$ $[72-14-0]$  | 86.   |
| <ul> <li>Benzenesulfonamide, 4-amino-N-2-pyrimi-<br/>dinyl- (sulfadiazine); C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S;</li> </ul>                 |   |
| [68-35-9]   | PREPARED BY:                                |
| (4) Benzenesulfonamide, 4-amino-N-(4-methyl-<br>2-pyrimidinyl)- (sulfamerazine);<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7] | R. Piekos                                   |
| (5) Phosphoric acid, monopotassium salt;<br>KH <sub>2</sub> PO <sub>4</sub> ; [7778-77-0]   | ······                                      |
| (6) Sodium hydroxide; NaOH; [1310-73-2]   |   |
| (7) Water; H <sub>2</sub> 0; [7732-18-5]  |   |
| VARIABLES: pH   | ]   |
| EXPERIMENTAL VALUES:  | -   |
| Solubility at 30 <sup>0</sup> C of a mix  | ture of sulfabenzamide 3,                   |
| sulfathiazole 4, sulfadiazi   | ne 8, and sulfamerazine                     |
| 5 parts in M/20 KH <sub>2</sub> PO <sub>4</sub> solu  | tion of pH corrected with                   |
| Initial pH M/20 NaOH solution   | Final pH                                    |
| (mg/ml sol  | ution)                                      |
| 6.18 188  | 6.23  |
| 7.05 469.   | 4 6.93                                      |
|   |   |
| AUXILIARY   | INFORMATION                                 |
| METHOD/APPARATUS/PROCEDURE:   | SOURCE AND PURITY OF MATERIALS:             |
| A weighed sample of the mixture of sulfon-  | Neither source nor purity of the materials, |
| amides was placed in a clean reagent bottle   | with the exception of water, was specified. |
| and a known vol of the buffer soln was added  |   |
| The mixt was shaken in a mech shaker at 80-   |   |
| 100 strokes/min. After at least 24 h the  |   |
| mixt was filtered through a clean, dried and  | I Į   |
| weighed sintered-glass crucible. At the end   |   |
| of the filtration the crucible was washed   |   |
| with about 1 ml of water, dried at $105^{\circ}$ C for  |   |
| 2-3 h, cooled, and weighed to const wt. The   |   |
| pH was detd with a Cambridge bench type pH  | Temp: ±0.2 <sup>°</sup> C (authors).        |
| meter using a glass electrode.  | pH : ±0.01 unit (authors).                  |
|   | REFERENCES:                                 |
|   |   |
|   |   |
| 4   |   |
|   |   |
|   |   |

| COMPONENTS:<br>(1) Benzenesulfonamide, 4-amino-N-2-thiazo-   | ORIGINAL MEASUREMENTS:  |
|--|---|
| ly1- (sulfathiazole); C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S;   | Frisk, A. R.; Hagerman, G.;   |
| [72-14-0]<br>(2) Benzenesulfonamide, 4-amino-N-2-pyrimi-   | Helander, S.; Sjögren, B.   |
| diny1- (sulfapyrimidine); C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S;<br>[68-35-9]  | Hygiea <u>1946</u> , 108(12), 639-51.   |
| (3) Benzenesulfonamide, 4-amino-N-(4-methyl-   |   |
| 2-pyrimidiny1)- (sulfamethylpyrimidine)<br>C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S; [127-79-7]   |   |
| (4) Acetamide, N-[4-[(2-thiazolylamino)sul-  | PREPARED BY:<br>R. Piekos   |
| fonyl]phenyl]- (acetyl sulfathiazole);<br>C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> 0 <sub>3</sub> S <sub>2</sub> ; [127-76-4]  |   |
| (5) Acetamide, N-[4-[(2-pyrimidinylamino)-<br>sulfonyl]phenyl]- (acetyl sulfapyrimi-<br>dine); C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S; [127-74-2]                           |   |
| <pre>(6) Acetamide, N-[4-[[(4-methyl-2-pyrimidin-<br/>yl)amino]sulfonyl]phenyl]- (acetyl sul-<br/>famethylpyrimidine); C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>0<sub>3</sub>S;<br/>[127-73-1]</pre> |   |
| <pre>(7) Phosphoric acid, disodium salt;<br/>Na<sub>2</sub>HPO<sub>4</sub>; [7558-94-4]</pre>  |   |
| <ul> <li>(8) Phosphoric acid, monopotassium salt;<br/>KH<sub>2</sub>PO<sub>4</sub>; [7778-77-0]</li> </ul>   |   |
| (9) Water; H <sub>2</sub> 0; [7732-18-5]   |   |
| VARIABLES:<br>One temperature: 37 <sup>0</sup> C; one pH: 6.1  |   |
| EXPERIMENTAL VALUES:   | J   |
|  |   |
| Solubility of a mixture of sulfathiazol  | e, sulfapyrimidine, sulfamethyl-  |
| pyrimidine, acetyl sulfathiazole, acety  | 1 sulfapyrimidine and acetyl  |
| sulfamethylpyrimidine in M/30 phosphate  | buffer of pH 6.1 at 37 <sup>0</sup> C is  |
| 283 mg/100 ml solvent.   |   |
|  |   |
|  |   |
|  |   |
| AUXILIARY  | INFORMATION   |
| METHOD /APPARATUS / PROCEDURE :  |   |
| An excess of the three sulfonamides and thei   | SOURCE AND PURITY OF MATERIALS:<br>n Neither source nor purity of the materials |
| acetyl derivatives in the phosphate buffer   | was specified.  |
| was shaken at $37^{\circ}$ C for 24 h. The concn of  |   |
| the dissolved compds was detd by the Bratton   |   |
| and Marshall method (1) using a photoelec  |   |
| colorimeter.   |   |
|  |   |
|  |   |
|  | ESTIMATED ERROR:  |
|  | Soly: precision: ±28 mg/100 ml (authors).                                       |
|  | Temp and pH: not specified.   |
|  | DEFEDENCES -  |
|  | REFERENCES:   |
|  | 1. Bratton, A. C.; Marshall, E. K., Jr.   |
|  | J. Biol. Chem. <u>1939</u> , 128, 537.  |
|  |   |
|  |   |

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```
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          + calcium chloride
                                                                      121
          + magnesium chloride
                                                                      121
                                                                      120
          + phosphoric acid, disodium salt
          + phosphoric acid, monoammonium salt
                                                                      121
          + phosphoric acid, monopotassium salt
                                                                      120
                                                                      121
          + potassium chloride
          + sodium chloride
                                                                      121
          + urea
                                                                      121
Acetamide, N-[4-[[[4-[(methylamino)sulfonyl]phenyl]amino]sulfonyl]-
phenyl]-
                                                                    15-17
          + water
Acetamide, N-[4-[[[4-[(methylamino)sulfonyl]phenyl]amino]sulfonyl]-
phenyl]-, (aq)
          + phosphoric acid, disodium salt
                                                                   15, 17
          + phosphoric acid, monopotassium salt
                                                                   16, 17
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          + water
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          + 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide
                                                                      485
          + 4-amino-N-2-pyrimidinylbenzenesulfonamide
                                                                      485
          + 4-amino-N-2-thiazolylbenzenesulfonamide
                                                                      485
          + calcium chloride
                                                                 481, 482
          + N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-
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                                                             477, 480-482
          + 2-hydroxy-1,2,3-propanetricarboxylic acid
                                                                      480
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                                                      274-278, 464, 465,
          + phosphoric acid, monopotassium salt
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          + potassium chloride
                                                                 481, 482
          + N-[4-[(2-pyrimidinylamino)sulfonyl]phenyl]acetamide
                                                           465, 473, 477,
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          + sodium chloride
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          + sodium hydroxide
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          + N-[4-[(2-thiazolylamino)sulfonyl]phenyl]acetamide
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          + trichloromethane
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          + phosphoric acid, monopotassium salt
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          + sodium hydroxide
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          + 4-amino-N-2-pyridinylbenzenesulfonamide
                                                            462, 475, 485
          + 4-amino-N-2-thiazolylbenzenesulfonamide
                                                                      485
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                                                                 481, 482
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          + 2-hydroxy-1,2,3-propanetricarboxylic acid
                                                                      480
          + 2-hydroxy-1,2,3-propanetricarboxylic acid, disodium salt
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          + magnesium chloride
                                                                 481, 482
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Acetamide, N-[4-[(2-pyrimidinylamino)sulfonyl]phenyl]- (aq)
                                                      236-242,
          + phosphoric acid, disodium salt
                                                               463, 465
                                                      473, 477,
                                                                480, 485
                                                                  481,482
          + phosphoric acid, monoammonium salt
                                                      235, 237-242, 463,
          + phosphoric acid, monopotassium salt
                                                      465, 473, 477, 485
          + potassium chloride
                                                                 481, 482
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          + sodium chloride
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          + sodium hydroxide
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                                                                  481,482
          + urea
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                                                      451, 463, 464, 473
          + water
Acetamide, N-[4-[(2-thiazolylamino)sulfonyl]phenyl]-, (aq)
          + 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide
                                                                      485
          + 4-amino-N-2-pyrimidinylbenzenesulfonamide
                                                                      485
          + 4-amino-N-2-thiazolylbenzenesulfonamide
                                                                 451, 485
          + N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]acetamide
                                                            464, 473, 485
463, 464, 473
          + phosphoric acid, disodium salt
          + phosphoric acid, monopotassium salt
                                                            463, 464, 473
          + N-[4-[(2-pyrimidinylamino)sulfonyl]phenyl]acetamide
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              sulfonyl]phenyl]-
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              phenyl]-
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              phenyl]-
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              phenyl]-
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          see acetamide, N-[4-[[(6-methoxy-2-pyridazinyl)amino]sulfonyl]-
              phenyl]-
3-(Nl-Acetylsulfanilamido)-6-methoxypyridazine
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              phenyl]-
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          see acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]-
N4-Acetylsulfapyridine
          see acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]-
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| + hydrochloric acid, disodium salt 410, 401<br>+ phosphoric acid, monopotassium salt 410, 411<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)-<br>+ water 365, 474<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(2-pyrimidinylbenzenesulfonamide 474<br>+ 4-amino-N-(2-pyrimidinylbenzenesulfonamide 474<br>+ 4-amino-N-(2,pyrimidinylbenzenesulfonamide 474<br>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 365<br>+ phosphoric acid, disodium salt 365, 474<br>+ phosphoric acid, disodium salt 365, 474<br>+ phosphoric acid, disodium salt 364<br>+ phosphoric acid, disodium salt 474<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ phosphoric acid, disodium salt 434<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ water 434<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ 1-butanol 396, 397<br>+ 1-butanol 396, 397<br>+ 1-butanol 396, 397<br>+ 1-butanol 396, 397<br>+ 1-butanol 384, 386, 401<br>+ ethanol 384, 386, 401<br>+ ethoxyethanol 384, 386, 401<br>+ detoxyethanol 382, 383<br>+ octanol 396, 397<br>+ 1-putanol 392, 393<br>+ 1-propanol 382, 383<br>+ dotanol 396, 387<br>+ truchloromethane 398, 401<br>+ water B367, 306-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ carbonic acid, disodium salt 372, 374<br>+ dethanol 386, 389<br>+ truchloromethane 396, 301<br>+ dethanol 392, 393<br>+ 1-propanol 386, 389<br>+ truchloromethane 396, 301<br>+ carbonic acid, disodium salt 373, 374<br>+ dethanol 386, 381<br>+ formic acid, disodium salt 373, 374<br>+ dethanol 380, 381<br>+ formic acid, disodium salt 373, 374<br>+ dethanol 380, 381<br>+ formic acid, disodium salt 375, 378<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478<br>+ phosphoric acid, disodium salt 375-378<br>+ phosphoric acid, disodium salt 375-378<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>+ a-mino-N-(4-methyl-2-pyrimidinyl)benze  | + water  | E404, 40    | 5-411    |
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| <pre>Benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)-</pre>  | + phosphoric acid, disodium salt   | 410         | , 411    |
| + water $365, 474$<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-2-pyrimidinylbenzenesulfonamide 474<br>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 365, 474<br>+ phosphoric acid, disodium salt 365, 474<br>+ phosphoric acid, disodium salt 364<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-<br>+ water 434<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ phosphoric acid, monopotassium salt 434<br>Benzenesulfonamide, 4-amino-N-[4-[(dimethylamino)sulfonyl]phenyl]-<br>+ 2-propanone 18<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ 1-butanol 396, 397<br>+ ethanol 384-386, 401<br>+ thoxyethanol 384-386, 401<br>+ thoxyethanol 384, 395<br>+ 1-qecanol 396, 391<br>+ 1-decanol 396, 391<br>+ trichloromethane 384, 383<br>+ octanol 384, 383<br>+ octanol 384, 395<br>+ 1-propanol 384, 395<br>+ 1-propanol 384, 395<br>+ 1-propanol 392, 393<br>+ 2-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 394, 395<br>+ 1-pentanol 394<br>+ 4-amino-N-(2,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 2303, 304-341, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzene               | + phosphoric acid, monopotassium salt  | _ 410       | , 411    |
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| $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$   |  |             |          |
| + 4-amino-N-2-pyrimidinylbenzenesulfonamide 474+ 2-hydroxy-1,2,3-propanetricarboxylic acid 365+ phosphoric acid, disodium salt 365,474+ phosphoric acid, disodium salt 367,474Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-+ water 434Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)+ phosphoric acid, disodium salt 434Benzenesulfonamide, 4-amino-N-[4-[(dimethylamino)sulfonyl]phenyl]-+ 2-propanome 386, 397+ 1-decanol 396, 397+ 1-decanol 386, 397+ ethanol 384-386, 401+ hexane 386, 401+ hexane 386, 401+ hexane 386, 387+ hexane 386, 387+ hexane 386, 387+ hexane 386, 387+ hexane 386, 389+ 1-pentanol 382, 383+ 1-propanol 388, 389+ trichloromethane 399, 400+ water B367, 368-381Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)+ carbonic acid, disodium salt 372, 374+ ethanol 388, 389+ trichloromethane 380, 381+ formic acid, disodium salt 372, 374+ ethanol 380, 381+ formic acid, sodium salt 372, 374+ ethanol 381+ formic acid, sodium salt 372, 374+ ethanol 381+ formic acid, sodium salt 372, 374+ ethanol 381+ formic acid, sodium salt 375-377Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 802Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478, 479Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478, 476, 478, 479+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 474, 476, 478, 479+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-+ water 478, 476, 478, 479+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479  | + 4-amino-N-(4-metny1-2-pyrimidiny1)benzenesulton                              | amide       | 474      |
| + phosphoric acid, disodium salt 365, 474<br>+ phosphoric acid, monpotassium salt 474<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ thosphoric acid, disodium salt 434<br>Enzenesulfonamide, 4-amino-N-(4,6-dimethylamino)sulfonyl]phenyl]-<br>+ 2-propanone 18<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ 1-butanol 390, 391<br>+ 1-butanol 396, 397<br>+ ethanol 384-386, 401<br>+ ethayethanol 384-386, 401<br>+ thoxyethanol 384, 383<br>+ octanol 384, 383<br>+ octanol 384, 383<br>+ octanol 384, 383<br>+ trichloromethane 399, 400<br>+ water E367, 366-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ athanol 382, 383<br>+ octanol 392, 393<br>+ 1-penpanot 392, 393<br>+ 1-propanot 394, 395<br>- 1 water E367, 366-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ water E30, 301<br>+ formic acid, monopotasium salt 375-378<br>+ phosphoric acid, disodium salt 375-378<br>+ phosphoric acid, monopotasium salt 375-378<br>+ phosphoric acid, disodium salt 375-377<br>+ water 203, 304-341, 476, 478, 479<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)-,  | + 4-amino-N-2-pyrimidinylbenzenesulfonamide                                    |             |          |
| + phosphoric acid, monpotassium salt 474<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ water 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ phosphoric acid, disodium salt 434<br>Benzenesulfonamide, 4-amino-N-(4-[(dimethylamino)sulfonyl]phenyl]-<br>+ 2-propanone 18<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ 1-butanol 396, 397<br>+ 1-butanol 384-386, 401<br>+ 1-decanol 384-386, 401<br>+ tethanol 384-386, 401<br>+ methanol 382, 383<br>+ octanol 394, 395<br>+ 1-pentanol 392, 393<br>+ trichloromethane 399, 400<br>+ water E367, 368-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ water 373, 374<br>+ carbonic acid, monosodium salt 372, 374<br>+ ethanol 380, 381<br>+ formic acid, sodium salt 375-377<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 474, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ barium chloride 327, 478, 479  | + 2-hydroxy-1,2,3-propanetricarboxylic acid                                    |             |          |
| $\begin{aligned} & \text{Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-} & 434 \\ & \text{Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)} & + phosphoric acid, disodium salt & 434 \\ & + phosphoric acid, monopotassium salt & 434 \\ & \text{Benzenesulfonamide, 4-amino-N-(4-[(dimethylamino)sulfonyl]phenyl]-} & 18 \\ & \text{Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-} & 18 \\ & \text{H-butanol} & 384, 386, 401 & 387 \\ & \text{H-thatanol} & 384, 386, 401 & 387 \\ & \text{H-thatanol} & 382, 383 \\ & \text{H-thatanol} & 384, 389 \\ & \text{H-trichoromethane} & 388, 389 \\ & \text{H-trichoromethane} & 389, 400 \\ & \text{Water} & E367, 366-381 \\ & \text{Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq) \\ & + carbonic acid, disodium salt & 372, 374 \\ & + carbonic acid, monosodium salt & 372, 374 \\ & + carbonic acid, monosodium salt & 372, 374 \\ & + formic acid, monopotassium salt & 375-378 \\ & + phosphoric acid, monoptassium salt & 375-378 \\ & + phosphoric acid, monoptassium salt & 375-377 \\ & + phosphoric acid, monoptassium salt & 375-377 \\ & + water & E303, 304-341, 476, \\ & 474, 476, 478, 479 \\ & \text{H-amino-N-(4,6-dimethyl-2-pyrimidinyl)-} \\ & + water & E303, 304-341, 476, \\ & 474, 476, 478, 479 \\ & + amino-N-(4-methyl-2-pyrimidinyl)-midenyl) \\ & + 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- \\ & + water & 202 \\ & + amino-N-(4-methyl-2-pyrimidinyl)-midenyl \\ & 474, 476, 478, 479 \\ & + aminon-N-(4-methyl-2-pyrimidinyl) \\ & + 4-amino-N-(4-methyl-2-pyrimidinyl) \\ & + aminon-N-(4-methyl-2-pyrimidinyl) \\ & + aminon-N-(4-methyl-2-pyrimidin$   | + phosphoric acid, disodium salt<br>+ phosphoric acid, monpotassium salt       | 365         |          |
| + water 434<br>Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-, (aq)<br>+ phosphoric acid, monopotassium salt 434<br>Benzenesulfonamide, 4-amino-N-(4(dimethylamino)sulfonyl]phenyl]-<br>+ 2-propanone 18<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-<br>+ 1-butanol 396, 397<br>+ 1-butanol 396, 397<br>+ 1-decanol 396, 397<br>+ ethanol 384-386, 401<br>+ ethoxyethanol 382, 383<br>+ octanol 392, 393<br>+ 1-pentanol 392, 393<br>+ 1-propanol 382, 383<br>+ octanol 394, 395<br>+ 1-pentanol 392, 393<br>+ 1-propanol 388, 389<br>+ trichloromethane 399, 400<br>+ carbonic acid, disodium salt 372, 374<br>+ carbonic acid, disodium salt 372, 374<br>+ carbonic acid, monosodium salt 380, 381<br>+ formic acid, sodium salt 372, 374<br>+ trichanol 381<br>+ formic acid, sodium salt 372, 374<br>+ carbonic acid, disodium salt 372, 374<br>+ tothanol 381<br>+ formic acid, sodium salt 375-377<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 474, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 474, 476, 478, 479<br>+ amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ water 474, 476, 478, 479<br>+ amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ dard, 474, 476, 478, 479<br>+ d-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ dard, 474, 476, 478, 479<br>+ d-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>+ dard, 476, 478, 479   | Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)                    | -           |          |
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| <pre>18 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19</pre>   | + phosphoric acid, monopotassium salt  |             |          |
| Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-       390, 391         + 1-butanol       396, 397         + 1-decanol       364-386, 401         + ethanol       384-386, 401         + ethanol       387         + ethanol       384-386, 401         + ethoxyethanol       387         + hexane       398, 401         + methanol       382, 383         + octanol       394, 395         + 1-pentanol       392, 393         + 1-propanol       388, 389         + trichloromethane       399, 400         + carbonic acid, disodium salt       373, 374         + carbonic acid, monosodium salt       372, 374         + ethanol       380, 381         + formic acid, sodium salt       381         + formic acid, sodium salt       375, 379         + hydrochloric acid       371         + phosphoric acid, disodium salt       375-378         + phosphoric acid, disodium salt       375-378         + phosphoric acid, disodium salt       375-377         Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-       478, 479         Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-       478, 479         + amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide  |  | henyl]-     | ·        |
| <pre>+ 1-butanol 390, 391<br/>+ 1-decanol 396, 397<br/>+ ethanol 396, 401<br/>+ ethoxyethanol 384-386, 401<br/>+ methanol 398, 401<br/>+ methanol 392, 383<br/>+ octanol 392, 393<br/>+ 1-pentanol 392, 393<br/>+ 1-pentanol 392, 393<br/>+ 1-propanol 388, 389<br/>+ trichloromethane 399, 400<br/>+ water E367, 368-381<br/>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br/>+ carbonic acid, disodium salt 372, 374<br/>+ ethanol 380, 381<br/>+ formic acid, sodium salt 372, 374<br/>+ ethanol 380, 381<br/>+ formic acid, sodium salt 372, 374<br/>+ ethanol 381<br/>+ formic acid, sodium salt 381<br/>+ formic acid, disodium salt 381<br/>+ formic acid, disodium salt 381<br/>+ formic acid, disodium salt 381<br/>+ phosphoric acid, disodium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 2303, 304-341, 476, 478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water 478, 476, 478, 479<br/>Henzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water 474, 476, 478, 479<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 474, 476, 478, 479<br/>+ ammonium chloride 327, 478, 479</pre>  |  |             | 18       |
| <pre>+ ethanol</pre>   |  |             |          |
| <pre>+ ethoxyethanol</pre>   |  |             |          |
| <pre>+ hexane 398, 401<br/>+ methanol 382, 383<br/>+ octanol 394, 395<br/>+ 1-pentanol 392, 393<br/>+ 1-propanol 388, 389<br/>+ trichloromethane 399, 400<br/>+ water E367, 368-381<br/>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br/>+ carbonic acid, disodium salt 372, 374<br/>+ ethanol 380, 381<br/>+ formic acid, monosodium salt 372, 374<br/>+ ethanol 380, 381<br/>+ formic acid, sodium salt 381<br/>+ formic acid, disodium salt 381<br/>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br/>+ hydrochloric acid 371<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476, 478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476, 478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>+ barium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcuum chloride 327, 478, 479</pre>   |  | 384-386     |          |
| + octanol 394, 395<br>+ 1-pentanol 302, 393<br>+ 1-propanol 388, 389<br>+ trichloromethane 399, 400<br>+ water E367, 368-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ carbonic acid, disodium salt 372, 374<br>+ carbonic acid, monosodium salt 372, 374<br>+ ethanol 380, 381<br>+ formic acid, sodium salt 381<br>+ formic acid, sodium salt 381<br>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br>+ hydrochloric acid, disodium salt 375-377<br>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride 326<br>+ barium chloride 325<br>+ benzoic acid 37, 341<br>+ calcium chloride 327, 478, 479  |  |             | , 401    |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   |  |             |          |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   |  |             |          |
| + water E367, 368-381<br>Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ carbonic acid, disodium salt 373, 374<br>+ carbonic acid, monosodium salt 372, 374<br>+ ethanol 380, 381<br>+ formic acid, sodium salt 381<br>+ formic acid, sodium salt 381<br>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br>+ hydrochloric acid, disodium salt 375-378<br>+ phosphoric acid, monopotassium salt 375-377<br>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476, 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide 326<br>+ barium chloride 325<br>+ benzoic acid 337, 341<br>+ calcum chloride 327, 478, 479  | + 1-propanol   |             |          |
| Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-, (aq)<br>+ carbonic acid, disodium salt 373, 374<br>+ carbonic acid, monosodium salt 372, 374<br>+ ethanol 380, 381<br>+ formic acid, sodium salt 381<br>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br>+ hydrochloric acid 371<br>+ phosphoric acid, disodium salt 375-378<br>+ phosphoric acid, monopotassium salt 375-377<br>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br>+ water 302<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride 325<br>+ benzoic acid 337, 341<br>+ calcuum chloride 327, 478, 479  |  |             |          |
| <pre>+ carbonic acid, disodium salt 373, 374<br/>+ carbonic acid, monosodium salt 372, 374<br/>+ ethanol 380, 381<br/>+ formic acid 380, 381<br/>+ formic acid, sodium salt 381<br/>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>+ hydrochloric acid, disodium salt 375-378<br/>+ phosphoric acid, disodium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 8303, 304-341, 476, 478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>  |  |             | 0-201    |
| <pre>+ ethanol 380, 381<br/>+ formic acid 381<br/>+ formic acid, sodium salt 381<br/>+ formic acid, sodium salt 381<br/>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>+ hydrochloric acid, disodium salt 375-378<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 302<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476,<br/>478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>  | + carbonic acid, disodium salt   | 373         |          |
| <pre>+ formic acid 381<br/>+ formic acid, sodium salt 381<br/>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>+ hydrochloric acid 378, 379<br/>= hydrochloric acid, disodium salt 375-378<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 302<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476,<br/>478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>   |  |             |          |
| <pre>+ formic acid, sodium salt 381<br/>+ 2-hydroxy-1,2,3-propanetricarboxylic acid 378, 379<br/>+ hydrochloric acid 371<br/>+ phosphoric acid, disodium salt 375-378<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 302<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476,<br/>478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>   |  | 200         |          |
| <pre>+ hydrochloric acid 371<br/>+ phosphoric acid, disodium salt 375-378<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 302<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476,<br/>478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 326<br/>+ barium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>   | + formic acid, sodium salt   |             | 381      |
| <pre>+ phosphoric acid, disodium salt 375-378<br/>+ phosphoric acid, monopotassium salt 375-377<br/>Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)-<br/>+ water 302<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br/>+ water E303, 304-341, 476,<br/>478, 479<br/>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br/>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br/>474, 476, 478, 479<br/>+ ammonium chloride 325<br/>+ benzoic acid 337, 341<br/>+ calcium chloride 327, 478, 479</pre>   |  | 378         | · .      |
| <pre>+ phosphoric acid, monopotassium salt 375-377 Benzenesulfonamide, 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)- + water 302 Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- + water E303, 304-341, 476, 478, 479 Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq) + 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479 + 4-amino-N-(2-pyrimidinyl)benzenesulfonamide 474, 476, 478, 479 + ammonium chloride 326 + barium chloride 325 + benzoic acid 337, 341 + calcium chloride 327, 478, 479</pre>  |  | 37          |          |
| + water 302<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, $304-341$ , 476,<br>478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride 326<br>+ barium chloride 325<br>+ benzoic acid 337, 341<br>+ calcium chloride 327, 478, 479  | + phosphoric acid, monopotassium salt  |             |          |
| Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-<br>+ water E303, 304-341, 476,<br>478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride 326<br>+ barium chloride 325<br>+ benzoic acid 337, 341<br>+ calcium chloride 327, 478, 479  |  |             | 202      |
| 478, 479<br>Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride<br>+ barium chloride<br>+ benzoic acid<br>+ calcium chloride<br>327, 478, 479  |  |             | 302      |
| Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (aq)<br>+ 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride<br>525<br>+ barium chloride<br>537, 341<br>+ calcium chloride<br>527, 478, 479   | + water E303,  |             |          |
| + 4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride<br>525<br>+ barium chloride<br>4337, 341<br>+ calcium chloride<br>327, 478, 479   | Benzenesulfonamide 4-amino-N-(4.6-dimethyl-2-pyrimidinyl)-                     | 478<br>(ag) | , 479    |
| 474, 476, 478, 479<br>+ 4-amino-N-(2-pyrimidinyl)benzenesulfonamide<br>474, 476, 478, 479<br>+ ammonium chloride<br>+ barium chloride<br>525<br>+ benzoic acid<br>+ calcium chloride<br>327, 478, 479  |  |             |          |
| + ammonium chloride       474, 476, 478, 479         + barium chloride       326         + benzoic acid       325         + calcium chloride       337, 341         + calcium chloride       327, 478, 479   | 474,   |             | , 479    |
| + ammonium chloride 326<br>+ barium chloride 325<br>+ benzoic acid 337, 341<br>+ calcium chloride 327, 478, 479  |  | 476. 478    | . 479    |
| + benzoic acid 337, 341<br>+ calcium chloride 327, 478, 479  | + ammonium chloride  |             |          |
| + calcium chloride 327, 478, 479   |  |             |          |
|  |  |             |          |
|  |  | -2,7 4,0    |          |
|  |  |             |          |

| Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, (ac                         |                  |
|--|------------------|
| + ethanol<br>+ 1-ethenyl-2-pyrrolidinone   | 338<br>340, 341  |
| + hydrochloric acid  | 328              |
| + α-hydro-ω-hydroxypoly(oxy-1,2-ethanediyl)  | 345              |
| + 2-hydroxy-1,2,3-propanetricarboxylic acid  | 332, 476         |
| + 2-hydroxy-1,2,3-propanetricarboxylic acid, disodium                                    |                  |
| ( ) this is a stand of   | 335, 336         |
| + lithium chloride<br>+ magnesium chloride 324,  | 313<br>478, 479  |
| + phosphoric acid, disodium salt 329-334, 336,   |                  |
| + phosphoric acid, monoammonium salt   | 478, 479         |
| + phosphoric acid, monopotassium salt 329-331,   |                  |
| + phosphoric acid, monosodium salt   | 333              |
| + potassium bromide<br>+ potassium chloride 315-317,                                     | 318, 319         |
| + potassium iodide   | 320, 321         |
| + 2-propanone  | 343              |
| + sodium chloride 314, 328,  | 478, 479         |
| + sodium hydroxide   | 335              |
| + thiocyanic acid, potassium salt<br>+ trichloromethane                                  | 322, 323         |
| + trichloromethane<br>+ urea   | 344<br>478, 479  |
| + sorbitan monooleate, polyoxyethylene deriv.  | 339              |
| Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, hem                         | mihydrate        |
| + sodium hydroxide   | 347              |
| + water<br>Rongonosulfonamido (4 amino-N=(4 and mothyl=2-pyrimidinyl) - mor              | 347              |
| Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, mor salt                    | iostiver(1+)     |
| + 4-morpholinepropanesulfonic acid   | 356              |
| + 4-morpholinepropanesulfonic acid, sodium salt  |                  |
|  | 356              |
| + nitric acid  | 352-355          |
| + nitric acid, potassium salt  | 352-356          |
| + water<br>Benzenesulfonamide, 4-amino-N-(2-ethoxy-5-pyridinyl)-                         | 352-356          |
| + water  | 87               |
| Benzenesulfonamide, 4-amino-N-(3-ethoxy-2-pyridinyl)-                                    |                  |
| + water  | 80               |
| Benzenesulfonamide, 4-amino-N-(4-ethoxy-2-pyrimidinyl)-<br>+ water                       | 296              |
| Benzenesulfonamide, 4-amino-N-(5-ethyl-1,3,4-thiadiazol-2-yl), (                         |                  |
| + N-[4-[[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]sulfonyl                                   |                  |
| acetamide  | 452              |
| + water  | 452              |
| Benzenesulfonamide, 4-amino-N-(2-hydroxy-5-pyridinyl)-<br>+ water                        | 05               |
| Benzenesulfonamide, 4-amino-N-hydroxy-N-2-pyrimidinyl-, calcium                          | 85<br>salt (1•1) |
| 2-propanone  | 55               |
| Benzenesulfonamide, 4-amino-N-hydroxy-N-2-pyrimidinyl-, calcium                          |                  |
| dihydrate  |                  |
| + 2-propanone  | 56               |
| Benzenesulfonamide, 4-amino-N-(5-iodo-2-pyridinyl)-<br>+ water                           | 77               |
| Benzenesulfonamide, 4-amino-N-(3-methoxypyrazinyl)-                                      | ••               |
| + 2-hydroxy-1,2,3-propanetricarboxylic acid  | 441              |
| + phosphoric acid, disodium salt   | 441              |
| + water  | 441              |
| Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-<br>+ trichloromethane           | 113, 114         |
| + water  | 102-114          |
| Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-                                 | •                |
| + calcium chloride   | 108              |
| + ethanol  | 110, 111         |
| + hydrochloric acid  | 103              |
| + α-hydro-ω-hydroxy-poly(oxy-1,2-ethanediyl) + 2-hydroxy-1,2,3-propanetricarboxylic acid | 111, 112<br>104  |
| + 2,2'-iminodiethanol  | 104              |
| + magnesium chloride   | 108              |
| + phosphoric acid, disodium salt   | 104-107          |
| + phosphoric acid, monoammonium salt   | 108              |
| + phosphoric acid, monopotassium salt  | 105-107          |
| + piperazine<br>+ potassium chloride   | 110-112<br>108   |
| . Loonssam enterted  |                  |
|  |                  |

| Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-  |              |
|---|--------------|
| + 1,3-propanediol 109,<br>+ sodium chloride   | 112<br>108   |
| + $\alpha$ -[(tetrahydro-2-furany1)methy1]- $\omega$ -hydroxy-(gy1cofuro1)p   |              |
| 1,2-ethanediyl)   | 110<br>108   |
| + urea<br>Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-, cobalt c  |              |
| see cobalt, bis[4-amino-N-(6-methoxy-3-pyridazinyl)benzene  | sulfon-      |
| amidato]diaqua<br>Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-, monosodiu                                 | m salt       |
| (aq)  |              |
| + acetic acid, cobalt(2+)<br>+ cobalt, bis[4-amino-N-(6-methoxy-3-pyridaziny1)benzenesu                               | 116<br>1fon- |
| amidato]benzenesulfonamide, diaqua  | 116          |
| + water   | 116          |
| Benzenesulfonamide, 4-amino-N-(2-methoxy-5-pyrimidinyl)-<br>+ water   | 284          |
| Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-  |              |
| + 2-ethoxyethanol<br>+ water 280,   | 282<br>281   |
| Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-, (aq)  | 201          |
| + 1,4,7,10,13,16-hexaoxacyclooctadecane<br>+ hydrochloric acid  | 283<br>283   |
| + $\alpha$ -hydro- $\omega$ -hydroxy-poly(oxy-1,2-ethanediy1) 280,  |              |
| Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-  |              |
| + benzene 290, 292,<br>+ 1,4,7,10,13,16-hexaoxacyclooctane 292,   | 293<br>293   |
| + trichloromethane  | 291          |
|   | -289         |
| Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-, aq<br>+ hydrochloric acid                                   | 287          |
| + phosphoric acid, disodium salt 288,   | 289          |
| + phosphoric acid, monosodium salt 288,<br>Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-, comp. wit        |              |
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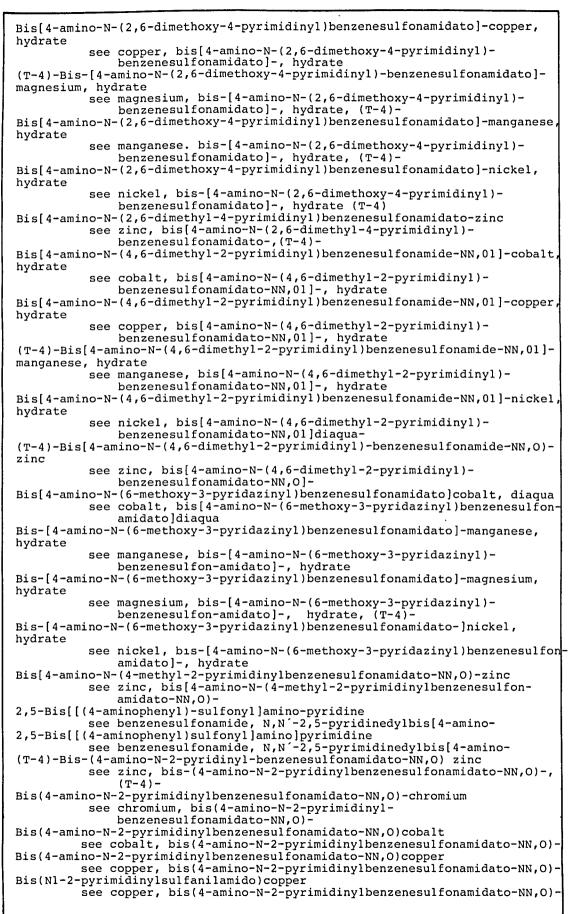
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          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
2,4-Dimethyl-6-sulfanilamidopyrimidine
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
Nl,Nl-Dimethyl-N4-sulfanilylsulfanilamide
          see benzenesulfonamide, 4-[[(4-aminophenyl)sulfonyl]amino]-
              N,N-dimethyl-
4'-(Dimethylsulfamoyl)sulfanilanilide
          see benzenesulfonamide, 4-[[(4-aminophenyl)sulfonyl]amino]-
              N,N-dimethyl-
4'-(Dimethylsulfamyl)sulfanilanilide
          see benzenesulfonamide, 4-[[(4-aminophenyl)sulfonyl]amino]-
              N,N-dimethyl-
Dimezathine
          see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-
Diseptal B
          see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl]-
              phenyl]-
Diseptal C
          see benzenesulfonamide, 4-amino-N-[4-(aminosulfonyl)phenyl]-
Disulfan-HCl
          see benzenesulfonamide, 4-amino-N-4-[(aminosulfonyl)phenyl]-,
              monohydrochloride
Disulfan
          see benzenesulfonamide, 4-amino-N-[4-(aminosulfonyl)phenyl]-
Disulon
          see benzenesulfonamide, 4-amino-N-[4-(aminosulfonyl)phenyl]-
DJ 1550
          see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-
Domian
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
DS 36
          see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-
Durasulf
          see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-
Durenat
          see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-
Elcosine
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
Elkosil
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
Elkosine
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
Elkosin
          see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-
Eskadiazine
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Nl-(4-Ethoxy-2-pyrimidinyl)sulfanilamide
          see benzenesulfonamide, 4-amino-N-(4-ethoxy-2-pyrimidinyl)-
Eubasin
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
Eubasinum
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
F.I. 5978
          see benzenesulfonamide. 4-amino-N-(3-methoxypryrazinyl)-
Fanasil
          see benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-
Fanasulf
          see benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-
Fe(III) sulfadiazine
          see iron, tris(4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN,0)-
Ferric sulfadiazine
          see iron, tris(4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN,O)-
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Flamazine
          see silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-
Haptocil
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
1,4,7,10,13,16-Hexaoxacyclooctadecane, comp. with 4-amino-N-(6-methoxy-
4-pyrimidinyl)benzenesulfonamide
          see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-, comp.
              with 1,4,7,10,13,16-hexaoxacyclooctadecane (1:1)
Honey Diazine
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
TCT 32525
          see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-
ICI 3435
          see benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)-
1H-Imidazole, silver complex
          see silver, (4-amino-N-2-pyrimidinylbenzene-sulfonamidato-NN,O)-
              bis(l-imidazole-N3)-,(T-4)-
Iron, tris(4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN,0)-
                                                                      214
          + vater
Kelametazine
          see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-
Kelfizina
          see benzenesulfonamide. 4-amino-N-(3-methoxypryrazinyl)-
Kelfizin
          see benzenesulfonamide. 4-amino-N-(3-methoxypryrazinyl)-
Kinex
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Kirocid
          see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-
Kiron
          see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-
Kynex
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Lederkin
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Lederkvn
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Lipo-Diazine
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Lipo-Levazine
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Liquadiazine
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Lisulfen
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Longasulf
          see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-
Longin
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Magnesium, bis-[4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfonamidato]-,
hydrate, (T-4)-
          + hydrochloric acid
                                                                      117
                                                                      117
          + water
Magnesium, bis-[4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)-
benzenesulfonamidato]-, hydrate, (T-4)-
                                                                      431
          + hydrochloric acid
          + water
                                                                      431
Manganese, bis-[4-amino-N-(6-methoxy-3-pyridaziny1)benzenesulfon-amidato]-,
hydrate
          + hydrochloric acid
                                                                      118
          + water
                                                                      118
Manganese, bis[4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)benzenesulfonamidato]+,
hydrate, (T-4)-
          + hydrochloric acid
                                                                      432
           water
                                                                      432
Manganese, bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-
NN,01]-, hydrate
          + hydrochloric acid
                                                                      350
                                                                      350
          + water
Mebacid
          see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-
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Medicel see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Mefenal see benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)-Mermeth see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-Mesulfa see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-N1-(3-Methoxy-2-pyrazinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(3-methoxypryrazinyl)-N-[4-[[(6-Methoxy-2-pyridazinyl)amino]sulfonyl]phenyl]-acetamide see acetamide, N-[4-[[(6-methoxy-2-pyridazinyl)amino]sulfonyl]phenyl]-N1-(6-Methoxy-3-pyridazinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-6-Methoxy-3-pyridazinylsulfanilamide see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-N1-(4-Methoxy-2-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(4-methoxy-2-pyrimidinyl)-Nl-(5-Methoxy-2-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-3-Methoxy-2-sulanilamidopyrazine see benzenesulfonamide, 4-amino-N-(3-methoxypryrazinyl)-5-Methoxy-2-sulfanilamidopyrimidine see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-3-Methoxy-2-sulfapyrazine see benzenesulfonamide, 4-amino-N-(3-methoxypryrazinyl)-4'-[(6-Methoxy-3-pyridaziny1)sulfamoy1]acetanilide see acetamide, N-[4-[[(6-methoxy-2-pyridaziny1)amino]sulfony1]phenyl]-6-Methoxy-3-sulfanilamidopyridazine see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Nl-(6-Methoxy-4-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-Nl-(6-Methoxy-4-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-6-Methoxy-4-sulfanilamidopyrimidine see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-3-Methoxy-6-sulfanilamidopyridazine see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-4-Methoxy-6-sulfanilamidopyrimidine see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-3-Methoxypyrazine sulfanilamide see benzenesulfonamide, 4-amino-N-(3-methoxypryrazinyl)-N1-(3-Methoxypyrazinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(3-methoxypryrazinyl)-Methoxypyrimal see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-N-4-[[(4-Methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]acetamide see acetamide, N-4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-4 -[ (4-Methyl-2-pyrimidinyl) sulfamoyl ]acetanilide see acetamide, N-4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-N1-(4-Methyl-2-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-N-(4-Methyl-2-pyrimidyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-Nl-(6-Methyl-3-pyridazinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-Nl-(2-Methyl-4-pyrimidinyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(2-methyl-4-pyrimidinyl)-Nl-Methyl-Nl-2-pyridylsulfanilamide see benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-Nl-Methyl-N4-sulfanilylsulfanilamide see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl]phenyl]-N-[4-[[[4-[(Methylamino)sulfonyl]phenyl]amino]sulfonyl]phenyl]acetamide see acetamide, N-[4-[[[4-[(Methylamino)sulfonyl]phenyl]amino]sulfonyl]phenyl]-Methylpyrimal see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-

4'-(Methylsulfamoyl)sulfanilanilide see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl]phenyl]-N1-Methylsulfapyridine see benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-Methylsulfazine see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-N1-[6-(Methylthio)-3-pyridazinylbenzenesulfonamide see benzenesulfonamide, 4-amino-N-[6-(methylthio)-3-pyridazinyl)-Metilsulfadiazin see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-Metilsulfazin see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-Microsulfon see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-Midicel see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Midikel see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Myasul see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Na disulfan monohydrate see benzenesulfonamide, 4-amino-N-4-[(aminosulfonyl)phenyl]-, monosodium salt monohydrate Na disulfan see benzenesulfonamide, 4-amino-N-[4-(aminosulfonyl)phenyl]-, monosodium salt Neasina see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-Neazina see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-Neazine see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-Neo-Uliran see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl] phenyl]-Neouliron see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl]phenyl]-Nickel, bis-[4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfon-amidato]-, hydrate + hydrochloric acid 119 + water 119 Nickel, bis[4-amino-N-(2,6-dimethoxy-4-pyrimidiny1)-benzenesulfonamidato]-, hydrate + hydrochloric acid 433 + water 433 Nickel, bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-NN.01] diagua-+ hydrochloric acid 351 + water 351 N1-(5-Nitro-2-pyridyl)sulfanilamide see benzenesulfonamide, 4-amino-N-(5-nitro-2-pyridinyl)-4-0xo-4-[[[4-(2-pyrimidinylamino)sulfonyl]phenyl]amino]-butanoicacid, disilver(1+) salt see butanoic acid, 4-oxo-4-[[[4-(2-pyrimidinylamino)sulfony]]phenyl]-amino]-, disilver(l+) salt Paramid Supra see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Paramid see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Percoccide see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-Piridazol see benzenesulfonamide, 4-amino-N-2-pyridinyl-Piridisir see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-Piridolo see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-Pirimal-M see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-Pirimal see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-

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Pirmazin
          see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-
Polycidal
          see benzenesulfonamide. 4-amino-N-(3-methoxypryrazinyl)-
Pyralcid
          see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-
        Pyrazinyl)sulfanilamide, monosodium saltsee benzenesulfonamide,
 N1-(
4-amino-N-pyrazinyl-, monosodium salt
Nl-(Pyrazinyl)sulfanilamide
          see benzenesulfonamide, 4-amino-N-pyrazinyl-
N1-2-Pyrazinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-pyrazinyl-
(N1-Pyrazinylsulfanilamido)sodium
          see benzenesulfonamide, 4-amino-N-pyrazinyl-, monosodium salt
Pyriamid
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
N1-3-Pyridazinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-3-pyridazinyl-
Pvridazol
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
Pyridine, 2,5-bis[[(4-aminophenyl)sulfonyl]amino]-
          see benzenesulfonamide, N,N'-(2,5-pyridinediyl)bis[4-amino-
1(2H)-Pyridineacetic acid, 2-[[(4-aminophenyl)sulfonyl]amino]-
          + water
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N-[4-[(2-Pyridinylamino)sulfonyl]phenyl]acetamide
          see acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]-
4-[(2-Pyridylamino)sulfonyl]aniline
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
N1-2(1H)-Pyridylidenesulanilamide
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
4'-(2-Pyridylsulfamoyl)acetanilide
          see acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]-
N1-3-Pyridylsulfanilamide
          see benzenesulfonamide, 4-amino-N-3-pyridinyl-
N1-2-Pyridylsulfanilamide
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
(N1-2-Pyridylsulfanilamido)sodium
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosodium salt
N1-2-Pyridylsulfapyridine, monosodium salt
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosodium salt
Pyrimal
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Pyrimal m
          see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-
N-[4-[(2-Pyrimidinylamino)sulfonyl]phenyl]acetamide
          see acetamide, N-[4-[(2-pyrimidinylamino)sulfonyl]phenyl]-
N1-2(1H)-Pyrimidinylidenesulfanilamide
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
4 - (2-Pyrimidinylsulfamoyl)acetanilide
          see acetamide, N-[4-[(2-pyrimidinylamino)sulfonyl]phenyl]-
N1-2-Pyrimidinylsulfanilamide, monosilver(1+) salt
          see silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-
N1-2-Pyrimidinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
N1-4-Pyrimidinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-4-pyrimidinyl-
Nl-5-Pyrimidinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-5-pyrimidinyl-
N1-2-Pyrimidinylsulfanilamide
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
(N1-2-Pyrinidinylsulfanilamido)sodium
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium salt
N1-2-Pyrimidylsulfanilamide
          see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-
Quinoseptyl
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Relbapiridine
          see benzenesulfonamide, 4-amino-N-2-pyridinyl-
Retamid
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
Retasulfin
          see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-
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| Retasulfine  |    |
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| see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)~<br>Ro 4-3506  |    |
| see benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)-   |    |
| Ro 4-4426<br>see benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-  | -  |
| Romezin see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-  |    |
| Ronin<br>see benzenesulfonamide, 4-amino-N-2-pyridinyl-  |    |
| RP 2652<br>see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-   |    |
| Salazodimethoxine<br>see benzoic acid, 5-[[4-[[2,6-dimethoxy-4-pyrimidinyl)amino]-<br>sulfonyl]-phenyl]azo]-2-hydroxy- |    |
| Sanasil<br>see benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-  | -  |
| Sanodiazine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-  | 1  |
| SDA see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-   |    |
| Septacil see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-   |    |
| Septipulmon<br>see benzenesulfonamide, 4-amıno-N-2-pyridinyl-  |    |
| SH 613<br>see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-   | I  |
| Silvadene<br>see silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-  | -  |
| Silver sulfadiazine<br>see silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-                                | ~  |
| Siver sulfamethazine<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-,                               | ,  |
| monosilver(l+) salt<br>Silver, (4-anino-N-2-pyrimidinylbenzene-sulfonamidato-NN,O)-<br>bis(1-imidazole-N3)-,(T-4)-     |    |
| + water 223<br>Silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-  |    |
| Slosul<br>see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-   |    |
| SMOP<br>see benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-   |    |
| SMP2<br>see benzenesulfonamide. 4-amino-N-(3-methoxypryrazinyl)-   |    |
| Sodium sulfadiazine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium sal                                | lt |
| Sodium sulfapyridine<br>see benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosodium salt                                |    |
| Sodium sulfapyrimidine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium sal                             | lt |
| Soluble sulfadiazine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium sal                               | lt |
| Soludagenan<br>see benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosodium salt   |    |
| Soludiazine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium sal  | lt |
| Sonilyn see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-  |    |
| Spanbolet<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-   |    |
| Spofadazine<br>see benzenesulfonamide, 4-amino-N~(6-methoxy-3-pyridazinyl)-  |    |
| Sporfadrizine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-  |    |
| Sterazine<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-  |    |
| Streptosilpyridine<br>see benzenesulfonamide, 4-amino-N-2-pyridinyl-   |    |
| Sulanilsulfanilmethylamide<br>see benzenesulfonamide, 4-amino-N-[4-[(methylamino)sulfonyl]-                            |    |
| phenyl]-<br>2-Sulfa-4-methylpyrimidine<br>see benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)-                  |    |

| 2-Sulfa-5-methoxypryimidine  |
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| see benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)-<br>Sulfachloropyridazine        |
| see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-<br>Sulfachlorpyridazine          |
| see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-<br>Sulfaclorazine                |
| see benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)-<br>Sulfadiazin                   |
| see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-<br>Sulfadiazine                             |
| see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-   |
| Sulfadiazine silver<br>see silver, (4-amino-N-2-pyrimidinylbenzenesulfonamidato-NN-01)-      |
| Sulfadiazine sodium<br>see benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosodium salt     |
| Sulfadimerazine<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-           |
| Sulfadimesin<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-              |
| Sulfadimesine<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-             |
| Sulfadimethoxypyrimidine<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)- |
| Sulfadimethyldiazine<br>see benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-      |
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