COMPONENTS:	EVALUATOR:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Water or (3) Aqueous phosphate buffers	Anthony N. Paruta Department of Pharmaceutics University of Rhode Island Kingston, Rhode Island, USA and Ryszard Piekos Faculty of Pharmacy, University of Gdansk 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

	10^3 mol dm^{-3} (*indicates mol Kg^{-1})		
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 x 10^{-3}mol dm^{-3} is too low with respect to the other values probably due to the poor control of temperature. Tréfouël'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^{-3}.

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 mol 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^{-3} phosphate buffer solutions. At pH 6,7 and 8 the recommended values are at 293K, 2.7 x 10^{-3} mol dm^{-3}, 2.8 x 10^{-3} mol dm^{-3} and 3.0 x 10^{-3} mol dm^{-3} 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 x 10^{-3} mol dm^{-3} and the solute is a fraction (≅ 2-3 x 10^{-3} mol dm^{-3}) of these highly soluble salts.

REFERENCES:

(1) Hug, E. *Rev. soc. Argentina biol.* 1940, *16,* 662-6.
(2) Lebel, H.; Schroeder, E.; Simesen, M. *Acta Med. Scand.* 1940, *105(4),* 395-410.
(3) Roblin, R.O., Jr.; Winnek, P.S. *J. Am. Chem. Soc.* 1940, *62,* 1999-2002.
(4) Durel, M.P.; Allinne, M. *Bull. Soc. Med. Hop. Paris* III 1941, 251-9.
(5) Tréfouël, M. *Bull. Acad. Med. Paris* 1941, *124,* 546-54.
(6) Clark, W.G.; Strakosch, E.A.; Levitan, N.I. *J. Lab. Clin. Med.* 1942, *28,* 188-9.
(7) Sapozhnikova, N.V.; Postovskii, I.Ya. *Zh. Prikl. Khim.* 1944, *17,* 427-34.
(8) Langecker, H. *Arch. Exptl. Path. Pharmakol.* 1948, *205,* 291-301.
(9) Neish, W.J.P. *Rec. trav. chim.* 1948, *67,* 361-71.
(10) Yamazaki, M.; Aoki.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1),* 37-40.
(11) Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21,* 2417-26.
(12) Krüger-Thiemer, E. *Arch. Dermatol. Syphilis* 1942, *183,* 90-116.
(13) Pulver, R.; Suter, R. *Schweiz. Med. Wochenschr.* 1943, *73(13),* 403-8.
(14) Langecker, H. *Arch. Exptl. Path. Pharmakol.* 1948, *205,* 291-301.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Hug, E. *Rev. soc. Argentina biol.* 1940, *16*, 662-6.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 54 mg% (2.2 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: A satd soln of sulfapyridine was prepd by heating on a water bath. The soln was then cooled down to 37°C and maintained at this temp for 7 days.	**SOURCE AND PURITY OF MATERIALS:** Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Lebel, H.; Schroeder, E.; Simesen, M. M. *Acta Med. Scand.* 1940, *105(4)*, 395-410.
VARIABLES: One temperature: 35°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 35°C is 1:1800 corresponding to 56 mg% (2.3 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Nothing specified	**SOURCE AND PURITY OF MATERIALS:** Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapydridine in water at 37°C is 49.5 mg/100 cm^3 solution (1.98×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

Sulfapyridine, mp 190-1°C, was probably prepd by the authors.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Durel, M. P.; Allinne, M.
Bull. Soc. Med. Hop. Paris III
1941, 251-9.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 0.45 g/liter (1.8 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A mixt of sulfapyridine and water was agitated for 24 hours at 37°C.

SOURCE AND PURITY OF MATERIALS:

Source and purity of sulfapyridine were not specified.

Distilled water was used.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Tréfouël, M.

Bull. Acad. Med. Paris 1941, *124*, 546-54.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 0.2 part per 100 parts water (8×10^{-3} mol kg^{-1} water, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine was diazotized, coupled with N-naphthyl-1-N-diethyl-3-propylenediamine and assayed colorimetrically.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Clark, W. G.; Strakosch, E. A.; Levitan, N. I. *J. Lab. Clin. Med.* 1942, *28*, 188-9.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^\circ C$	Solubility	
	g/100 g water	10^3 mol kg^{-1}water[a]
25	0.0268	1.07
37	0.0486	1.95

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small tinted glass container contg excess sulfapyridine in water was shaken in a water bath thermostat for 24 h. The satd soln was then filtered by aspiration through a 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), using a photoelectric colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of sulfapyridine was specified.

CO_2-free distd water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Water; H_2O; [7732-18-5]	Sapozhnikova, N. V.; Postovskii, I. Ya. *Zh. Prikl Khim.* 1944, *17*, 427-34.
VARIABLES:	PREPARED BY:
Temperature	R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility Weight %	Solubility 10^3 mol kg^{-1} water[a]
20	0.0194	0.778
37	0.0470	1.89
50	0.094	3.8
75	0.24	9.6
99	0.61[b]	25

[a] Calculated by compiler

[b] Calculated from the heat of dissolution (10,040 cal mol^{-1})

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine was dissolved in water to form a satd soln which was occasionally agitated in a glass vessel immersed in a thermostat. The equilibrium was usually attained after 1 h. Five to 100-cm^3 samples of the satd soln were placed in Pt crucibles or dishes and evapd to dryness at temps lower than 110-115°C. The residue was dried to const wt at 105-110°C and weighed.

SOURCE AND PURITY OF MATERIALS:

Pure, recrystd sulfapyridine was used. Its mp conformed to that reported in the literature.

Purity of the water was not specified.

ESTIMATED ERROR: Soly: quite reliable results were obtained over the temp range 20-75°C. At higher temps the accuracy was poor due to evapn of water during sampling (authors).
Temp: ±0.05°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Langecker, H.

Arch. Exptl. Path. Pharmakol. 1948, *205*, 291-301.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 53 mg% (2.1×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfapyridine in water was boiled and left for 24 h in a vessel protected from access of CO_2. The concn of sulfapyridine 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.

SOURCE AND PURITY OF MATERIALS:

Source and purity of the materials were not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Bratton, A. G.; Marshall, E. K. *J. Biol. Chem.* 1939, *128*, 537.
2. Havemann, R. *Klin. Wochenschr.* 1940, p. 503.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Neish, W. J. P. *Rec. trav. chim.* 1948, *67*, 361-71.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 370 γ/ml (1.48×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A suspension of sulfapyridine (10 mg/5 ml) in water was kept for 5 h at 37°C and 1 h 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 comparing the color with that of a std soln in a Klett colorimeter.

SOURCE AND PURITY OF MATERIALS:

Sulfapyridine: not specified.

Distd water was used.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Westfall, B. B. *J. Nat. Cancer Inst.* 1945, *6*, 23.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.

VARIABLES:

One temperature: 30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 30°C is 2.01 mmol/L (0.501 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine (0.5 g) was placed in an L-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 spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in water at 37°C is 2.09 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfapyridine concn in the aq soln (pH 6) was detd by diazotization. No details were given.

SOURCE AND PURITY OF MATERIALS:

Comm available sulfapyridine was used as supplied.

Deionized water was used.

ESTIMATED ERROR:

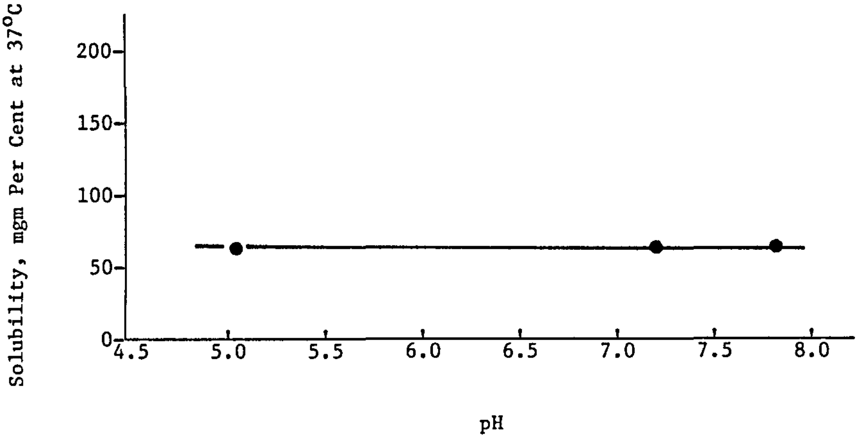
Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Sodium hydroxide; NaOH; [1310-73-2] (3) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Rose, F. L.; Martin, A.R.; Bevan, H. G. L. *J. Pharm. Exp. Therap.* 1943, *77*, 127-42.
VARIABLES: pH	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfapyridine was stirred in boiling water, the soln was cooled to 37°C, the temp being maintained thermostatically, and 0.1N NaOH was added to increase the pH. The pH was measured by means of a glass electrode - calomel half-cell system, and was permitted to reach equilibrium before a reading was taken. The concn of sulfapyridine in soln was detd colorimetrically by withdrawing a sample through a filter-tip into a preheated micropipet.

SOURCE AND PURITY OF MATERIALS:

The source and purity of sulfapyridine was not specified.

Water was doubly distilled.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Sodium chloride; NaCl; [7647-14-5] (3) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Avico, U.; Cavazutti, G.; di Francesco, R.; Signoretti Ciranni, E.; Zuccaro, P. *Farmaco, Ed. Pratica* <u>1975,</u> *30(1),* 40-6.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility of amorphous sulfapyridine in equimolal NaCl solutions	
	g/100 g water	10^3 mol kg^{-1} water[a]
25	0.61	2.4
35	0.75	3.0
40	0.81	3.2

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A soln of Na salt of sulfapyridine was added to a HCl soln contg stoichiometric quantity of the acid to neutralize the salt. The neutralization was carried out in a thermostat and the pH of the mixt was maintained close to that of a satd sulfapyridine soln. The procedure was repeated using various initial concn of the reagents to find the max concn of sulfapyridine at which no pptn occurred.

SOURCE AND PURITY OF MATERIALS:

Source and purity of sulfapyridine was not specified. The mp of crystalline sulfapyridine was 191-3°C.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]
(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]
(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:
Krüger-Thiemer, E.
Arch. Dermatol. Syphilis 1942, *183*, 90-116.

VARIABLES:
One temperture: ca 20°C; one pH: 8.74

PREPARED BY:
R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in a 0.705M (10%) Na_2HPO_4 solution of pH 8.74, at room temperature (about 20°C), is 0.075 g% (3.0 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
Sulfapyridine (0.5 g) was dissolved in the 0.705M (10%) Na_2HPO_4 soln (pH 8.74), at room temp (about 20°C), shaken for 2 h, and filtered. A 1-cm^3 aliquot of the filtrate was withdrawn, cooled, acidified with 2N HCl, and the sulfapyridine content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultra-ionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:
Sulfapyridine was the product manufd by Nordmark under the name Eubasin.
The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:
Soly: precision ±5% (author).
Temp: not specified.
pH : ±0.05 pH unit (author).

REFERENCES:
1. Kimmig, J. *Arch. Dermatol.* *176*, 722; *Erg. Hyg.* 1941, *24*, 398.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Krüger-Thiemer, E.

Arch. Dermatol. Syphilis 1942, *183*, 90-116.

VARIABLES:

One temperature: ca 20°C; one pH: 4.37

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in a 0.735M (10%) KH_2PO_4 solution of pH 4.37, at room temperature (about 20°C), is 0.054 g% (2.17 mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine was dissolved in a 0.735M (10%) KH_2PO_4 soln in amt of 0.5 g/10 cm^3, shaken for 2 h, and filtered. A 1-cm^3 aliquot of the filtrate was withdrawn, cooled, acidified with 2N HCl, and the sulfapyridine 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 glass electrode.

SOURCE AND PURITY OF MATERIALS:

Sulfapyridine was the product manufd by Nordmark under the name Eubasin.

The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Soly: precision ±5% (author).

Temp: not specified.

pH : ±0.05 pH unit (author).

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Krüger-Thiemer, E.

Arch. Dermatol. Syphilis 1942, *183*, 90-116.

VARIABLES:

Temperature; pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Composition of 1/15M phosphate buffer solutions				Solubility			
				Room temp (ca 20°C)		37°C	
Na_2HPO_4	KH_2PO_4	%Content	pH	g%	10^3 mol dm^{-3} solution[a]	g%	10^3 mol dm^{-3} solution[a]
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[b]	7.51	0.060	2.407	-	-
94.7	5.3	0.95	8.018	0.081	3.249	-	-

[a] Calculated by compiler.

[b] Molar content; 10% buffer solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine (0.5 g) was dissolved in 10 cm^3 of a buffer soln, shaken for 2 h at 20°C (or left for 48 h at 37°C), and filtered at respective temp. A 1-cm^3 aliquot of the filtrate was then withdrawn, cooled (dild for expts at 37°C), acidified with 1 cm^3 of 2N HCl, and the sulfapyridine 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.

SOURCE AND PURITY OF MATERIALS:

Sulfapyridine was the product manufd by Nordmark under the name Eubasin.

The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Soly: precision ±7% (author).

Temp: not specified.

pH : ±0.05 pH unit (author).

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Pulver, R.; Suter, R.

Schweiz. Med. Wochenschr. 1943, *73(13)*, 403-8.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility of sulfapyridine in M/15 phosphate buffers (according to Sørensen) at 20°C	
	mg%	10^3 mol dm^{-3} [a]
6.0	64	2.6
7.0	67	2.7
8.0	70	2.8

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonmaide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Langecker, H.

Arch. Exptl. Path. Pharmakol. 1948, *205,* 291-301.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH of the 1/15M phosphate buffer	Solubility at 37°C	
	mg%	10^3 mol dm^{-3} [a]
4.9	44	1.8
5.9	60	2.4
7.0	58	2.3
7.5	62	2.5

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfapyridine was added to the buffer soln and boiled for 1 h in a sealed ampul followed by keeping the ampul at 37°C. The concn of sulfapyridine 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.

SOURCE AND PURITY OF MATERIALS:

Source and purity of the materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Bratton, A. G.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *128,* 537.
2. Havemann, R. *Klin. Wochenschr.* 1940, p. 503.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku,* 1967, *27(1),* 37-40.

VARIABLES:

One temperature: 30°C; one pH: 7.4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 1.91 mmol/L (0.476 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine (0.5 g) was placed in an L-shaped tube together with 20 ml of the buffer 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.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Hekster, Y. A.; Vree, T. B.; Damsma, J.E.; Friesen, W. T. *J. Antimicrob. Chemother.* 1981, *8*, 133-44.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^4 mol dm^{-3} a
5.5	120	4.81
7.5	200	8.02

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfapyridine were prepd in phosphate buffers of pH 5.5 and 7.5 at room temp (25°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 column (10 cm x 4.6 mm i.d.) was packed with Lichrosorb RPS, 5 μm, obtained from Chrompack. An injection loop of 100 μl was used. The oven temp was 40°C. Detection of sulfapyridine was performed at 260 nm.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials were not specified.

ESTIMATED ERROR:

The detection limit of the solute by HPLC was 0.5 mg/l (authors). The error in temperature and pH was not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Calcium chloride; $CaCl_2$; [10043-52-4]

(3) Potassium chloride; KCl; [7447-40-7]

(4) Sodium chloride; NaCl; [7647-14-5]

(5) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Hawking, F.

Lancet, 1941, *240*, 786-8.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility of bicarbonate-free Locke's solution^{a}	
	mg/100 ml	10^4 mol dm^{-3} ^{a}
17	17	6.8
36	41	16.5

^{a}The solution contained NaCl 9 g, KCl 0.2 g, $CaCl_2$ 0.2 g, water 1 liter, and had a pH of 6.8.

^{b}Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine was shaken up with the bicarbonate-free Locke's soln for many hours in a tube which was corked to prevent loss of CO_2. The supernatant was filtered through a paper, dild in a hot room to prevent pptn, and sulfapyridine was detd by the method of Marshall and Litchfield (1).

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

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* 1938, *88*, 85.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]
(2) Ethanol; C_2H_6O; [64-17-5]
(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Sapozhnikova, N. V.; Postovskii, I. Ya.
Zh. Prikl. Khim. 1944, *17*, 427-34.

VARIABLES:

Concentration of ethanol, temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of ethanol	Solubility			
	at 37°C		at 75°C	
Weight%	Weight%	10^2 mol kg^{-1} solvent[a]	Weight%	10^2 mol kg^{-1} solvent[a]
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

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine was dissolved in EtOH-water mixts to form satd solns which were occasionally agitated in glass vessels immersed in a thermostat. The equilibrium was usually attained after 1 h. Five- to 100-cm^3 samples of the satd soln were placed in Pt crucibles or dishes and evapd to dryness at temps lower than 110-115°C. The residue was dried to const wt at 105-110°C and weighed.

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.

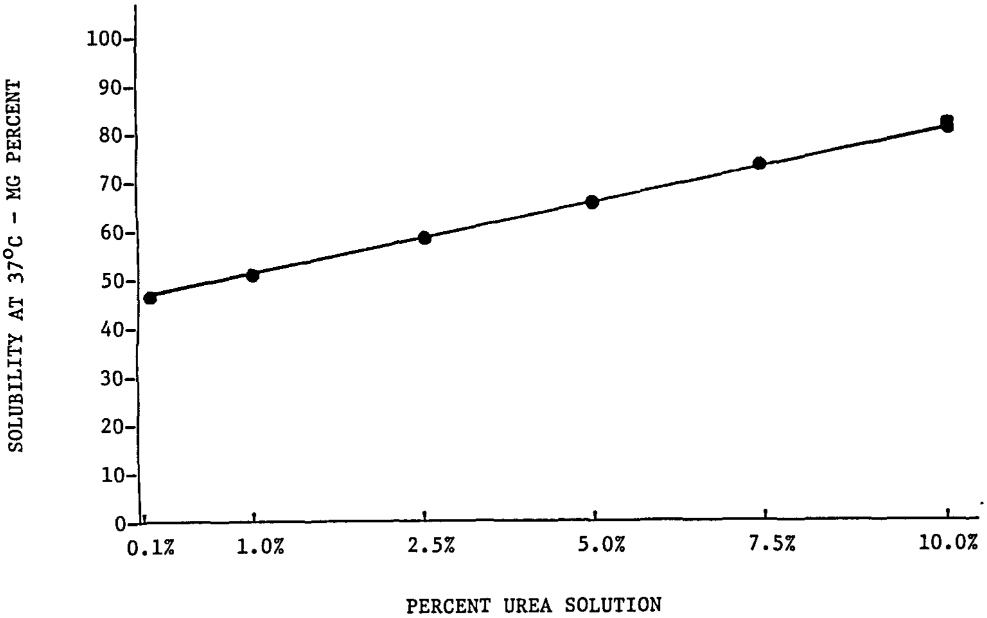
ESTIMATED ERROR:

Soly: quite reliable results were obtained (authors).
Temp: ±0.05°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Urea; CH_4NO; [57-13-6] (3) Water; H_2O; [7732-18-5]	Sobin, S. S. *J. Lab. Clin. Med.* 1942, *27*, 1657-8.
VARIABLES: Concentration of urea	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:



Solubility in a 10 per cent solution at 37°C is 73.3 mg per 100 cm^3 (2.94×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Urea solns of varying concns from 0.1 to 10% were incubated at 37°C with an excess of sulfapyridine, shaken at intervals, and filtered through two thicknesses of Whatman No. 42 filter paper. After appropriate diln the free sulfonamide was detd by the method of Bratton and Marshall (1) using the Evelyn colorimeter and a No. 540 filter.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Ethanol; C_2H_6O; [64-17-5] (3) 1,2,3-Propanetriol; C_3H_8O; [56-81-5] (4) Water; H_2O; [7732-18-5]	Dolique, R.; Foucault, J. *Trav. soc. pharm. Montpellier* 1952, *12*, 145-53.
VARIABLES: One temperature: 26-28°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in a mixture of 1,2,3-propanetriol and 95% ethanol (2:1 by wt) at 26-28°C is 0.575% (2.32×10^{-2} mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The sulfapyridine content was detd by diazotization of the amine group in a cold acidified 0.1N KNO_2 soln. an excess of KNO_2 was detected by using iodinated starch.	Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) Ethanol; C_2H_6O; [64-17-5]

(3) 1,2,3-propanetriol; $C_3H_8O_3$; [56-81-5]

(4) Urea; CH_4N_2O; [57-13-6]

(5) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Dolique, R.; Foucault, J.

Trav. soc. pharm. Montpellier 1952, *12*, 145-53.

VARIABLES:

One temperature: 26-28°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine at 26-28°C in a saturated solution of urea in a mixture of 1,2,3-propanetriol and 95° ethanol (2:1 by wt.), containing 54.5 g of urea per 100 g of the mixture, is 0.78% (3.2×10^{-2} mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfapyridine content was detd by diazotization of the amine group in a cold acidified 0.1N KNO_2 soln. An excess of KNO_2 was detected by using iodinated starch.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (caffeine); $C_8H_{10}N_4O_2$; [58-08-2]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Neish, W. J. P. *Rec. trav. chim.* 1948, *67*, 361-71.

VARIABLES:

Concentration of caffeine

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of caffeine g/100 ml	Solubility of sulfapyridine at 37°C	
	γ /ml	10^3 mol dm^{-3} a
0.5	470	1.88
0.75	480	1.92

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A suspension of sulfapyridine in caffeine soln was kept for 5 h at 37°C and 1 h at room temp before filtration. Soly was detd by the Westfall's method (1) based on diazotization of the sulfonamide, coupling with Na 2-napthol-3,6-disulfonate and comparing the color with that of a std soln in a Klett colorimeter.

SOURCE AND PURITY OF MATERIALS:

Sulfapyridine: not specified.

Anhydrous caffeine was a good commercial product (source not specified).

Distd water was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Westfall, B. B. *J. Nat. Cancer Inst.* 1945, *6*, 23.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	**ORIGINAL MEASUREMENTS:** Yamazaki, M.; Aoki, M. ; Kamada, A.; Yata, N. *Yakuzaigaku,* 1967, *27(1),* 37-40.
VARIABLES: One temperature: 30°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in chloroform at 30°C is 3.27 mmol/L (0.815 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyridine (0.5 g) was placed in an L-shaped tube together with 20 ml of chloroform. The mixt was 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.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}N_{11}N_3O_2S$; [144-83-2]

(2) Methane, trichloro-; $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A.

1973, *21*, 2417-26.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in $CHCl_3$ at 37°C is 2.86 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

One ml of the sulfapyridine soln in $CHCl_3$ at equilibrium was taken into a test tube. After evapn of the solvent, the residue was dissolved in 1N NaOH, the soln was properly dild with deionized water and the concn of sulfapyridine was detd by diazotization.

SOURCE AND PURITY OF MATERIALS:

Comm available sulfapyridine was used as supplied.

Neither source nor purity of $CHCl_3$ was specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) 2-Propanol; C_3H_8O; [67-63-0]

ORIGINAL MEASUREMENTS:

Burlage, H. M. *J. Am. Pharm. Assoc., Sci. Ed.* 1948, *37*, 345.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyridine in 2-propanol at 25°C is 0.1750 g/100 cm^3 solution (7.020×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfapyridine in 2-propanol were prepd at 25°C and definite vols of the solns were measured into tared dishes by means of standard pipets. The alcohol was allowed to evap at room temp and the residue was dried at 105°C. In the case of losses due to apparent decompn, the residue was dried in a desiccator (1).

SOURCE AND PURITY OF MATERIALS:

The sulfapyridine was manufd by Merck and was of the U.S.P. purity. The source and purity of 2-propanol were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Burlage, H. M. *J. Am. Pharm. Assoc., Sci. Ed.* 1947, *36(1)*, 16.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2]

(2) 2-Propanone (acetone); C_3H_6O; [67-64-1]

ORIGINAL MEASUREMENTS:

Gutierrez, F. H.

Anales fis. quim. (Madrid) 1945, *41*, 537-60.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	G^a	E^b	X_g/l^c	mol/l^d acetone	mmol/mol acetone	$1:X_g^e$	$1 + X_{cc}^f$
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

$^aG = \dfrac{p\ 100}{P - p}$, where p and P are weights of solute and solution, resp.

Continued on the next page.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A special all-glass app was contructed enabling the prepn of satd solns, agitation by bubbling a stream of acetone-satd N, filtration, and distn off the solvent without contact with air. Two exchangeable dissoln vessels of 15 and 8 cm^3 working capacity were used depending on the soly of solute. The app was immersed in a thermostat. The vols of acetone used were 15 or 5 cm^3, and the equilibration time was 2-2.5 h. The satd solns were filtered, weighed, the solvent was distd off, the residues were dried at 105°C, weighed, and examd for the presence of solvated acetone.

SOURCE AND PURITY OF MATERIALS:

The source of the materials was not specified. Pure, anhyd acetone was used. The absence of impurities and water was confirmed by procedures of the German Pharmacopeia VI and Spanish Pharmacopeia VIII.

The purity of sulfapyridine was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated until 2 values not differeing in the second decimal were obtained (author).

Temp: ±0.1°C (author).

REFERENCES:

Continued from previous page.

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

[e] g of acetone required to dissolve 1 g of solute; [f] volume (cm^3) of acetone required to dissolve 1 g of solute.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [144-83-2] (2) Methylcyclohexanone; $C_7H_{12}O$; [1331-22-2]	Barber, H. J.; Wilkinson, J. H. *Quart. J. Pharm. Pharmacol.* 1946, *19*, 248-55.
VARIABLES:	PREPARED BY:
One temperature: 25°C	R. Piekos

EXPERIMENTAL VALUES:

Approximate solubility of sulfapyridine in methylcyclohexanone at 25°C is 3.5 per cent w/v (0.14 mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Nothing specified.	Nothing specified.
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl- (sulfapyridine); $C_{11}H_{11}N_3O_2S$; [114-83-2]

(2) Methylcyclohexanone; $C_7H_{12}O$; [1331-22-2]

ORIGINAL MEASUREMENTS:

Barber, H. J.; Wilkinson, J. H.
Pharm. J. 1946, 105-6.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Approximate solubility of sulfapyridine in methylcyclohexanone at 25°C is 3.5 per cent w/v (0.14 mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-3-pyridinyl-; $C_{11}H_{11}N_3O_2S$; [599-81-5]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-3-pyridinylbenzenesulfonamide in water at 37°C is 3.3 mg/100 cm^3 solution (1.3×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 258-9°C (dec), was probably prepd by the authors by reacting 3-aminopyridine with acetylsulfanilyl chloride followed by hydrolysis. Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Hydroxycalcium, (4-amino-N-2-pyridinylbenzenesulfonamidato)-; $C_{11}H_{11}CaN_3O_3S$; [77400-70-5]

(2) 2-Propanone (acetone); C_3H_6O; [67-64-1]

ORIGINAL MEASUREMENTS:

Gutierrez, F. H.

Anales fis. quim. (Madrid) 1945, *41*, 537-60.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	G[a]	E[b]	X_g/l[c]	mol/l[d] acetone	mmol/mol acetone	1:X_g[e]	1 + X_{cc}[f]
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

[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/l acetone; [d] should be mmol/l acetone (compiler);

[e] g of acetone required to dissolve 1 g of solute; [f] volume (cm^3) of acetone required to dissolve 1 g of solute.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A special all-glass app was constructed enabling the prepn of satd solns, agitation by bubbling a stream of acetone-satd N, filtration, and distn off the solvent without contact with air. Two exchangeable dissoln vessels used depending on the soly of solute. The app was immersed in a thermostat. The vols of acetone used were 15 or 8 cm^3, and the equilibration time was 2-2.5 h. The satd solns were filtered, weighed, the solvent was distd off, the residues were dried at 105°C, weighed, and examd for the presence of solvated acetone.

SOURCE AND PURITY OF MATERIALS:

The source of the materials was not specified. Pure, anhyd acetone was used. The absence of impurities and water in it was confirmed by procedures of the German Pharmacopeia VI and Spanish Pharmacopeia VIII. The purity of the solute was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated until 2 values not differing in the second decimal were obtained (author).

Temp: ±0.1°C (author).

REFERENCES:

COMPONENTS:

(1) Hydroxycalcium, (4-amino-N-2-pyridinylbenzenesulfonamidato)-, dihydrate; $C_{11}H_{11}CaN_3O_3S \cdot 2H_2O$; [77400-71-6]

(2) 2-Propanone (acetone); C_3H_6O; [67-64-1]

ORIGINAL MEASUREMENTS:

Gutierrez, F. H.

Anales fis. quim. (Madrid) 1945, *41*, 537-60.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	G^a	E^b	X_g/l^c	mol/l^d acetone	mmol/mol acetone	$1{:}X_g^e$	$1 + X_{cc}^f$
0	0.526	0.523	4.285	12.6	0.90	190.80	233.10
5	0.531	0.528	4.295	12.7	0.91	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	1.10	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	1.00	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

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

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

^{e}g of acetone required to dissolve 1 g of solute; ^{f}volume (cm^3) of acetone required to dissolve 1 g of solute.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A special all-glass app was constructed enabling the prepn of satd solns, agitation by bubbling a stream of acetone-satd N, filtration, and distn off the solvent without contact with air. Two exchangeable dissoln vessels of 15 and 8 cm^3 working capacity were used depending on the soly of solute. The app was immersed in a thermostat. The vols of acetone used were 15 or 5 cm^3, and the equilibration time was 2-2.5 h. The satd solns were filtered, weighed, the solvent was distd off, the residues were dried at 105°C, weighed, and examd for the presence of solvated acetone.

SOURCE AND PURITY OF MATERIALS:

The source of the materials was not specified. Pure, anhyd acetone was used. The absence of impurities and water in it was confirmed by procedures of the German Pharmacopeia VI and Spanish Pharmacopeia VIII. The purity of the solute was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated until 2 values not differing in the second decimal were obtained (author).

Temp: ±0.1°C (author).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosodium salt (sodium sulfapyridine); $C_{11}H_{10}N_3NaO_2S$; [127-57-1]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Clark, W. G.; Strakosch, E. A.; Levitan, N.I. *J. Lab. Clin. Med.* 1942, *28*, 188-9.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	Solubility	
	g/100 g water	mol kg^{-1} water[a]
25	52.0	1.92
37	80.0	2.95

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small tinted glass container contg excess Na sulfapyridine in water was shaken in a water bath thermostat for 24 h. The satd soln was then filtered by aspiration through a 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), using a photoelectric colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of Na sulfapyridine was specified.

CO_2-free distd water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Zinc, (T-4)-bis(4-amino-N-2-pyridinylbenzenesulfonamidato-N^N,O)-Zn(II) sulfapyridine); $C_{22}H_{18}N_6O_4S_2Zn$; [71261-89-7] (2) Water; H_2O; [7732-18-5]	Fox, Ch. L., Jr.; Modak, S. Standford, J. W.; Fox, P. L. *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.
VARIABLES: One temperture: 28-30°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of Zn(II) sulfapyridine in water at room temperature (28-30°C)[a] is 44.6 mg% (7.94×10^{-4} mol dm^{-3} solution, compiler).

[a] Value given by one of the authors (S. M.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd soln of Zn(II) sulfapyridine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfapyridine content using the colorimeter method of Bratton and Marshall (1). The soly value was then calcd from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

The Zn(II) sulfapyridine was prepd by the authors as follows: an inorg Zn salt was reacted with Na salt of sulfapyridine and the ppt was analyzed and characterized.
No details were given, however.
Purity of the materials were not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *120*, 537.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosilver salt; (Ag sulfapyridine); $C_{11}H_{10}AgN_3O_2S$ [24342-38-9]

(2) Nitric acid; HNO_3; [7697-37-2]

(3) Potassium nitrate; KNO_3; [7757-79-1]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Nesbitt, R. U., Jr.; Sandmann, B. J.

J. Pharm. Sci. 1978, *67(7)*, 1012-17.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Comparison of Total Silver Sulfapyridine Molar Solubility, S, Determined by the Method of Known Subtraction with the Molar Concentration of the Silver Ion Determined by Direct Potentiometry on Identical Samples at 25±0.1°, 0.1M Ionic Strength, in Nitric Acid Buffer

pH 2.294

	$S \times 10^3$	$[Ag^+] \times 10^3$
	8.973	8.143
	8.889	8.018
	9.030	8.143
	9.030	8.143
	8.889	8.018
Mean	8.962	8.093

pH 2.486

$S \times 10^3$	$[Ag^+] \times 10^3$
5.472	7.425
5.514	7.514
5.579	7.632
5.304	7.484
5.514	7.514
5.660	7.454
5.508	7.504

pH 2.583

	$S \times 10^3$	$[Ag^+] \times 10^3$
	5.366	4.540
	5.336	4.488
	5.356	4.401
	5.346	4.505
	5.366	4.470
	5.356	4.436
Mean	5.354	4.473

pH 2.848

$S \times 10^3$	$[Ag^+] \times 10^3$
3.031	2.954
2.974	2.874
2.866	2.774
2.979	2.863
2.788	2.678
2.928	2.839

to be contd.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Mixts of 100 g of Ag sulfapyridine and 25 or 27 ml of the nitric acid buffer were placed in paraffin-coated vials, adjusted to an ionic strength 0.1M with KNO_3, and rotated end over end in a thermostated bath until equilibrium soly was obtained (3-7 days). After filtration through 20M glass filtering crucibles, the solns were analyzed at 25±0.1 °C in paraffin coated beakers for Ag^+ ions with a silver-ion selective electrode (No. 94-16, Orion Res. Cambridge, Mass) standardized at the temp indicated and 0.1M ionic strength. The pH was measured with a triple-purpose pH electrode (Corning Sci. Instruments, Medfield, Mass) standardized using buffers meeting NBS requirements. The nitric acid buffers were prepd by diln of 0.1M HNO_3 and were adjusted to an ionic strength of 0.1M with KNO_3.

SOURCE AND PURITY OF MATERIALS:

All reagents were anal or USP grade. Ag sulfapyridine was prepd by the method of Rosenzweig and Fuchs (1) and recrystd from concd ammonia (2).

Water had a sp cond of (1-10) x 10^{-7} ohm^{-1} cm^{-1}.

The source of the reagent was not specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors)

pH : accuracy ±0.001 pH unit (authors).

REFERENCES:

1. 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.* 1974, *63*, 948.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyridinyl-, monosilver salt, (Ag sulfapyridine); $C_{11}H_{10}AgN_3O_2S$; [24342-38-9]

(2) 4-Morpholinepropanesulfonic acid; $C_7H_{15}NO_4S$; [1132-61-2]

(3) 4-Morpholinepropanesulfonic acid, sodium salt; $C_7H_{14}NNaO_4S$; [71119-22-7]

(4) Potassium nitrate; KNO_3; [7757-79-1]

(5) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Nesbitt, R. U., Jr.; Sandmann, B. J.

J. Pharm. Sci. 1978, *67(7)*, 1012-17.

VARIABLES:

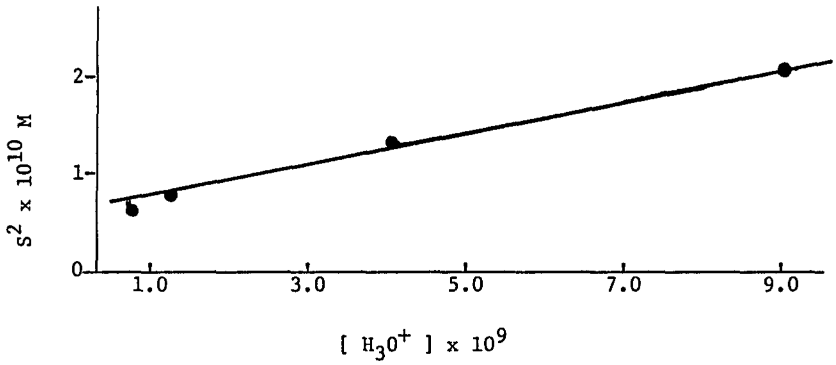
Hydronium-ion concentration

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Equilibrium values of S^2 (S = total molar solubility) versus $[H_3O^+]$ for Ag sulfapyridine in 0.05M 4-morpholinepropanesulfonic acid buffer at 0.1M ionic strength (KNO_3) and 25±0.1°C.



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Mixts of 100 mg of Ag sulfapyridine and 25 or 27 ml of the 4-morpholinepropanesulfonic acid buffer were placed in paraffin-coated vials, adjusted to an ionic strength 0.1M with KNO_3, and rotated end over end in a thermostated bath until equilibrium soly was obtained (3-7 days). After filtration through 20M glass filtering crucibles, the solns were analyzed at 25±0.1°C in paraffin-coated beakers for Ag^+ ions with a silver-ion selective electrode (No. 94-16, Orion Res., Cambridge, Mass) standardized at the temp indicated and 0.1M ionic strength. The pH was measured with a triple-purpose pH electrode (Corning Sci. Instruments, Medfield, Mass) standardized using buffers meeting NBS requirements. The buffers were prepd with a total molar concn of 0.05M and adjusted to an ionic strength of 0.1M with KNO_3

SOURCE AND PURITY OF MATERIALS:

All reagents used were anal or USP grade.

Ag sulfapyridine was prepd by the method of Rosenzweig and Fuchs (1) and recrystd from concd ammonia (2).

Water had a sp cond of (1-10) x 10^{-7} $ohm^{-1}cm^{-1}$

The buffer soln was from US Biochem. Corp., Cleveland, Ohio (purity not specified).

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors)

pH : accuracy ±0.001 pH unit (authors)

REFERENCES:

1. Rosenzweig, S.; Fuchs, W. *U.S. pat* 2,536,095 (1951)
2. Sandmann, B.J.; Nesbitt, R.U., Jr.; Sandmann, R. A. *J. Pharm.* 1974, *63*, 948.

COMPONENTS:

Continued from previous page

ORIGINAL MEASUREMENTS:

Nesbitt, R. U., Jr.; Sandmann, B. J.
J. Pharm. Sci. 1978, *67(7)*, 1012-17.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Calculation of the Solubility Product of Ag Sulfapyridine[a], K_s, at 25°C and 0.1M Ionic Strength

pH	f_o	$[Ag^+]$	S	K_s
2.294	1.418×10^{-7}	8.093×10^{-3}	8.890×10^{-3}	1.02×10^{-11}
2.486	3.066×10^{-7}	5.508×10^{-3}	7.504×10^{-3}	1.27×10^{-11}
2.583	4.480×10^{-7}	4.473×10^{-3}	5.354×10^{-3}	1.07×10^{-11}
2.848	1.184×10^{-6}	2.828 x 10-3	2.937×10^{-3}	9.80×10^{-12}
			Mean	$(1.09 \pm 0.13)10^{-11}$

[a] from eq. $K_s = f_o\,[Ag^+]S$, where

$$f_o = \left(1 + \frac{[H_3O^+]}{K_2} + \frac{[H_3O^+]^2}{K_1\ K_2}\right)^{-1}$$

S is the total molar solubility, and K_1 and K_2 are the apparent dissociation constants of the N^4 - (amino) and N^1 - (amido) hydrogens of sulfapyridine, respectively.

[a] K_s reported as mean ± SD.

to be contd

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

(1) Ag sulfapyridine; $C_{11}H_{10}AgN_3O_2S$; [24342-38-9]

(2) Nitric acid; HNO_3; [7693-37-2]

(3) Potassium nitrate; KNO_3; [7757-79-1]

(4) Water; H_2O; [7732-18-5]

for details see previous page

ORIGINAL MEASUREMENTS:

Nesbitt, R. U., Jr.; Sandmann, B. J.

J. Pharm. Sci. <u>1978</u>, *67(7)*, 1012-17.

VARIABLES:

pH

PREPARED BY:

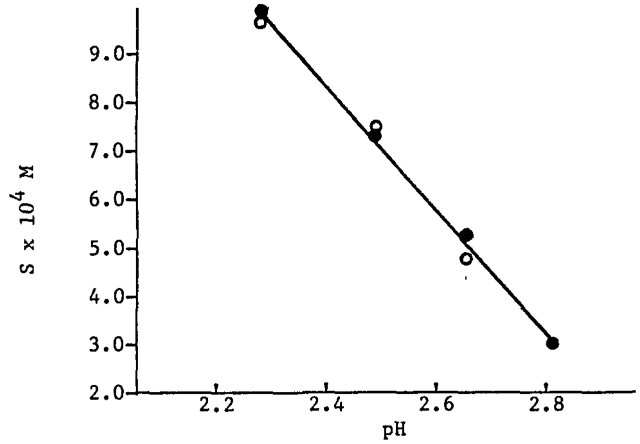
R. Piekos

EXPERIMENTAL VALUES:

Molar solubility, S, of Ag sulfapyridine versus pH at 0.1M ionic strength and 25±0.1°C. Key: ● calculated from the equation

$$S = \left(\frac{[H_3O^+]^2 K_s}{K_1 K_2} + \frac{K_s}{K_2} [H_3O^+] \right)^{0.5} \left(1 + \frac{f_o S}{K_d}\right),$$

where K_s is the solubility product of Ag sulfapyridine, and K_1, K_2, and K_d are the apparent dissociation constants of the N^4 (amido) hydrogen, N^1 (amino) hydrogens and Ag sulfapyridine, respectively; o , experimental values.



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:	EVALUATOR:
(1) Acetamide, N-[4-[(2-pyridinylamino)-sulfonyl]phenyl]- (acetyl sulfapyridine) $C_{13}H_{13}N_3O_3S$; [19077-98-6]	Anthony N. Paruta Department of Pharmaceutics University of Rhode Island Kingston, Rhode Island, USA and
(2) Water	Ryszard Piekos Faculty of Pharmacy, University of Gdansk Gdansk, Poland 1986

CRITICAL EVALUATION:

Table I: Solubility of Acetyl sulfapyridine in water, 310K

Reference	10^3 mol dm^{-3} 310K
1	2.4
2	0.721
3	1.1
4	0.51
5	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^{-3} 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^{-3} 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

Reference	pH	10^3 mol dm^{-3} 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 Krüger-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^{-3} in phosphate buffer 0.067 mol dm^{-3} 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^{-3}.

REFERENCES:

(1) Hug, E. *Rev. soc. Argentina biol.* 1940, *16*, 662-6.
(2) Lebel, H.; Schroeder, E.; Simesen, M. *Acta Med. Scand.* 1940, *105(4)*, 395-410
(3) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P. *J. Am. Chem. Soc.* 1940, *62*, 2002-5.
(4) Durel, M.P.; Allinne, M. *Bull. Soc. Med. Hop. Paris* III 1941, 251-9.
(5) Sapozhnikova, N.V.; Postovskii, I.Ya. *Zh. Prikl. Khim.* 1944, *17*, 427-34.
(6) Langecker, H. *Arch. Exptl. Path. Pharmakol.* 1948, *205*, 291-301.
(7) Krüger-Thiemer, E. *Arch. Dermatol. Syphilis* 1942, *183*, 90-116.
(8) Pulver, R.; Suter, R. *Schweiz. Med. Wochenschr.* 1943, *73(13)*, 403-8.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6] (2) Water; H_2O; [7732-18-5]	Hug, E.; *Rev. soc. Argentina biol.* 1940, *16*, 662-6.
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 = 2.4×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A satd soln of acetyl sulfapyridine was prepd by heating on a water bath. The soln was then cooled down to 37°C and maintained at this temp for 7 days.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Lebel, H.; Schroeder, E.; Simesen, M.

Acta. Med. Scand. 1940, *105(4)*, 395-410.

VARIABLES:

One temperature: 35°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyridine in water at 35°C is 1:1750 corresponding to 57 mg% (2.1 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4-[(2-pyridinylamino) sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6] (2) Water; H_2O; [7732-18-5]	Roblin, R. O., Jr.; Williams, J. H.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1940, *62*, 2002-5.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyridine in water at 37°C is 21.0 mg/100 cm^3 solution (7.21×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess acetyl sulfapyridine 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 spectrophotometer for comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyridine was prepd by condensing recrystd acetylsulfanilyl chloride with 2-aminopyridine in a pyridine soln. The crude product was recrystd from EtOH or PrOH (2).

Purity of the water was not specified.

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.* 1940, *62*, 160.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6] (2) Water; H_2O; [7732-18-5]	Durel, M. P.; Allinne, M. *Bull. Soc. Med. Hop. Paris III* <u>1941,</u> 251-9.
VARIABLES:	PREPARED BY:
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyridine in water at 37°C is 0.32 g/liter (1.1×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
A mixt of acetyl sulfapyridine and water was agitated for 24 hours at 37°C.	Source and purity of acetyl sulfapyridine was not specified. Distilled water was used.
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Sapozhnikova, N. V.; Postovskii, I. Ya.
Zh. Prikl. Khim. 1944, *17*, 427-34.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	Solubility	
	Weight%	10^3 mol kg^{-1} water[a]
20	0.0056	0.19
37	0.015	0.51
50	0.026[b]	0.89
75	0.067	2.30
99	0.20	6.88

[a] calculated by compiler

[b] calculated from the heat of dissolution (10,480 cal mol^{-1})

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was dissolved in water to form a satd soln which was occasionally agitated in a glass vessel immersed in a thermostat. The equilibrium was usually attained after 1 h. Five -' to 100-cm^3 samples of the satd soln were placed in Pt crucibles or dishes and evapd to dryness at temps lower than 110-115°C. The residue was dried to const wt at 105-110°C and weighed.

SOURCE AND PURITY OF MATERIALS:

Pure, recrystd sulfonamide was used.

Its mp conformed to that reported in the literature.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: quite reliable results were obtained over the temp range 20-75°C. At higher temps the accuracy was poor due to evapn of water during sampling (authors). Temp: ±0.05°C (authors)

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Langecker, H.

Arch. Exptl. Path. Pharmakol. 1948, *205*, 291-301.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 37°C	
	mg%	10^3 mol dm^{-3} [a]
7.2	31	1.1
6.6	24	0.82

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfapyridine in water was boiled for 1 h in a sealed ampul followed by keeping the soln at 37°C. Before assaying, the solute was treated with 2.6N NaOH soln (1) to cleave the acetyl group and the sulfapyridine was detd colorimetrically by the method of Bratton and Marshall (2) using a Havemann colorimeter (3), as well as by microanal detn of the solid residue.

SOURCE AND PURITY OF MATERIALS:

Source and purity of the materials were not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Scudi, J. V. *J. Lab. Clin. Med.* 1940, *25*, 404.
2. Bratton, A. G.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *128*, 537.
3. Havemann, R. *Klin. Wochenschr.* 1940, p. 503.

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Sodium hydroxide; NaOH; [1310-73-2]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Rose, F. L.; Martin, A. R.; Bevan, H. G. L. *J. Pharm. Exp. Therap.* 1943, *77*, 127-42.

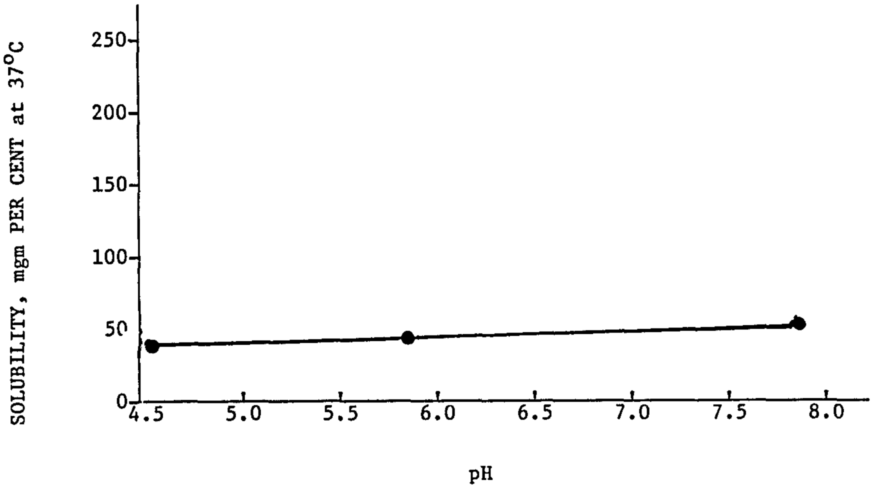
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfapyridine was stirred in boiling water, the soln was cooled to 37°C, the temp being maintained thermostatically, and 0.1N NaOH was added to increase the pH. The pH was measured by means of a glass electrode - calomel electrode half-cell system and was permitted to reach equilibrium before a reading was taken. The drug was then de-acetylated and the concn of sulfapyridine in soln was detd colorimetrically by withdrawing a sample through a filter-tip into a preheated micropipet.

SOURCE AND PURITY OF MATERIALS:

The source and purity of acetyl sulfapyridine were not specified.

Water was doubly distilled.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Phosphoric acid, disodium salt; Na_2HPO_4 [7558-94-4]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Krüger-Thiemer, E.

Arch. Dermatol. Syphilis 1942, *183*, 90-116.

VARIABLES:

One temperature: ca 20°C; one pH: 8.74

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyridine in a 0.705M (10%) Na_2HPO_4 solution of pH 8.74 at room temperature (about 20°C) is 0.042 g% (1.4 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyridine (0.5 g) was dissolved in 10 cm^3 of the 0.705M (10%) Na_2HPO_4 soln of pH 8.74, shaken for 2 h at room temp (about 20°C), and filtered. The filtrate was treated with equal vol of 2N HCl and refluxed for 15 min. After proper diln, a 1-cm^3 aliquot was withdrawn, acidified, cooled, and the sulfonamide content was detd colorimetrically (as sulfapyridine) by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyridine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyridine. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Soly: precision ±5% (author).

Temp: not specified.

pH : ±0.05 pH unit (author).

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Phosphoric acid, monopotassium salt; KH_2PO_4 [7778-77-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Krüger-Thiemer, E.

Arch. Dermatol. Syphilis 1942, *183*, 90-116.

VARIABLES:

One temperature: ca 20°C; one pH: 4.37

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyridine in a 0.735M (10%) KH_2PO_4 solution of pH 4.37 at room temperature (about 20°C) is 0.020 g% (6.9 x 10^{-4} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyridine (0.5 g) was dissolved in 10 cm^3 of the 0.735M (10%) KH_2PO_4 soln, shaken for 2 h at room temp (about 20°C), and filtered. The filtrate was treated with equal vol of 2N HCl, and refluxed for 15 min After proper diln, a 1-cm^3 aliquot was withdrawn, acidified, cooled, and the sulfonamide content was detd colorimetrically by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyridine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyridine. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Soly: precision ±5% (author).

Temp: not specified.

pH : ±0.05 pH unit (author).

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

VARIABLES:

Temperature; pH

ORIGINAL MEASUREMENTS:

Krüger-Thiemer E.

Arch. Dermtol. Syphilis 1942, *183*, 90-116.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Composition of 1/15M phosphate buffer solutions			pH	Solubility			
				Room temp (ca 20°C)		37°C	
Na_2HPO_4	KH_2PO_4	%Content		g%	10^3 mol dm^{-3} solution[a]	g%	10^3 mol dm^{-3} solution[a]
1.0	99.0	0.91	4.944	0.030	1.03	-	-
10.0	90.0	0.91	5.906	0.031	1.06	0.030	1.03
61.1	38.9	0.93	7.005	0.032	1.10	0.033	1.13
9.5	0.5	0.733[b]	7.51	0.026	0.89	-	-
94.7	5.3	0.95	8.018	0.047	1.60	-	-

[a] Calculated by compiler.

[b] Molar content; 10% buffer solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyridine (0.5 g) was dissolved in 10 cm^3 of a buffer soln, shaken for 2 h at 20°C (or left for 48 h at 37°C), and filtered at respective temp. The filtrate was treated with equal vol of 2N HCl and refluxed for 15 min. After proper diln, a 1-cm^3 aliquot was withdrawn, acidified, cooled, and the sulfonamide content was detd (as sulfapyridine) colorimetrically by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyridine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyridine. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Soly: precision ±5% (author).

Temp: not specified.

pH : ±0.05 pH unit (author).

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)sulfonyl]phenyl]- (acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

VARIABLES:

pH

ORIGINAL MEASUREMENTS:

Pulver, R.; Suter, R.

Schweiz. Med. Wochenschr. 1943, *73(13)*, 403-8.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility of acetyl sulfapyridine in M/15 phosphate buffers (according to Sørensen) at 20°C	
	mg%	10^3 mol dm^{-3} [a]
6.0	22	0.75
7.0	30	1.0
8.0	39	1.3

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyridinylamino)-sulfonyl]phenyl]- ($\underline{N}^4$-acetyl sulfapyridine); $C_{13}H_{13}N_3O_3S$; [19077-98-6]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Hekster, Y. A.; Vree, T. B.
Damsma, J. E.; Friesen, W. T.
J. Antimicrob. Chemother. 1981, *8*,
133-44.

VARIABLE:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^3 mol dm^{-3} [a]
5.5	313	1.07
7.5	440	1.51

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of $\underline{N}^4$-acetylsulfapyridine were prepd in phosphate buffers of pH 5.5 and 7.5 at room temp (25°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 column (10 cm x 4.6 mm i.d.) was packed with Lichrosorb RPS 5 μm, obtained from Chrompack. An injection loop of 100μl was used. The oven temp was 40° C. Detection of $\underline{N}^4$-acetylsulfapyridine was performed at 260 nm.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials were not specified.

ESTIMATED ERROR:

The detection limit of the solute was 0.5 mg/l (authors).
The error in temperature and pH was not specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-bromo-2-pyridinyl)-; $C_{11}H_{10}BrN_3O_2S$; [16805-99-5] (2) Water; H_2O; [7732-18-5]	Roblin, R. O., Jr.; Winnek, P. S. *J. Am. Chem. Soc.* 1940, *62*, 1999-2002.
VARIABLES:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(5-bromo-2-pyridinyl)benzenesulfonamide in water at 37°C is 3.8 mg/100 cm^3 solution (1.2 x 10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 199-200°C (cor), was prepd by the authors. Anal: %C 40.2 (calcd 40.2); %H 3.0 (3.0).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-iodo-2-pyridinyl); $C_{11}H_{10}N_3O_2S$; [71119-21-6]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek P. S.
J. Am. Chem. Soc. 1940, *62*, 1990-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N(5-iodo-2-pyridinyl)benzenesulfonamide in water at 37°C is 1.3 mg/100 cm^3 solution (3.5×10^{-5} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 220-1°C (cor), was prepd by the authors. Anal: %C 35.2 (calcd 35.2); %H 2.5 (2.7). Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-nitro-2-pyridinyl)-; $C_{11}H_{10}N_4O_4S$; [39588-36-8]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(5-nitro-2-pyridinyl)benzenesulfonamide in water at 37°C is 3.7 mg/100 cm^3 solution (1.3 x 10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 220-1°C (cor) was prepd by the authors. Anal: %C 45.0 (calcd 44.9); %H 3.2 (3.4).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-amino-2-pyridinyl)-; $C_{11}H_{12}N_4O_2S$; [16840-28-1]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(5-amino-2-pyridinyl)benzenesulfonamide in water at 37°C is 418 mg/100 cm^3 solution (1.58×10^{-2} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 157-8°C (cor), was prepd by the authors. Anal: %C 49.8 (calcd 50.0); %H 4.5 (4.5).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(3-ethoxy-2-pyridinyl)-; $C_{13}H_{15}N_3O_3S$; [71119-19-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(3-ethoxy-2-pyridinyl)benzenesulfonamide in water at 37°C is 23.5 mg/100 cm^3 (8.47×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excesss 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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 198-200°C (cor), was prepd by the authors. Anal: %C 53.0 (calcd 53.2); %H 5.0 (5.1).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-[1(2-hydroxyethyl)-1,2-dihydro-2-pyridinyl]-; $C_{13}H_{17}N_3O_3S$; [71119-27-2]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C. *J. Am. Chem. Soc.* 1942, *64*, 2532-7.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-[1-(2-hydroxyethyl)-1,2-dihydro-2-pyridinyl]-benzenesulfonamide at 37°C is 440 mg% (1.5×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was assayed colorimetrically (1). No details were reported.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, m.p. 184-5°C, was synthesized by the authors. Analysis: %C 53.41 (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.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(1-carboxymethyl-1,2-dihydro-2-pyridinyl)-; $C_{13}H_{15}N_3O_4S$; [71119-28-3] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C., *J. Am. Chem. Soc.* 1942, *64*, 2532-7.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(1-carboxymethyl-1,2-dihydro-2-pyridinyl)benzenesulfonamide in water at 37°C is 754 mg% (2.45 x 10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: The sulfonamide was assayed colorimetrically (1). No details were reported.	**SOURCE AND PURITY OF MATERIALS:** The sulfonamide, m.p. 165°C (dec) was synthesized 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.
	ESTIMATED ERROR: Nothing specified
	REFERENCES: 1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *128*, 537.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2-chloro-5-pyridinyl)-; $C_{11}H_{10}ClN_3O_2S$; [34392-82-0]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-chloro-5-pyridinyl)benzenesulfonamide in water at 37°C is 18.0 mg/100 cm^3 (6.34×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of the sulfonamide was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h at 37°C. A sample of the satd. soln. was withdrawn 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 Electric recording spectrophotometer was used in comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide: m.p. (cor.) 186-7°C.

Purity of the water was not specified.

ESTIMATED ERROR:

None specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2-bromo-5-pyridinyl)-; $C_{11}H_{10}BrN_3O_2S$; [17103-43-4]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.
J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-bromo-5-pyridinyl)benzenesulfonamide in water at 37°C is 12.2 mg/100 cm^3 (3.72×10^{-4} mol dm^{-3} - compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of the sulfonamide was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h at 37°C. A sample of the satd. soln. was withdrawn 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 Electric recording spectrophotometer was used in comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide: m.p. (cor.) 196-7°C.
Purity of the water was not specified.

ESTIMATED ERROR:

None specified

REFERENCES:

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

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2-hydroxy-5-pyridinyl)-; $C_{11}H_{11}N_3O_3S$; [71119-20-5] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Roblin, R. O., Jr.; Winnek, P. S. *J. Am. Chem. Soc.* 1940, *62*, 1999-2002.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-hydroxy-5-pyridinyl)benzenesulfonamide in water at 37°C is 258 mg/100 cm^3 solution (9.72×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: 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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing colors with those of the standards.	**SOURCE AND PURITY OF MATERIALS:** The sulfonamide, mp 243-4°C (dec, cor) was prepd by the authors. Anal: %C 49.8 (calcd 49.8); %H 4.2 (4.2). Purity of the water was not specified. **ESTIMATED ERROR:** Nothing specified **REFERENCES:** 1. Bratton, A. C.; Marshall, E. K., Jr. *J. Pharmacol.* 1939, *66*, 4.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2-amino-5-pyridinyl)-; $C_{11}H_{12}N_4O_2S$; [17103-45-6]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-amino-5-pyridinyl)benzenesulfonamide in water at 37°C is 129 mg/100 cm^3 solution (4.88×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 glass filter, dild, and analyzed by the modified Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 207-8°C (cor), was probably that synthesized by Winterbottom (2). Purity of the water was not specified.

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.* 1940, *62*, 160.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2-ethoxy-5-pyridinyl)-; $C_{13}H_{15}N_3O_3S$; [71720-65-5]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.

J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-ethoxy-5-pyridinyl)benzenesulfonamide in water at 37°C is 3.6 mg/100 cm^3 solution (1.3 x 10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 207-8°C (cor), was prepd by the authors. Anal: %C 53.2 (calcd 53.2); %H 5.1 (5.1).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-; $C_{12}H_{13}N_3O_2S$; [51543-29-4]

(2) Water

EVALUATOR:

Anthony N. Paruta
Department of Pharmaceutics
University of Rhode Island
Kingston, Rhode Island, USA
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 insoluble in water and the average of the two reported values should be considered as the recommended value at 310K in water, 4.96×10^{-3} mol dm^{-3}.

REFERENCES:

(1) Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C. *J. Am. Chem. Soc.* 1942, *64*, 2532-7.

(2) Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-; $C_{12}H_{13}N_3O_2S$; [51543-29-4]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C.; *J. Am. Chem. Soc.* 1942, *64*, 2532-7.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubilty of 4-amino-N-methyl-N-2-pyridinylbenzenesulfonamide in water at 37°C is 136 mg% (5.17×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was assayed colorimetrically (1). No details were given.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 86.5-7.0°C, was synthesized 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:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-; $C_{12}H_{13}N_3O_2S$; [51543-29-4] (2) Water; H_2O; [7732-18-5]	Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.
VARIABLES:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-methyl-N-2-pyridinylbenzenesulfonamide in water at 37°C is 4.74 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was assayed by diazotization. No details were given.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide was synthesized by the authors. Its purity was not specified. Deionized water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-methyl-N-2-pyridinyl-; $C_{12}H_{13}N_3O_2S$; [51543-29-4]

(2) Methane, trichloro-; $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A.

Chem. Pharm. Bull. 1973, *21*, 2417-26.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-methyl-N-2-pyridinylbenzenesulfonamide in $CHCl_3$ at 37°C is more than 2630 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

One ml of the sulfonamide soln in $CHCl_3$ at equilibrium was taken into a test tube. After evapn of the solvent, the residue was dissolved in 1N HCl, the soln was properly dild with deionized water, and the concn of the sulfonamide was detd by diazotization.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide was prepd by the authors. Its purity was not specified. Neither source nor purity of the $CHCl_3$ was specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(1-methyl-1,2-dihydro-2-pyridinyl)-;
$C_{12}H_{13}N_3O_2S$; [51543-30-7]

(2) Water

EVALUATOR:

Anthony N. Paruta
Department of Pharmaceutics
University of Rhode Island
Kingston, Rhode Island, USA
and
Ryszard Piekos
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 4.25×10^{-3} mol dm^{-3} in 1942. Kitao et al. (2) gave a value of 3.69×10^{-3} mol dm^{-3}. These values are about 15% in difference, and can be used to indicate a tentative value of 3.97×10^{-3} mol dm^{-3} in water at 310K.

REFERENCES:

(1) Shepherd, R. G.; Bratton, A. C.; Blanchard, K. C. *J. Am. Chem. Soc.* 1942, *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-(1-methyl-1,2-dihydro-2-pyridinyl)-; $C_{12}H_{13}N_3O_2S$; [51543-30-7] (2) Water; H_2O; [7732-18-5]	Shepherd, R. G.; Bratton, A. C.; Blanchard, K.C. *J. Am. Chem. Soc.* 1942, *64*, 2532-7.
VARIABLES:	**PREPARED BY:**
One temperature: 37 °C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(1-methyl-1,2-dihydro-2-pyridinyl)benzenesulfonamide in water at 37°C is 112 mg% (4.25 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was assayed colorimetrically (1). No details were given.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide , mp 232-3°C, was synthesized 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.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(1-methyl-1,2-dihydro-2-pyridinyl)-; $C_{12}H_{13}N_3O_2S$; [51543-30-7]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A.

Chem. Pharm. Bull. 1973, *21*, 2417-26.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(1-methyl-1,2-dihydro-2-pyridinyl)benzenesulfonamide in water at 37°C is 3.69 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfonamide was assayed by diazotization. No details were given.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide was synthesized by the authors. Its purity was not specified. Deionized water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(1-methyl-1,2-dihydro-2-pyridinyl)-;
$C_{12}H_{13}N_3O_2S$; [51543-30-7]

(2) Methane, trichloro-; $CHCl_3$;
[67-66-3]

ORIGINAL MEASUREMENTS:

Kitao, K.; Kubo, K.; Morishita, T.;
Yata, N.; Kamada, A.
Chem. Pharm. Bull. 1973, *21*, 2417-26.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-methyl-1,2-dihydro-2-pyridinyl)benzenesulfonamide in $CHCl_3$ at 37°C is 5.53 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

One ml of the sulfonamide soln in $CHCl_3$ at equilibrium was taken into a test tube. After evapn of the solvent the residue was dissolved in 1N HCl, the soln was properly dild with deionized water, and the concn of the sulfonamide was detd by diazotization.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide was prepd by the authors. Its purity was not specified.
Neither source nor purity of the $CHCl_3$ was specified.

ESTIMATED ERROR:

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

REFERENCES:

COMPONENTS:

(1) Pyridine, 2,5-bis[[(4-aminophenyl)-sulfonyl]amino]-; $C_{17}H_{17}N_5O_4S_2$; [71119-18-1]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.
J. Am. Chem. Soc. 1940, *62*, 1999-2002.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 2,5-bis[[(4-aminophenyl)sulfonyl]amino]pyridine in water at 37°C is 49.5 mg/100 cm^3 solution (1.18×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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 modified Marshall method (1) using a General Electric recording spectrophotometer for comparing colors with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 215-6°C (cor), was prepd by the authors. Anal: %C 48.8 (calcd 48.7); %H 4.1 (4.1).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-3-pyridazinyl-; $C_{10}H_{10}N_4O_2S$; [515-62-8]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Anderson, G. W.; Faith, H. E.; Marson, H.W. Winnek, P. S.; Roblin, R. O., Jr.

J. Am. Chem. Soc. 1942, *64*, 2902-5.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-3-pyridazinylbenzenesulfonamide in water at 37°C is 221 mg/100 cm^3 solution (8.83×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 189-90°C, was prepd by the authors. Anal: %C 47.7 (calcd 48.0); %H 4.0 (4.0); %N 22.8 (22.4). Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)- (sulfachlorpyridazine); $C_{10}H_9ClN_4O_2S$; [80-32-0]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Riess, W.

Intern. Congr. Chemotheraphy, Proc. 3rd, Stuttgart 1963, *1*, 627-32.

VARIABLES:

One temperature: 20°C; one pH: 7.4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfachlorpyridazine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 1200 mg% (4.215×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solns of pH varying between 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).

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-chloro-3-pyridazinyl)- (sulfachlorpyridazine); $C_{10}H_9ClN_4O_2S$; [80-32-0]

(2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Riess, W.

Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart 1963, *1,* 627-32.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfachlorpyridazine in chloroform at 20°C is 59 mg%

(2. 1 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(6-methyl-3-pyridazinyl)-(sulfamethylpyridazine); $C_{11}H_{12}N_4O_2S$; [5433-63-6] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-77-0] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Riess, W. *Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart* <u>1963,</u> *1*, 627-32.
VARIABLES: One temperature: 20°C; one pH: 7.4	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethylpyridazine in M/15 Sörensen buffer solution (pH 7.4) at 20°C is 140 mg% (5.30 x 10^{-3} dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfamethylpyridazine at 20°C, their pH was measured at equilibrium, and the sulfamethylpyridazine 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).	**SOURCE AND PURITY OF MATERIALS:** Nothing specified **ESTIMATED ERROR:** Nothing specified **REFERENCES:**

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methyl-3-pyridazinyl)- (sulfamethylpyridazine); $C_{11}H_{12}N_4O_2S$; [5433-63-6]

(2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Reiss, W.

Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart 1963, *1*, 627-32.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethylpyridazine in chloroform at 20°C is 144 mg%

(5.45×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.

VARIABLES:

One temperature: 30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in water at 30°C is 3.36 mmol/L (0.942 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamethoxypyridazine (0.5 g) was placed in an L-shaped tube together with 20 ml of water. The mixt was shaken in a thermostat until equilibrium was attained. The sulfamethoxypyridazine was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Soly: not specified

Temp: ±1°C (authors)

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Hydrochloric acid; HCl; [7647-01-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Ogata, H.; Shibazaki, T.; Inoue, T.; Ejima, A. *Chem. Pharm. Bull.* 1979, *27(6)*, 1281-6.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in 0.1N HCl at 37°C is 17.243 mg/ml

(6.1516×10^{-2} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A centrifuge tube contg 30 ml of 0.1N HCl and 0.5-3.0 g of the sulfamethoxypyridazine powder was tightly sealed and shaken at 37°C. The concn of the dissolved drug was detd spectrophotometrically following filtration through a Millipore filter (type EH, pore size 0.5 μm), and the procedure was repeated every 24 h until a const concn was obtained.

SOURCE AND PURITY OF MATERIALS:

Comm available 250-mg uncoated tablets of sulfamethoxypyridazine were used. Hydrochloric acid was of reagent grade.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (citric acid); $C_6H_8O_7$; [77-92-9]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Bertazzoli, C.; Buogo, A.; Ciceri, C.; Ghione, M.; Turolla, E.; Zavaglio, V.

Minerva Med. 1961, *52(40)*, 1789-96.

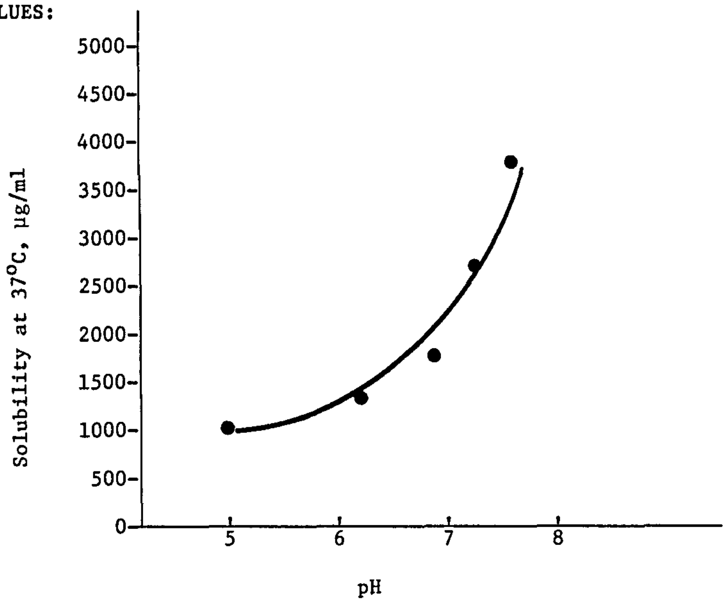
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly of sulfamethoxypyridazine in McIlvaine's Na_2HPO_4 - citric acid buffer solns was detd under agitation at 37°C. No details were given.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

VARIABLES:

pH

ORIGINAL MEASUREMENTS:

Bandelin, F. J.; Malesh, W.

J. Am. Pharm. Assoc., Sci. Ed. 1959, *48*, 177-81.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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

Initial pH	Solubility	
	mg/100 ml	10^2 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

[a] calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Solns were prepd by adding an excess of sulfamethoxypyridazine to 10 ml of buffer soln at each pH level in 18 x 150-mm test tubes, stoppering the tubes and placing them in a water bath at 37°C with gentle agitation for 24 h. The mixt was then filtered and a 1-ml aliquot was accurately pipetted into a volumetric flask for diln and analysis. The balance was retained for pH detn to ascertain any change in pH value. The sulfonamide was assayed colorimetrically by the method of Bratton and Marshall as described in detail by Biamonte and Schneller (1). A standard curve was prepd using accurately prepd standard solutions.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the reagents were specified. Distilled water was used.

ESTIMATED ERROR:

Soly: av values of duplicate runs are reported (authors).

Temp and pH: not specified.

REFERENCES:

1. Biamonte, A. R.; Schneller, G. E. *J. Am. Pharm. Assoc., Sci. Ed.*, 1952, *41*, 341.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

VARIABLES:

One temperature: 20°C; one pH: 7.4

ORIGINAL MEASUREMENTS:

Riess, W.

Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart 1963, *1*, 627-32.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 200 mg% (7.13 x 10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solutions of pH varying between 7 and 8 were prepd, satd with sulfamethoxypyridazine at 20°C, their pH was measured at equilibrium, and the sulfamethoxypyridazine was assayed 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: (1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40
VARIABLES: One temperature: 30°C; one pH: 7.4	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 6.12 mmol/L (1.71 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Sulfamethoxypyridazine (0.5 g) was placed in an L-shaped tube together with 20 ml of the buffer soln. The mixt was shaken in a thermostat until equilibrium was attained. The sulfamethoxypyridazine was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration curve.	SOURCE AND PURITY OF MATERIALS: Nothing specified.
	ESTIMATED ERROR: Soly and pH: not specified. Temp: ±1°C (authors)
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Calcium chloride; $CaCl_2$; [10043-52-4]

(3) Magnesium chloride; $MgCl_2$; [7786-30-3]

(4) Phosphoric acid, monoammonium salt; $NH_4H_2PO_4$; [7722-76-1]

(5) Potassium chloride; KCl; [7447-40-7]

(6) Sodium chloride; NaCl; [7647-14-5]

(7) Urea; CH_4N_2O; [57-13-6]

(8) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Bandelin, F. J.; Malesh, W.

J. Am. Pharm. Assoc., Sci. Ed. 1959, *48*, 177-81.

VARIABLES: pH at 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in a solution containing $CaCl_2$ 0.1143, $MgCl_2$ 0.121, $NH_4H_2PO_4$ 0.300, KCl 1.660, NaCl 2.950 and urea 20 g/dm^3 (synthetic urine, Mosher Vehicle) at 37°

Equilibrium pH	Solubility	
	mg/100 ml	10^2 mol/dm^3 [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

[a] calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess sulfamethoxypyridazine was added to aliquots of synthetic urine solns 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 was attained. Then the solns were filtered and in aliquots the sulfonamide was assayed spectrophotometrically by the method described by Biamonte and Schneller (1).

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Soly: average values of 2 detns were given.

Temp: not specified.

pH ; not specified

REFERENCES:

1. Biamonte, A. R.; Schneller, G. E. *J. Am. Pharm. Assoc., Sci. Ed.* 1952, *41*, 341.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Ethanol, 2,2'-iminodi-(diethanolamine); $C_4H_{11}NO_2$; [111-42-2]

(3) 1,3 -Propanediol; $C_3H_8O_2$; [504-63-2]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Lombardi, R. B.
Rev. Farm. (Buenos Aires) 1968, *110(7-8)*, 154-9.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Maximum concentration of sulfamethoxypyridazine in a mixture of diethanolamine 1 ml, 1,3-propanediol 60 ml, and water 39 ml, at 20°C, is 14% (0.50 mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

To the diethanolamine solution in water warmed up to 40°C, sulfamethoxypyridazine was added followed by 1,3-propanediol previously warmed to 50°C, and the mixt was agitated. The pH of the mixt was 7.9 at 20°C.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials, with the exception of water, was not specified.

Distd water was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Ethanol; C_2H_6O; [64-17-5]

(3) Piperazine; $C_4H_{10}N_2$; [110-85-0]

(4) Poly(oxy-1,2-ethanediyl), α-[(tetrahydro-2-furanyl)methyl]-ω-hydroxy-(glycofurol); $(C_2H_4O)_nC_5H_{10}O_2$; [31692-85-0]

(5) Water; H_2O; [7732-18-5]

VARIABLES: One temperature: 20°C

ORIGINAL MEASUREMENTS:

Lombardi, R. B.

Rev. Farm. (Buenos Aires) 1968, *110(7-8)*, 154-9.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

To glycofurol, warmed to 60°C, through which a stream of nitrogen was bubbled, sulfamethoxypyridazine was added, followed by an aq piperazine soln and EtOH. The stream of nitrogen was bubbled throughout. The pH of the soln was 7.9 at 20°C.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials were not specified, with the exception of water. Water for injection was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide,4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Ethanol; C_2H_6O; [64-17-5]

(3) Piperazine; $C_4H_{10}N_2$; [110-85-0]

(4) Poly(oxy-1,2-ethanediyl), α-hydro -ω-hydroxy- (PEG 300); $(C_2H_4O)_nH_2O$; [25322-68-3] 300

(5) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Lombardi, R. B.

REv. Farm. (Buenos Aires) 1968, *110(7-8)*, 154-9.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Maximum concentration of sulfamethoxypyridazine in a mixture of ethanol 96°GL 10 ml, piperazine 2 g, PEG 300 50 ml, and water 40 ml, at 20°C , is 18% (0.64 mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

To a soln of piperazine in water, EtOH was added, followed by sulfamethoxypyridazine, and PEG 300 previously warmed to 50-55°C. Nitrogen was bubbled through the mixt to ensure agitation. The pH of the mixt was 7.8 at 20°C.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials, with the exception of water, were not specified. Water for injections was used.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-(sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3]

(2) Piperazine; $C_4H_{10}N_2$; [110-85-0]

(3) Poly(oxy-1,2-ethanediyl), α-hydro- ω -hydroxy- (PEG 300); $(C_2H_4O)_nH_2O$; [25322-68-3] 300

(4) 1,3-Propanediol; C_3H_8O; [504-63-2]

(5) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Lombardi, R. B.

Rev. Farm. (Buenos Aires) 1968, *110(7-8)*, 154-9.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Maximum concentration of sulfamethoxypyridazine in a mixture of piperazine 3.5 g, PEG 300 40 ml, 1,3-propanediol 40 ml, and water 27.5 ml, at 20°C, is 15% (0.54 mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

To a soln of piperazine in water, a mixt of PEG 300 and 1,3-propanediol, previously heated to 50°C, was added, followed by sulfamethoxypyridazine. Nitrogen was bubbled through the mixt to ensure agitation. The pH of the mixt was 7.8 at 20°C.

SOURCE AND PURITY OF MATERIALS:

The source and purity of the materials, with the exception of water, were not specified.

Water for injections was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide,4-amino-N-(6-methoxy-3-pyridazinyl)-(sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-3] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	**ORIGINAL MEASUREMENTS:** Riess, W. *Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart* 1963, *1,* 627-32.
VARIABLES: One temperature: 20°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in chloroform at 20°C is 390 mg%

(1.39×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Nothing specified	**SOURCE AND PURITY OF MATERIALS:** Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)- (sulfamethoxypyridazine); $C_{11}H_{12}N_4O_3S$; [80-35-5]

(2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.

VARIABLES:

One temperature: 30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxypyridazine in chloroform at 30°C is 14.03 mmol/L (3.933 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamethoxypyridazine (0.5 g) was placed in an L-shaped tube together with 20 ml of chloroform. The mixt was shaken in a thermostat until equilibrium was attained. The sulfamethoxypyridazine was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Soly: not specified

Temp: ±1°C (authors)

REFERENCES:

COMPONENTS:

(1) Cobalt, bis [4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfonamidato-]diaqua-
($CoR_2 \cdot 2H_2O$); $C_{22}H_2CoN_8O_6S_2 \cdot 2H_2O$;
[72384-11-3]

(2) Hydrochloric acid; HCl; [7647-01-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Gogorishvili, P. V.; Tskitishvili, M. G.; Chrelashvili, M. V.

Izv. Akad. Nauk Gruz. SSR, Ser. Khim 1979, *5(3)*, 199-204.

VARIABLES:

Concentration of HCl (pH)

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of HCl	pH	Solubility (mol/l) at 25°C based on		$10^{11} \times K_{so}$
		$[Co^{2+}]$	$[RH_2^+]$	
2.5×10^{-2}	6.15	1.3×10^{-2}	8.09×10^{-3}	-
1.0×10^{-2}	6.25	6.6×10^{-3}	5.15×10^{-3}	1.51
5.0×10^{-3}	6.62	3.6×10^{-3}	4.36×10^{-3}	1.56
2.5×10^{-3}	6.92	2.0×10^{-3}	2.80×10^{-3}	1.50
1.0×10^{-3}	7.31	1.28×10^{-3}	8.45×10^{-4}	1.53
5.0×10^{-4}	7.54	1.05×10^{-3}	8.32×10^{-4}	1.51
2.5×10^{-4}	7.78	5.84×10^{-4}	8.23×10^{-4}	1.55
1.0×10^{-4}	7.92	5.67×10^{-4}	7.90×10^{-4}	1.50
5.0×10^{-5}	8.12	5.51×10^{-4}	7.87×10^{-4}	1.50
2.5×10^{-5}	8.23	5.48×10^{-4}	7.15×10^{-4}	1.52
			Mean	1.52

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

$CoR_2 \cdot 2H_2O$ was placed in a glass vessel, 100 ml of aq HCl was added, and the mixt was shaken for 6 h in a thermostat at 25°C. After attaining equilibrium, the contents of Co^{2+} and S were detd, and the pH measured.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Soly: not specified

K_{so} : standard deviation 5.64×10^{-13} (compiler).

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Cobalt, bis[4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfonamidato]diaqua- ($CoR_2 \cdot 2H_2O$); $C_{22}H_{22}CoN_8O_6S_2 \cdot 2H_2O$; [72384-11-3]

(2) Acetic acid, cobalt(2+) salt; $C_4H_6CoO_4$; [71-48-7]

(3) Benzenesulfonamide, 4-amino-N-(6-methoxy-3-pyridazinyl)-, monosodium salt, (NaR); $C_{11}H_{11}NaN_4O_3S$; [2577-32-4]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Gogorishvili, P. V.; Tskitishvili, M. G.; Chrelashvili, M. V.

Izv. Akad. Nauk Gruz. SSR, Ser. Khim. 1979, *5(3)*, 199-204.

VARIABLES:

Co^{2+}/R^- ratio; pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Volume ratio of 0.1M solns of Co^{2+}acetate and NaR	pH	$[Co^{2+}]$ mol/l	Excess of NaR or Co^{2+} acetate mol/l	$[R^-]$ mol/l	pLi[a] based on $[Co^{2+}]$	pLi[a] based on $[R^-]$
10:90	9.25	7.09×10^{-6}	7.0×10^{-3}	7.02×10^{-3}	5.16	5.45
20:80	9.09	2.12×10^{-5}	4.0×10^{-3}	4.04×10^{-3}	4.69	4.71
25:75	8.75	3.90×10^{-5}	2.5×10^{-3}	2.58×10^{-3}	4.44	4.43
30:70	8.14	2.06×10^{-4}	1.0×10^{-3}	1.43×10^{-3}	3.80	3.79
1:20	7.95	7.52×10^{-4}	-	1.49×10^{-3}	3.32	3.30
35:65	7.85	4.76×10^{-4}	2.5×10^{-4}	4.83×10^{-4}	3.91	3.82
40:60	7.75	1.37×10^{-3}	1.0×10^{-3}	7.59×10^{-4}	3.65	3.64
50:50	7.62	4.04×10^{-3}	2.5×10^{-3}	1.47×10^{-3}	3.10	3.09
60:40	7.49	7.67×10^{-3}	4.0×10^{-3}	7.48×10^{-3}	2.78	2.44
70:30	7.46	1.14×10^{-2}	5.5×10^{-3}	1.19×10^{-2}	2.59	2.59
80:20	7.40	1.51×10^{-2}	7.0×10^{-3}	1.50×10^{-2}	2.48	2.46
90:10	7.33	1.88×10^{-2}	8.5×10^{-3}	2.02×10^{-2}	2.41	2.41

[a] pLi = -log (solubility), solubility being expressed in mol/l and measured at 25°C.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The effect of the concns of Co^{2+} and R^- on the soly of $CoR_2 \cdot H_2O$ was detd by the method of isomolar series of solns. The ppt of CoR_2 was obtained by mixing together 0.1M solns of Co^{2+} acetate and NaR taken in proportions specified in the Table (cf. Experimental Values box). The total vol after mixing was always 100 ml. After attaining equilibrium by shaking for 6 h, the pH, and the Co^{2+} and S content were detd in soln.

SOURCE AND PURITY OF MATERIALS:

$CoR_2 \cdot H_2O$ was obtained by mixing together 0.1M solns of Co^{2+} acetate and NaR. Neither source nor purity of the reagents was specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Magnesium, (T-4)-bis[4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfonamidato]-hydrate; $C_{22}H_{20}MgN_8O_6S_2\cdot nH_2O$; [84812-83-9] (2) Hydrochloric acid; HCl; [7647-01-0] (3) Water; H_2O; [7732-18-5]	Tskitishvili, M. G.; Shvelashvili, A. E.; Mikadze, I. I.; Zhorzholiani, N. B.; Chrelashvili, M. V. *Izv. Akad. Nauk Gruz. SSR, Ser. Khim.* 1981, *7(4)*, 300-4.
VARIABLES:	**PREPARED BY:**
pH	R. Piekos

EXPERIMENTAL VALUES:

K_{so} over the HCl concentration range 5.0×10^{-3} to 1.5×10^{-5} mol dm^{-3}, at 25°C, is 2.00×10^{-3}.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
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^{2+} and S content was determined to calculate K_{so} The pH was measured on a pH-673 pH meter.	0.1M solns of chem pure $Mg(OAc)_2$, monosodium salt of sulfapyridazine , and HCl as well as doubly distd water were used. The source of the materials was not specified.
	ESTIMATED ERROR:
	Nothing specified
	REFERENCES:
	1. Tskitishvili, M. G.; Mikadze, I. I. *Soobshch. Akad. Nauk Gruz. SSR* 1978, *89(3)*, 589.

COMPONENTS:

(1) Manganese, bis[4-amino-N-(6-methoxy-3-pyridazinyl)benzenesulfonamidato)-hydrate; $C_{22}H_{20}MnN_8O_6S_2 \cdot nH_2O$; [84812-82-8]

(2) Hydrochloric acid; HCl; [7647-01-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Tskitishvili, M. G.; Shvelashvili, A. E.; Mikadze, I. I.; Zhorzholiani, N. B.; Chrelashvili, M. V. *Izv. Akad. Nauk Gruz. SSR, Ser. Khim* 1981, *7(4)*, 300-4.

VARIABLES:

pH

PREPARED BY:

R. Peikos

EXPERIMENTAL VALUES:

Concentration of HCl (mol/l)	pH	10^6 K_{so} at 25°C
1.0×10^{-2}	7.65	1.99
5.0×10^{-3}	7.71	1.97
2.5×10^{-3}	7.73	1.94
1.0×10^{-3}	7.75	1.99
5.0×10^{-4}	7.76	2.00
2.5×10^{-4}	7.78	1.97
1.0×10^{-4}	7.80	2.02
5.0×10^{-5}	7.82	2.04
1.5×10^{-5}	7.83	1.99
	Mean	1.99

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 Mn^{2+} and S content was determined to calculate K_{so}. The pH was measured on a pH-673 pH meter.

SOURCE AND PURITY OF MATERIALS:

0.1M solns of chem pure $Mn(OAc)_2$, monosodium salt of sulfapyridazine, and HCl as well as doubly distd water were used. The source of the materials was not specified.

ESTIMATED ERROR:

K_{so} : std deviation 3×10^{-8} (compiler).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Nickel, bis[4-amino-N-6-methoxy-3-pyridazinyl)benzenesulfonamidato]-hydrate; $C_{22}H_{20}N_8NiO_6S_2 \cdot nH_2O$; [84825-01-4]

(2) Hydrochloric acid; HCl; [7647-01-0]

(3) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Tskitishvili, M. G.; Shvelashvili, A. E.; Mikadze, I. I.; Zhorzholiani, N. B.; Chrelashvili, M. V.;

Izv. Akad. Nauk Gruz. SSR, Ser. Khim. 1981, *7(4)*, 300-4.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of HCl (mol/l)	pH	10^7 K_{so} at 25°C
1.0×10^{-2}	7.15	1.88
5.0×10^{-3}	7.38	1.87
2.5×10^{-3}	7.65	1.86
1.0×10^{-3}	7.90	1.87
5.0×10^{-4}	8.01	1.84
2.5×10^{-4}	8.04	1.83
1.0×10^{-4}	8.07	1.79
5.0×10^{-5}	8.07	1.80
2.5×10^{-5}	8.07	1.80
	Mean	1.84

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 Ni^{2+} and S content was determined to calculate K_{so} The pH was measured on a pH-673 pH meter.

SOURCE AND PURITY OF MATERIALS:

0.1M solns of chem pure $Ni(OAc)_2$, monosodium salt of sulfapyridazine, and HCl as well as doubly distd water were used. The source of the materials was not specified.

ESTIMATED ERROR:

K_{so}: std deviation 3.5×10^{-9} (compiler).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(6-methoxy-2-pyridazinyl)amino]sulfonyl]phenyl]-(acetyl sulfamethoxypyridazine); $C_{13}H_{14}N_4O_4S$; [127-75-3]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7889-77-0]

(4) Water; H_2O; [7732-18-5]

VARIABLES:

pH

ORIGINAL MEASUREMENTS:

Bandelin, F. J.; Malesh, W.

J. Am. Pharm. Assoc., Sci. Ed. 1959, *48*, 177-81.

PREPARED BY:

R. Piekos

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^{-3}, compiler) and KH_2PO_4 (36.3 g/l distilled water; 0.27 mol dm^{-3}, compiler) at 37°C

Equilibrium pH	Solubility (based on sulfamethoxypyridazine)	
	mg/100 ml	10^3 mol dm^{-3} [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:

Solns were prepd by adding an excess of acetyl sulfamethoxypyridazine to 10 ml of buffer 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 hydrolyzate was accurately pipetted into a volumetric flask for diln and analysis. The sulfonamide was assayed colorimetrically by the method of Bratton and Marshall as described in detail by Biamonte and Schneller (1). A standard curve was prepd using accurately prepd standard solutions.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the reagents were specified. Distilled water was used.

ESTIMATED ERROR:

Soly: av values of duplicate runs are reported (authors).

Temp and pH: not specified.

REFERENCES:

1. Biamonte, A. R.; Schneller, G. E. *J. Am. Pharm. Assoc., Sci. Ed.* 1952, *41*, 341.

COMPONENTS:

(1) Acetamide, N-[4[[(6-methoxy-2-pyridazinyl)amino]sulfonyl]phenyl]-(acetyl sulfamethoxypyridazine); $C_{13}H_{14}N_4O_4S$; [127-75-3]

(2) Calcium chloride; $CaCl_2$; [10043-52-4]

(3) Magnesium chloride; $MgCl_2$; [7786-30-3]

(4) Phosphoric acid, monoammonium salt; $NH_4H_2PO_4$; [7722-76-1]

(5) Potassium chloride; KCl; [7447-40-7]

(6) Sodium chloride; NaCl; [7647-14-5]

(7) Urea; CH_4N_2O; [57-13-6]

(8) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Bandelin, F. J.; Malesh, W.

J. Am. Pharm. Assoc., Sci. Ed.

<u>1959</u>, *48*, 177-81.

VARIABLES:

pH at 37°C

PREPARED BY:

R. Piekos

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^3 (synthetic urine, Mosher vehicle) at 37°C

Equilibrium pH	Solubility	
	mg/100 ml	10^2 mol/dm^3 [a]
	as sulfamethoxypyridazine	
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

[a] calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess acetyl sulfamethoxypyridazine was added to aliquots of synthetic urine solns 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 was attained. Then the solns were filtered and in aliquots the acetylsulfonamide was assayed spectrophotometrically by the method described by Biamonte and Schneller (1). Before detn the soln was refluxed with 5% H_2SO_4 for 1 h to liberate the free amino compound.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Soly: average values of 2 detns were given.

Temp: not specified .

pH : not specified.

REFERENCES:

1. Biamonte, A. R.; Schneller, G. E. *J. Am. Pharm. Assoc., Sci. Ed.* <u>1952</u>, *41*, 341.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-[6-(methylthio)-3-pyridazinyl]- (sulfamethylmercaptopyridazine); $C_{11}H_{12}N_4O_2S_2$; [7758-81-8]

(2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Riess, W.

Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart 1963, *1*, 627-32.

VARIABLES:

One temperature: 20°C; one pH: 7.4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethylmercaptopyridazine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 29 mg% (9.8 x 10^{-4} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfamethylmercaptopyridazine at 20°C, their pH was measured at equilibrium, and the sulfamethylmercaptopyridazine was assayed 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:

(1) Benzenesulfonamide, 4-amino-N-(6-methylthio)-3-pyridazinyl]- (sulfamethylmercaptopyridazine); $C_{11}H_{12}N_4O_2S_2$; [7758-81-8]

(2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]

ORIGINAL MEASUREMENTS:

Reiss, W.
Intern. Congr. Chemotherapy, Proc. 3rd, Stuttgart <u>1963</u>, *1*, 627-32.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethylmercaptopyridazine in chloroform at 20°C is 150 mg% (5.06×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Nothing specified

REFERENCES: