COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Water

EVALUATOR:

Anthony N. Paruta
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Gdansk, Poland 1986

CRITICAL EVALUATION:

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

Table I: Solubility of Sulfapyrimidine in water at various temperatures

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

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

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (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:	PREPARED BY:
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyrimidine in water at 37°C is 12.3 mg/100 cm^3 solution (4.91×10^{-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 Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

Sulfapyrimidine, mp 255-6°C (dec, cor), was prepd by the authors. Anal: %C 48.1 (calcd 48.0); %H 4.0 (4.0); %N 21.7 (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-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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/°C	Solubility	
	g/100 g water	10^4 mol kg^{-1} water[a]
25	0.0077	3.08
37	0.0127	5.07

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small tinted glass container contg excess sulfadiazine 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 sulfadiazine 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:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Kikuth, W.

Med. Welt 1943, *17(26/27)*, 483-6.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyrimidine in water at 37°C is 53.5 mg/100 cm^3 solution (2.14×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified

SOURCE AND PURITY OF MATERIALS:

Sulfapyrimidine was a product of Bayer. The pH of the water was 7.0.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in water at 37°C is 12 mg% (4.8×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine was boiled with water and left for 24 h in a vessel protected from access of CO_2. The concn of sulfadiazine 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Bhattacharyya, R.; Basu, U. P.

Indian Pharmacist 1950, *6(3)*, 77-8, 86.

VARIABLES:

One temperature: 30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in water at 30°C is 15 mg per 100 ml (6.0×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A weighed sample of sulfadiazine was placed in a clean reagent bottle and a known vol of water was added. The mixt was shaken in a mech shaker at 80-100 strokes/min. After at least 24 h the mixt was filtered through a clean, dried and weighed sintered-glass crucible. At the end of the filtration the crucible was washed with about 1 ml of water, dried at 105°C for 2-3 h, cooled, and weighed to const wt.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the sulfadiazine was specified.

Doubly distd water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Higuchi, T.; Lach, J. L.
J. Amer. Pharm. Assoc., Sci. Ed.
1954, *43*, 349-54.

VARIABLES:

One temperature: 30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in water at 30°C is 3.46×10^{-4} mol dm^{-3} solution (9.11×10^{-2} g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess sulfadiazine (25 mg) was placed in a 125-ml glass-stoppered bottle together with 50 ml of water. The bottle was placed in a mech shaker in a const temp bath and equilibrated for 8 h at 30°C. Aliquot of the supernatant liquid was analyzed for sulfadiazine by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Recrystd sulfadiazine (U.S.P.), mp 255-6°C, and distilled water were used.

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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in water at 30°C is 0.54 mmol/L (0.14 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadiazine (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 sulfadiazine content 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-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Elworthy, P. H.; Worthington, H. E. C.

J. Pharm. Pharmac. 1968, *20*, 830-5.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	Weight %	10^6 mole fraction	10^4 mol kg^{-1} water[a]
20	0.00454	3.27	1.81
30	0.00760	5.47	3.04
40	0.01290	9.29	5.15

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Solns were presatd by shaking with powd sulfadiazine for 24 h and transferred to a soly app which was of the percolation type and a modification of that used by Davies and Griffiths (1). The soln was recycled in the app through a sintered-glass filter until satd (7 - 14 days). Samples were dild with water and assayed spectrophotometrically at 270 nm. Suitable calibration lines were prepd.

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (B. P. quality) was twice recrystd from an EtOH - DMF mixt (3:1 by vol) and dried over P_2O_5. Its mp was 255°C. Assay by the Pharmacopeial method gave 100.0% purity calcd with reference to the material dried at 105°C.

Purity of the water was not specified.

ESTIMATED ERROR:

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

Temp: ±0.05°C (authors).

REFERENCES:

1. Davies, M; Griffiths, D. M. L. *Trans. Faraday Soc.* 1953, *49*, 1405.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Corby, T. C.; Elworthy, P. H.

J. Pharm. Pharmac. 1971, *23*, Suppl. 39S-48S.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of sulfadiazine in a saturated aqueous solution at 20°C is 0.236 millimolal (5.91×10^{-3}% by wt, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly was detd in an app where water percolated through a plug of sulfadiazine supported on a 5/3 sintered glass disc. The percolation was continued until the soln was satd (5-6 days). The concn of sulfadiazine was detd spectrophotometrically from a calibration curve using a Uvispek spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (Macarthy's Ltd, Romford) was a British Pharmacopeia product. It was recrystd twice from a DMF-EtOH mixt (1:3) and dried at 40°C over P_2O_5. Its mp was 254° (decompn).

Tap water once distd from glass was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Elworthy, P. H.; Lipscomb, F. J. *J. Pharm. Pharmac.* 1968, *20*, 790.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Watari, N.; Kaneniwa, N.

Chem. Pharm. Bull. <u>1976</u>, *24(11)*, 2577-84.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Total solubility of sulfadiazine in water at 37°C is 0.127 mg/ml solution

(5.07×10^{-4} mol dm^{-3}, compiler.)

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine, required to saturate water, was placed in a flask contg 25 ml of water. The flask was shaken (2 strokes/s) at the amplitude of 3 cm in a thermostatically controlled water bath at 37°C. One-ml sample was removed every 6 h (total equilibration period 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 µ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically (1).

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine of the Japanese Pharmacopeia grade and distd water were used.

ESTIMATED ERROR:

Temp: ±0.05°C (authors).

Soly: not specified.

REFERENCES:

1. Kaneniwa, N.; Watari, N.
Chem. Pharm. Bull. <u>1974</u>, *22*, 1699.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Water; H_2O; [7732-18-5]	Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1978, *26(3)*, 813-26.
VARIABLES:	PREPARED BY:
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in water at 37°C is 0.128 mg/ml solution (5.11×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine was placed in a flask contg 25 ml of water. The flask was shaken (2 strokes/s at the amplitude of 3 cm) in a thermostatically controlled water bath at 37°C. One-ml sample was withdrawn every 6 h (total equilibration period was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 µ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically (1).

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine of the Japanese Pharmacopeia grade and distd water were used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1974, *22*, 1699.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Watari, N.; Kaneniwa, N.; Hanano, M.
Int. J. Pharm. 1980, *6(2)*, 155-66.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in water at 37°C is 12.8 mg/100 ml (5.11×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method was employed (1), whereby an excess of sulfadiazine, required to saturate medium, was placed in a flask contg 25 ml of water. The flask was stroked (2 strokes/s) at an amplitude of 3 cm, in a thermostatically controlled bath. One-ml sample was removed every 6 h (total equilibration time was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine was of the Japanese Pharmacopeia grade.

Distilled water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1974, *22*, 1699.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A.

Chem. Pharm. Bull. 1966, *14(4)*, 339-50.

VARIABLES:

Concentration of HCl

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of HCl	Solubility of sulfadiazine at 37°C	
mol dm^{-3}	mg/100 ml	10^4 mol dm^{-3} [a]
10^{-1}	92.0	36.8
10^{-2}	18.0	7.19
10^{-3}	11.1	4.43

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

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

ORIGINAL MEASUREMENTS:

Krebs, H. A. ; Speakman, J. C.

J. Chem. Soc. 1945, 593-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH at saturation	Solubility of sulfadiazine at 25.0°C in solution of ionic strength 0.1M maintained by NaCl	
	mg/100 ml	10^3 mol dm^{-3} [a]
1.00[b]	68	2.7
1.26	66	2.6
1.55	25.2	1.01
1.89	16.5	0.659

[a] Calculated by compiler

[b] in 0.15N HCl

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The HCl solns were satd by shaking them with an excess of solid sulfadiazine for at least 3 h. They were then quickly filtered. The sulfadiazine concn was detd by the method of Bratton and Marshall (1), and the pH values were measured with the glass electrode, which was standardized in terms of the buffer solns recommended by Hitchcock and Taylor (2).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine, mp 256°C, was obtained by recrystg a comm specimen (source not specified) from water.

Purity of the remaining materials was not specified.

ESTIMATED ERROR:

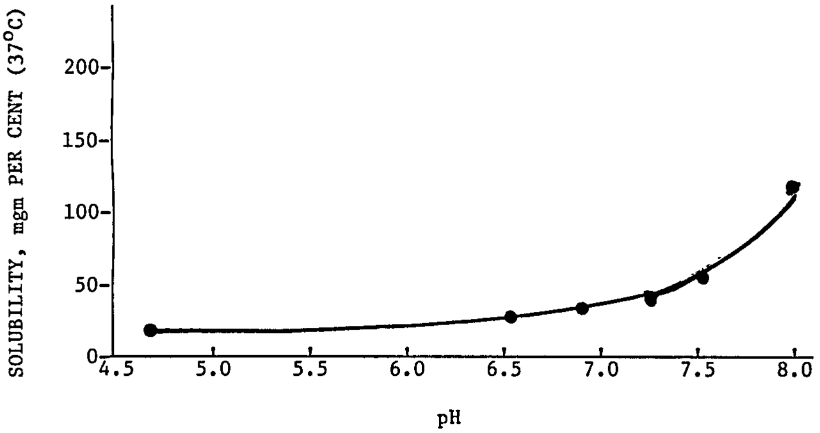
Nothing specified.

REFERENCES:

1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *128*, 537.
2. Hitchcock, D. I.; Taylor, A. C. *J. Am. Chem. Soc.* 1937, *59*, 1812.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Sodium hydroxide; NaOH; [1310-73-2] (3) Water; H_2O; [7732-18-5]	Rose, F. L.; Martin, A. R.; Bevan, H. G. L. *J. Pharm. Exp. Therap.* 1943, *77*, 127-42.
VARIABLES:	PREPARED BY:
pH	R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
An excess of sulfadiazine 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 sulfadiazine in soln was detd colorimetrically by withdrawing a sample through a filter-tip into a preheated micropipet.	The source and purity of sulfadiazine were not specified. Water was doubly distilled.
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Sodium hydroxide; NaOH; [1310-73-2] (3) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Holz, E.; Garcia Onandia, A.; Holz, S. *Acta Cient. Venezolana* 1955, *6(2)*, 68-73.
VARIABLES: Concentration of NaOH	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of NaOH soln	Volume of NaOH soln required to dissolve 1 g of sulfadiazine at 26°C	Solubility of sulfadiazine at 26°C
N	cm^3	mol dm^{-3} NaOH soln[a]
1/10	43.3	0.0923
1/4	17.3	0.231
1/2	8.35	0.478
1	4.5	0.89
1.5	2.8	1.4
2	2.1	1.9
2.5	1.65	2.42
3	1.4	2.8
3.5	1.2	3.3
3.75	1.2	3.3
4	101	0.0396

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified.

SOURCE AND PURITY OF MATERIALS:

Nothing specified. Distd water was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A.

Chem. Pharm. Bull. 1966, *14(4),* 339-50.

VARIABLES:

Concentration of sodium hydroxide

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of NaOH	Solubility of sulfadiazine at 37°C	
10^3 mol dm^{-3}	mg/100 ml	10^3 mol dm^{-3}
1	35.2	1.41
1.4	46.9	1.88
2	68.1	2.72
3	96.0	3.84
4	118	4.72
5	153	6.12
10	272	10.9
30	760	30.4
50	1270	50.8
100	2520	100.8

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Potassium hydroxide; KOH; [1310-58-3]

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A.

Chem. Pharm. Bull. 1966, *14(4)*, 339-50.

VARIABLES:

Concentration of KOH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of KOH	Solubility of sulfadiazine at 37°C	
10^2 mol dm^{-3}	mg/100 ml	10^2 mol dm^{-3}
0.1	35	0.141
0.5	131	0.524
1.0	326	1.30
5.0	1350	5.40
10.0	2710	1.08[a]

[a] should be 10.8 - compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Carbonic acid, disodium salt; Na_2CO_3; [497-19-8]

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.

VARIABLES:

One temperature: 37°C; one pH: 11.3

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in a Na_2CO_3 solution (2.120 g Na_2CO_3/100 ml water) of pH 11.3 at 37°C is 29.12 mg/ml solution[a] (0.1163 mol dm^{-3} solution, compiler).

[a] Numerical value to the graphical data given by one of the authors (S.T.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the Na_2CO_3 soln were placed in glass-stoppered flasks with excess of sulfadiazine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfadiazine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine was of pharmaceutical purity. The source and purity of Na_2CO_3 were not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Carbonic acid, monosodium salt; $NaHCO_3$; [144-55-8]

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.

VARIABLES:

One temperature: 37°C; one pH: 8.4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in a $NaHCO_3$ solution (1.680 g $NaHCO_3$/100 ml water) of pH 8.4 at 37°C is 8.06 mg/ml solution[a] (3.22×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the $NaHCO_3$ soln were placed in glass-stoppered flasks with excess of sulfadiazine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfadiazine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine was of pharmaceutical grade. The source and purity of $NaHCO_3$ was not specified.

Distd. water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku*, 1971, *31*, 298.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Sodium chloride; NaCl; [7647-14-5] (3) 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 sulfadiazine in a 0.9 % w/w NaCl solution at 37°C is 16 mg%

(6.4×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine in a 0.9% w/w NaCl soln was boiled for 1 h in a sealed ampul followed by keeping the ampul at 37°C. The sulfadiazine concn was detd colorimetrically by the method of Bratton and Marsahll (1) using a Havemann colorimeter (2), and 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A.

Chem. Pharm. Bull. 1966, *14(4)*, 339-50.

VARIABLES:

Concentration of sodium chloride

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of NaCl	Solubility of sulfadiazine at 37°C	
mol dm^{-3}	mg/100 ml	10^4 mol dm^{-3} [a]
10^{-3}	12.1	4.83
10^{-2}	11.3	4.51
10^{-1}	10.2	4.07
1	9.0	3.6

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Avico, U.; Cavazuti, G.; di Francesco, R.; Signoretti Ciranni, E.; Zuccaro, P.

Farmaco, Ed. Practica 1975, *30(1)*, 40-6.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility of amorphous sulfadiazine in equimolal NaCl solutions	
	g/100 g water	10^3 mol kg^{-1} water[a]
25	0.151	6.03
35	0.151	6.03
40	0.151	6.03

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A soln of Na salt of sulfadiazine 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 sulfadiazine soln. The procedure was repeated using various initial concns of the reagents to find the max concn of sulfadiazine at which no pptn occurred.

SOURCE AND PURITY OF MATERIALS:

Source and purity of sulfadiazine was not specified. The mp of crystalline sulfadiazine was 253-6°C.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfapyrimidine in a 0.735M (10%) KH_2PO_4 solution of pH 4.37 at room temperature (about 20°C) is 0.0070 g% (2.8 x 10^{-4} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyrimidine (0.5 g) was dissolved in 10 cm^3 of a 0.735M (10%) KH_2PO_4 soln of pH 4.37, shaken for 2 h at room temp (about 20°C), and filtered. A 1-cm^3 aliquot of the filtrate was withdrawn, cooled, acififled with 1 cm^3 of 2N HCl, and the sulfapyrimidine content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Sulfapyrimidine was manufd by Schering (purity not specified). 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A. *Chem. Pharm. Bull.* 1966, *14(4)*, 339-50.

VARIABLES:

Concentration of Na_2HPO_4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of Na_2HPO_4	Solubility of sulfadiazine at 37°C	
mol dm^{-3}	mg/100 ml	10^{-3} mol dm^{-3}
10^{-4}	15.8	0.63
10^{-3}	33.1	1.3
10^{-2}	104	4.2
10^{-1}	242	9.7

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]
(2) Hydrochloric acid; HCl; [7647-01-0]
(3) Phosphoric acid, trisodium salt; Na_3PO_4; [7601-54-9]
(4) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Stricker, H.
Pharm. Ind. 1971, *33(7)*, 446-54.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 37°C	
	g/100 ml	10^3 mol dm^{-3} [a]
5.7	ca 0.03	1.2
7.5	ca 0.11	4.4

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd in a Sartorius-Loesemodell SM 16 751 soly apparatus contg 100 ml of solvent. The solvent consisted of 0.06N HCl whose pH was adjusted to the desired value by addn of a concd Na_3PO_4 soln.
Aliquots of solns were acidifed, diazotized and coupled with N-(1-naphthyl)-ethylenediammonium chloride. After subsequent addn of an acetate buffer soln of pH 5 and acetone, extinction of the solns was measured at 500 nm.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: not specified.
Temp: ±0.5°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Carbonic acid, disodium salt; Na_2CO_3; [497-19-8]

(3) Carbonic acid, monosodium salt; $NaHCO_3$; [144-55-8]

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M.

Chem. Pharm. Bull. 1973, *21(7)*, 1440-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Na_2CO_3	$NaHCO_3$	pH	Solubility at 37°C	
g/100 ml water	g/100 ml water		mg/ml soln[a]	10^2 mol dm^{-3} soln[b]
0.212	1.512	9.1	9.32	3.724
0.848	1.008	9.8	18.82	7.520
1.908	0.168	10.7	26.94	10.764

[a] Numerical values to the graphical ones were given by one of the authors (S. T.) in personal communication.

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the carbonate buffer solns were placed in glass-stoppered flasks with excess of sulfadiazine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfadiazine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine was of pharmaceutical grade. The source and purity of Na_2CO_3 and $NaHCO_3$ were not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Composition of 1/15M phosphate buffer solutions			pH	Solubility at room temperature (about 20°C)	
Na_2HPO_4	KH_2PO_4	%Content		g%	10^3 mol dm^{-3} solution[a]
1.0	99.0	0.91	4.944	0.0087	0.35
10.0	90.0	0.91	5.906	0.0101	0.403
61.1	38.9	0.93	7.005	0.033	1.3
9.5	0.5	0.733[b]	7.51	0.065	2.6
94.7	5.3	0.95	8.018	0.127	5.07

[a] Calculated by compiler

[b] Molar content; 10% buffer solution

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfapyrimidine (0.5 g) was dissolved in 10 cm^3 of the buffer soln, shaken for 2 h at room temp (about 20°C), and filtered. A 1-cm^3 aliquot of the filtrate was withdrawn, cooled, acidified with 1 cm^3 of 2N HCl, and the sulfapyrimidine content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Sulfapyrimidine was manufd by Schering (purity not specified). 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in M/15 phosphate buffers (according to Sørensen) at 20°C	
	mg%	10^3 mol dm^{-3} [a]
6.0	13	0.52
7.0	45	1.80
8.0	191	7.63

[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) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

Gilligan, D. R.; Garb, S.; Plummer, M. N. *Proc. Soc. Exp. Biol. Med.* 1943, *52*, 248-50.

VARIABLES:

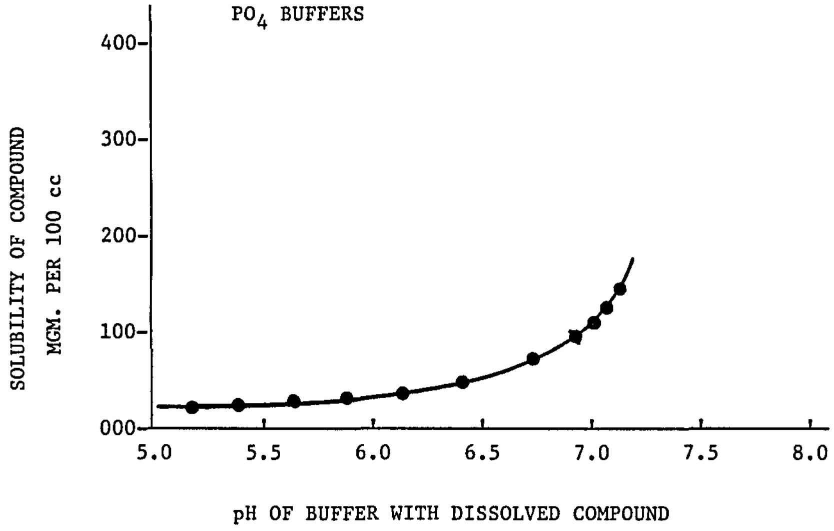
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The curve of solubility of sulfadiazine in M/15 phosphate buffer solutions of varying pH's at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An amt of sulfadiazine in large excess of that to be dissolved was added to M/15 phosphate buffer solns, shaken for 18 h in a water bath at 37°C and filtered at the same temp. The pH of the filtrate was measured immediately with a Beckmann pH meter and appropriate temp corrections were made. Sulfadiazine was assayed by the method of Bratton and Marshall.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

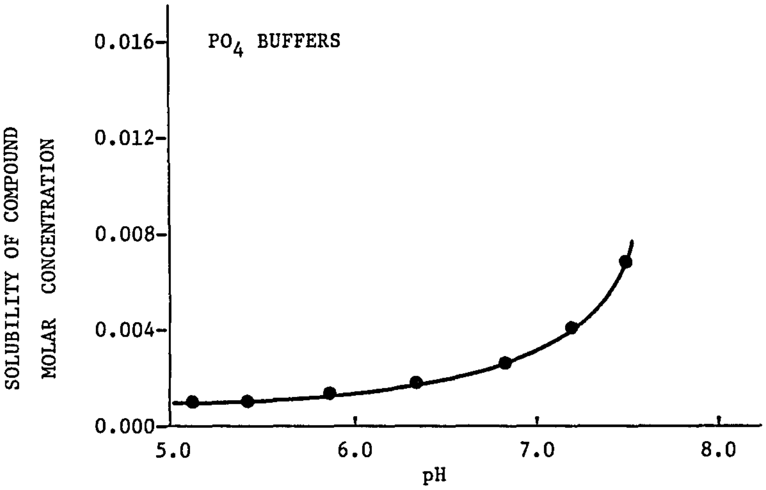
REFERENCES:

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

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (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:** Gilligan, D. R.; Plummer, M. N. *Proc. Soc. Exp. Biol. Med.* 1943, *53*, 142-5.
VARIABLES: pH	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in M/15 phosphate buffer solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann electrode pH meter and appropriate corrections for the difference between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were 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-pyrimidinyl- (sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

Frisk, A. R.; Hagerman, G.; Helander, S.; Sjögren, B.

Hygiea 1946, *108(12)*, 639-51.

VARIABLES:

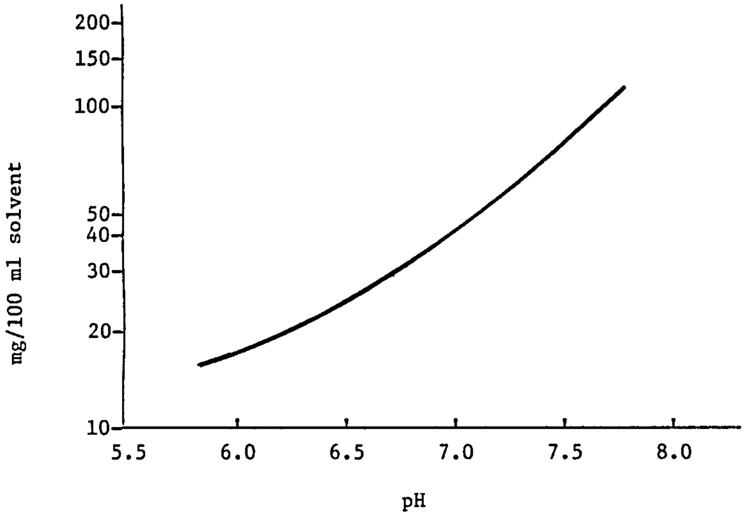
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfapyrimidine at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfapyrimidine in the phosphate buffer was shaken at 37°C for 24 h. The concn of the solute was detd by the Bratton and Marshall method (1) using a photoelec colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

ESTIMATED ERROR:

Soly: precision ±2 mg/100 ml (authors).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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%	10^4 mol dm^{-3} [a]
4.9	16	6.4
5.9	21	8.4
6.9	29	12
7.0	54	22
7.5	81	32

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine was added to a buffer soln and boiled for 1 h in a sealed ampul followed by keeping the ampul at 37°C. The concn of sulfadiazine 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 65 mg% (2.6×10^{-3} mol dm^{-3} solutions, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfadiazine at 20°C, their pH was measured at equilibrium, and the sulfadiazine 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) Benzensulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 2.70 mmol/L (0.676 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadiazine (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 sulfadiazine 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 and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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	10^3 mol dm^{-3} [a]
5.5	265	1.06
7.5	950	3.80

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadiazine 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 sulfadiazine 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 in bicarbonate-free Locke's solution[a]	
	mg/100 ml	10^4 mol dm^{-3} [b]
17	7.8	3.12
36	18.0	7.19

[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:

Sulfadiazine 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 sulfadiazine 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Boric acid, disodium salt; $Na_2B_4O_7$; [1330-43-4]

(3) Phosphoric acid; H_3PO_4; [7664-38-2]

(4) Phosphoric acid; monosodium salt; NaH_2PO_4; [7558-80-7]

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

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

ORIGINAL MEASUREMENTS:

Krebs, H. A.; Speakman, J. C.

J. Chem. Soc. <u>1945,</u> *42,* 593-5.

PREPARED BY:

R. Piekos

VARIABLES:

pH

EXPERIMENTAL VALUES:

pH at saturation	Solubility of sulfadiazine at 25.0°C in phosphate - borate buffer solutions[a]	
	mg/100 ml	10^3 mol dm^{-3} [b]
6.01	8.5	0.34
6.35	11.1	0.443
6.82	19.4	0.775
7.23	43.5	1.74
7.56	86	3.4
7.67	114	4.56
8.00	229	9.15

[a] The buffer solutions were prepared by adding NaOH to a solution of 0.0375M H_3PO_4 + 0.00938M Na tetraborate (i.e. equivalent to 0.0188M H_3PO_4 + 0.0188M NaH_2PO_4 + 0.0375M HBO_2) chosen so as to give an approx uniform buffering capacity over the range of pH, diluting and adding the appropriate quantity of N-NaCl to maintain the ionic strength at 0.1M. After dilution, the final total concentration of each acid was 0.0268M.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The buffer solns were satd by shaking them vigorously with an excess of solid sulfadiazine for at least 3 h. They were then quickly filtered. The sulfadiazine concn was detd by the method of Bratton and Marshall (1), and the pH values were measured with the glass electrode, which was standardized in terms of the buffer solns recommended by Hitchcock and Taylor (2).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine, mp 256°C, was obtained by recrystg a common specimen from water. Neither source nor purity of the remaining materials was specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* <u>1939,</u> *128,* 537.
2. Hitchcock, D. I.; Taylor, A. C. *J. Am. Chem. Soc.* <u>1937,</u> *59,* 1812.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]
(2) Acetic acid; $C_2H_4O_2$; [64-19-7]
(3) Acetic acid, sodium salt; $C_2H_3NaO_2$; [127-09-3]
(4) Phosphoric acid; H_3PO_4; [7664-38-2]
(5) Phosphoric acid, monosodium salt; NaH_2PO_4; [7558-80-7]
(6) Sodium chloride; NaCl; [7647-14-5]
(7) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Krebs, H. A.; Speackman, J. C.
J. Chem. Soc. 1945, *42*, 593-5.

PREPARED BY:

R. Piekos

VARIABLES:

pH

EXPERIMENTAL VALUES:

pH at saturation	Solubility of sulfadiazine at 25.0°C in acetate - phosphate buffer solutions[a]	
	mg/100 ml	10^4 mol dm^{-3} [a]
2.31	9.3	3.7
2.69	7.5	3.0
3.06	6.9	2.8
4.89	6.3	2.5

[a] The buffer solutions were prepared by adding NaOH to a solution of 0.0375M H_3PO_4 + 0.0375M CH_3COOH chosen so as to give an approx uniform buffering capacity over the range of pH, diluting, and adding the appropriate quantity of N-NaCl to maintain the ionic strength at 0.1M.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The buffer solns were satd by shaking them vigorously with an excess of solid sulfadiazine for at least 3 h. They were then quickly filtered. The sulfadiazine concn was detd by the method of Bratton and Marshall (1), and the pH values were measured with the glass electrode, which was standardized in terms of the buffer solns recommended by Hitchcock and Taylor (2).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine, mp 256°C, was obtained by recrystg a common specimen from water. Neither source nor purity of the remaining materials was specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Bratton, A. C.; Marshall, E.K., Jr. *J. Biol. Chem.* 1939, *128*, 537.
2. Hitchcock, D. I.; Taylor, A. C. *J. Am. Chem. Soc.* 1937, *59*, 1812.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy, disodium salt; (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Garb, S.; Plummer, M. N. *Proc. Soc. Exp. Biol. Med.* 1943, *52*, 248-50.

VARIABLES:

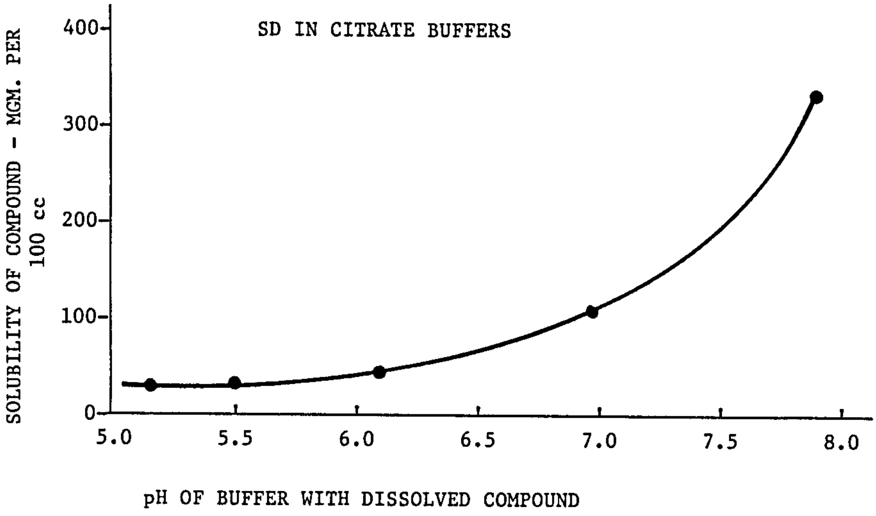
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The curve of solubility of sulfadiazine in M/10 citrate plus NaOH buffer solutions at 37°C.



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt; (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Plummer, M. N.

Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

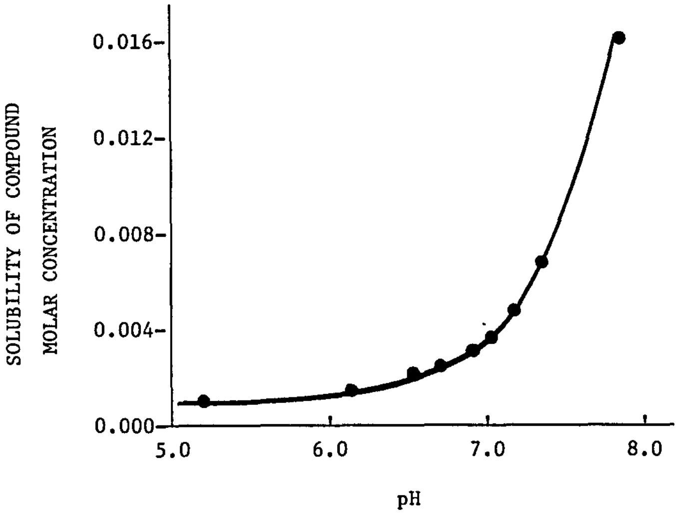
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in M/10 Na citrate + NaOH solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were 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-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (citric acid); $C_6H_8O_7$; [77-92-9] (3) Water; H_2O; [7732-18-5]	Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.
VARIABLES:	PREPARED BY:
One temperature: 37°C; one pH: 2.1	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadiazine in a citric acid solution (2.100 g citric acid per 100 ml water) of pH 2.1 at 37°C is 0.20 mg/ml solution[a] (8.0×10^{-4} mol dm^{-3} solution, compiler).

[a] Numerical value to the graphical data was given by one of the authors (S. T.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the citric acid soln were placed in glass-stoppered flasks with excess of sulfadiazine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfadiazine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine was of pharmaceutical grade. The source and purity of the citric acid was not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

Nogami, H.; Nagai, T.; Suzuki, A.
Chem. Pharm. Bull. 1966, *14(4)*, 339-50.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH of Mc'Ilvaine buffer solutions^a at constant ionic strength of 0.35.		Solubility of sulfadiazine at 37°C	
at the beginning of the run	at the end of the run	mg/100 ml	10^3 mol dm^{-3} ^{b}
4.17	4.19	10.7	0.4275
5.06	5.09	11.0	0.4395
6.56	6.59	93.0	3.716
7.23	7.10	175	6.992
8.14	7.30	242	9.669

[a] Obtained by mixing together Na_2HPO_4 and citric acid solutions of proper concentrations.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Citric acid	Na_2HPO_4	pH	Solubility at 37°C	
g/100 ml water	g/100 ml water		mg/ml soln[a]	10^3 mol dm^{-3} soln[b]
1.680	0.572	3.1	0.13	0.519
1.260	1.144	4.2	0.11	0.439
0.840	1.716	5.8	0.16	0.639
0.420	2.228	6.8	0.49	1.96

[a] Numerical values to the graphical data were given by one of the authors (S. T.) in personal communication.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the buffer solns were placed in glass-stoppered flasks with excess of sulfadiazine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfadiazine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfadiazine was of pharmaceutical grade. The source and purity of Na_2HPO_4 and citric acid was not specified. Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Ethanesulfonic acid, 2-[[3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-amino]-, monosodium salt (Na taurocholate); $C_{26}H_{45}NO_7S{\cdot}Na$; [145-42-6]

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

(4) Phosphoric acid, monosodium salt; NaH_2PO_4; [7558-80-7]

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

ORIGINAL MEASUREMENTS:

Gasco, M. R.; Aimonetto, S.

Atti Accad. Sci. Torino, Cl. Sci. Fis., Mat. Nat. 1979, *113(1-2)*, 119-22.

VARIABLES:

Concentration of Na taurocholate; pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of Na taurocholate mM/l solution[a]	Solubility of sulfadiazine at 25°C µM/ml solution[a]	
	pH 6.3	pH 7.2
2.25	0.52	1.43
4.50	0.47	1.34
6.00	0.47	1.39
8.00	0.47	1.35
12.00	0.47	1.43
16.00	0.47	1.43
20.00	0.47	1.43

[a] Numerical values given by the first author in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly of sulfadiazine was detd by the method of Hofmann (1). In a series of 15-ml glass cylinders with ground-in stoppers, 50 mg of sulfadiazine was placed in 15 ml of phosphate buffer solns of increasing Na taurocholate concn. The suspensions were agitated for 20 h at 25°C and filtered. The quantity of sulfadiazine dissolved was detd by measuring surface tension by means of a Dognon-Abribat (Prolabo) tensiometer and spectrophotometrically on a Perkin Elmer EPS-35 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

The phosphate buffer was 0.3M in respect of the Na^+ ion concentration.

ESTIMATED ERROR:

Soly: precision ±2% (authors).

pH : precision ±0.02 pH unit (authors).

Temp: ±0.5°C (authors).

REFERENCES:

1. Hofmann, A. F., *Biochem. J.* 1963, *89*, 57.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Ethanesulfonic acid, 2-[[[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxacholan-24-yl]amino]acetyl]amino]-, sodium salt (Na tauroglycocholate); $C_{28}H_{48}N_2O_8S\cdot Na$ [11006-55-6]

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

(4) Phosphoric acid, monosodium salt; NaH_2PO_4; [7558-80-7]

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

ORIGINAL MEASUREMENTS:

Gasco, M. R.; Aimonetto, S.

Atti Accad. Sci. Torino, Cl. Sci. Fis., Mat. Nat. 1979, *113(1-2)*, 119-22.

PREPARED BY:

R. Piekos

VARIABLES:

Concentration of Na tauroglycochlolate; pH

EXPERIMENTAL VALUES:

Concentration of Na tauroglycocholate mM/l solution	Solubility of sulfadiazine at 25°C μml solution^a	
	pH 6.3	pH 7.2
2.25	0.43	1.34
4.50	0.39	1.21
6.00	0.41	1.26
8.00	0.41	1.26
12.00	0.43	1.26
16.00	0.43	1.28
20.00	0.47	1.30

^{a}Numerical values given by the first author in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly of sulfadiazine was detd by the method of Hofmann (1). In a series of 15-ml glass cylinders with ground-in stoppers, 50 mg of sulfadiazine was placed in 15 ml of phosphate buffer solns of increasing Na tauroglycocholate concn. The suspensions were agitated for 20 h at 25°C and filtered. The quantity of dissolved sulfadiazine was detd by measuring surface tension by means of a Dognon-Abribat (Prolabo) tensiometer and spectrophotometrically on a Perkin Elmer EPS-35 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

The phosphate buffer was 0.3M in respect of the Na^+ ion concn.

ESTIMATED ERROR:

Soly: precision ±2% (authors).

pH : precision ±0.02 pH unit (authors).

Temp: ±0.5°C (authors).

REFERENCES:

1. Hofmann, A. F.; *Biochem. J.* 1963, *89*, 57.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Sulfuric acid monododecyl ester, sodium salt (Na lauryl sulfate); $C_{12}H_{25}NaO_4S$; [151-21-3]

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

ORIGINAL MEASUREMENTS:

Watari, N.; Kaneniwa, N.
Chem. Pharm. Bull. 1976, *24(11)*, 2577-84.

VARIABLES:

Concentration of Na lauryl sulfate

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of Na lauryl sulfate	Total solubility of sulfadiazine at 37°C	
% w/v	mg/ml solution	10^4 mol dm^{-3} [a]
0.01	0.124	4.954
0.05	0.132	5.274
0.10	0.151	6.033
0.25	0.165	6.592
0.50	0.179	7.152
1.00	0.207	8.270
2.00	0.258	10.31
3.00	0.309	12.35
4.00	0.361	14.42
5.00	0.410	16.38
6.00	0.463	18.50

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadiazine was added to 15 ml of the Na lauryl sulfate soln contained in a 50-ml flask and the flask was shaken (2 strokes/s at the amplitude of 3 cm) in a thermostatically controlled water bath at 37°C. One-ml sample was removed every 6 h (total equilibration period was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically (1).

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine of the Japanese Pharmacopeia grade and distd water were used.

Na lauryl sulfate was of the reagent grade (Wako Pure Chemical Industries Ltd, lot No. PA10233) and used without further purification.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Kaneniwa, N.; Watari, N.
Chem. Pharm. Bull. 1974, *22*, 1699.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

(4) 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 sulfadiazine in a mixture of 1,2,3-propanetriol and 95° ethanol (2:1 by wt) at 26-28°C is 0.27% (1.1×10^{-2} mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfadiazine content was detd by diazotization of the amine group in a cold acidified 0.1N KNO_2 soln. An excess of KNO_3 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine at 26-28°C in a saturated solution of urea in a mixture of 1,2,3-propanetriol and 95°C ethanol (2:1 by wt), containing 54.5 g of urea per 100 g of the mixture, is 0.26% (1.1 x 10^{-2} mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfadiazine content was detd by diazotization of the amine group in a cold acidified 0.1N KNO_2 soln. An excess of KNO_3 was detected by using iodinated starch.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Ethanol; 2,2'-iminobis- (diethanolamine); $C_4H_{11}NO_2$; [111-42-2] (3) Water; H_2O; [7732-18-5]	Nogami, H.; Nagai, T.; Suzuki, A. *Chem. Pharm. Bull.* 1966, *14(4)*, 339-50.
VARIABLES:	**PREPARED BY:**
Concentration of diaethanolamine	R. Piekos

EXPERIMENTAL VALUES:

Concentration of diethanolamine	Solubility of sulfadiazine at 37°C	
mol dm^{-3}	mg/100 ml	10^2 mol dm^{-3}
10^{-3}	33.8	0.135
10^{-2}	266.0	1.06
10^{-1}	2510.0	10.0

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl; (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Ethanol, 2,2',2''-nitrilotris-(triethanolamine); $C_6H_{15}NO_3$; [102-71-6] (3) Water; H_2O; [7732-18-5]	Nogami, H.; Nagai, T.; Suzuki, A. *Chem. Pharm. Bull.* 1966, *14(4)*, 339-50.
VARIABLES:	PREPARED BY:
Concentration of triethanolamine	R. Piekos

EXPERIMENTAL VALUES:

Concentration of triethanolamine	Solubility of sulfadiazine at $37^{\circ}C$	
mol dm^{-3}	mg/100 ml	10^2 mol dm^{-3}
10^{-3}	31.4	0.15
10^{-2}	286.0	1.10
10^{-1}	2550.0	10.0

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl-; (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Formamide, N, N-dimethyl- (DMF); C_3H_7NO; [68-12-2]

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

ORIGINAL MEASUREMENTS:

Elworthy, P. H.; Worthington, H. E. C.

J. Pharm. Pharmac. 1968, *20*, 830-5.

VARIABLES:

Temperature: Concentration of DMF

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Solns were presatd by shaking with powd sulfadiazine for 24 h, and transferred to a soly app which was of the percolation type and a modification of that used by Davies and Griffiths (1). The soln was recycled in the app until satd (7-14 days). The solute concn was detd by one of the three methods: (a) concn 1.5%, by evapn of solvent and drying the residue to const wt; (b) concn 0.02 to 1.5%, samples were dild to give a 70% DMF solvent mixt and assayed spectrophotometrically at 270 nm; (c) concn $< 0.02\%$, samples were dild with water and assayed as in (b). In all spectrophotometric assays suitable calibration lines were prepd.

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (B. P. quality) was twice recrystd from an EtOH-DMF mixt (3:1 by vol) and dried over P_2O_5. Its mp was 255°C. Assay by the Pharmacopeial method gave 100.0% purity calcd with reference to the material dried at 105°C. DMF (May and Baker Ltd) was distd under reduced pressure and gave $n_D^{25} = 1.4283$. Purity of the water was not specified.

ESTIMATED ERROR:

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

Temp: ±0.05°C (authors).

REFERENCES:

1. Davies, M.; Griffiths, D. M. L. *Trans. Faraday Soc.* 1953, *49*, 1405.

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

Elworthy, P. H.; Worthington, H. E. C.
J. Pharm. Pharmac. 1968, *20*, 830-5.

VARIABLES:
Temperature: Concentration of DMF

PREPARED BY:
R. Piekos

EXPERIMENTAL VALUES:

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

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

Elworthy, P. H.; Worthington, H. E. C.
J. Pharm. Pharmac. 1968, *20*, 830-5.

VARIABLES:

Temperature: Concentration of DMF

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

% w/w DMF	Mole fraction sulfadiazine in solution		
	20°C	30°	40°C
0.5	3.54×10^{-6}	5.47×10^{-6}	9.97×10^{-6}
1.0	3.78×10^{-6}	6.39×10^{-6}	1.07×10^{-5}
2.0	4.37×10^{-6}	7.21×10^{-6}	1.21×10^{-5}
3.0	5.00×10^{-6}	8.18×10^{-6}	1.38×10^{-5}
5.0	6.44×10^{-6}	1.06×10^{-5}	1.74×10^{-5}
10.0	1.33×10^{-5}	1.97×10^{-5}	3.19×10^{-5}
20.0	3.35×10^{-5}	4.87×10^{-5}	8.21×10^{-5}
30.0	7.91×10^{-5}	1.14×10^{-4}	1.75×10^{-4}
50.0	4.08×10^{-4}	5.84×10^{-4}	8.81×10^{-4}
70.0	2.94×10^{-3}	3.73×10^{-3}	5.50×10^{-3}
78.0	7.75×10^{-3}	8.84×10^{-3}	1.14×10^{-2}
89.0	2.32×10^{-2}	2.60×10^{-2}	2.90×10^{-2}

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

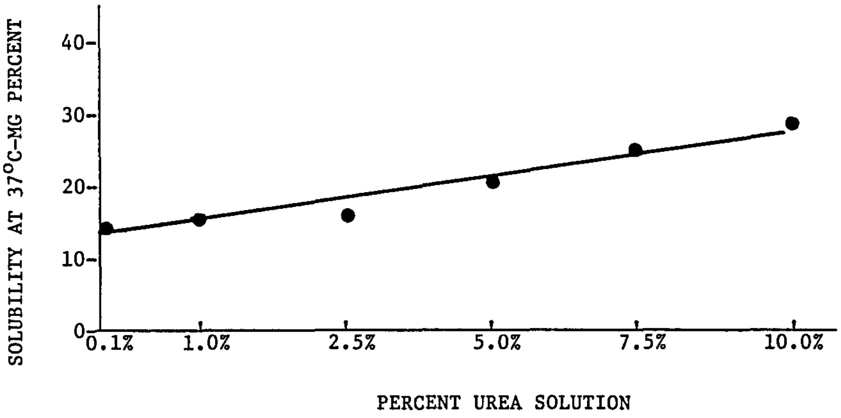
SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (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:	**PREPARED BY:**
Concentration of urea	R. Piekos

EXPERIMENTAL VALUES:



Solubility in a 10 percent urea solution at 37°C is 31.5 mg per 100 cm^3 (1.26×10^{-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 sulfadiazine, 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:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

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

ORIGINAL MEASUREMENTS:

Nogami, H.; Nagai, T.; Suzuki, A.
Chem. Pharm. Bull. 1966, *14(4)*,
339-50.

VARIABLES:

Concentration of urea; temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of urea	Solubility of sulfadiazine					
	25°C		37°C		50°C	
mol dm^{-3}	mg/100 ml	concn^a	mg/100 ml	concn^b	mg/100ml	concn^b
10^{-3}			15.9	0.635		
10^{-2}			20.2	0.807		
10^{-1}	10.2	4.07	28.8	1.150	34.4	1.37
5×10^{-1}			31.4	1.250		
1			42.3	1.690		

Note: molar concentrations of the solute calculated by compiler.

a - 10^4 mol dm^{-3}

b - 10^3 mol dm^{-3}

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.

SOURCE AND PURITY OF MATERIALS:

Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Dextrin; $(C_6H_{10}O_5)_n$; [90004-53-9]

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

ORIGINAL MEASUREMENTS:

Lach, J. L.; Cohen, J.

J. Pharm. Sci. 1963, *52*, 137-42.

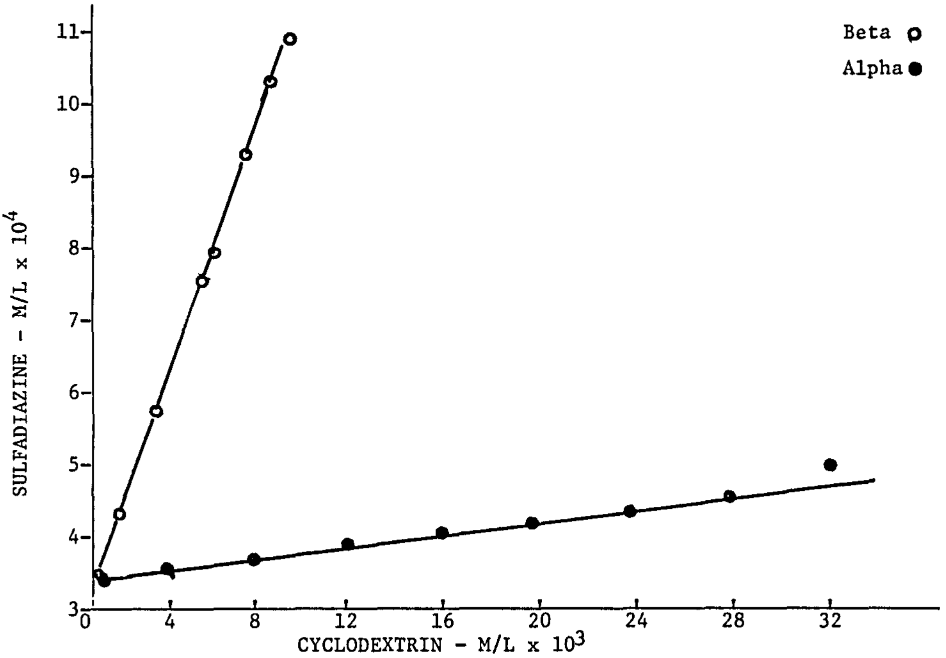
VARIABLES:

Concentration of dextrin

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Solubility of sulfadiazine in aqueous solutions of cyclodextrins at 30°C

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly method of Higuchi and Lach was employed (1). Procedure: excess quantity of sulfadiazine was placed in 125-ml glass-stoppered bottles together with varying but accurately weighed amts of dextrin and 50 ml of water. The bottles were placed in a mech shaker in a const temp bath and equilibrated for 8 h at 30°C. Aliquot portions of the supernatant liquid were removed and analyzed for the sulfadiazine concn at the end of this time. Sulfadiazine was assayed spectrophotometrically at 266 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine, m.p. 255-6°C. Source not specified.

The Schardinger dextrins were prepd by accepted methods (2,3).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Higuchi, T.; Lach, J. L.
J. Pharm. Sci. 1954, *43*, 349.
2. French, D.; Lavine, M. L.; Pazur, J. H.; Norberg, E., *J. Am. Chem. Soc.* 1949, *71*, 353.
3. Tilden, E. B.; Hudson, C. S., *J. Bacteriol.* 1942, *43*, 527.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Poly(oxy-1,2-ethanediyl), α - hexadecyl-ω -hydroxy-, mixt with α- octadecyl- ω -hydroxypoly(oxy-1,2-ethanediyl) (cetomacrogol) [8065-80-3]

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

ORIGINAL MEASUREMENTS:

Corby, T. C.; Elworthy, P. H.

J. Pharm. Pharmac. <u>1971,</u> *23,* Suppl. 39S-48S.

VARIABLES:

Concentration of cetomacrogol

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of cetomacrogol % w/v	Maximum additive concentration of sulfadiazine at 20°C	
	mmol kg^{-1} solvent	% by wt [a]
1	0.272	0.0680
8	0.535	0.134
10	1.01	0.252

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly was detd in an app where the aqueous soln of cetomacrogol was percolated through a plug of sulfadiazine supported on a 5/3 sintered glass disc. The percolation was continued until the soln was satd (5-6 days). The concn of sulfadiazine was detd spectrophotometrically from a calibration curve using a Uvispek spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (Macarthy's Ltd, Romford) was a British Pharmacopeia product. It was recrystd twice from a DMF-EtOH mixt (1:3) and dried at 40°C over P_2O_5. Its mp was 254°C (decompn). Cetomacrogol 1000 B.P.C. was of the same origin and was used as received. Tap water once distd from glass was used.

ESTIMATED ERROR:

Soly: nothing specified.

Temp: ±0.05°C (authors).

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Poly(oxy-1,2-ethanediyl), α-hydro- ω-hydroxy- (PEG 1000); $(C_2H_4O)_nH_2O$; [25322-68-3] 1000

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

ORIGINAL MEASUREMENTS:

Corby, T. C.; Elworthy, P. H.

J. Pharm. Pharmac. 1971, *23*, Suppl. 39S-48S.

VARIABLES:

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of PEG 1000	Solubility of sulfadiazine at 20°C	
% w/v	mmol kg^{-1} solvent	% by wt [a]
10	0.719	0.180
30	2.11	0.525
50	4.20	1.04

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly was detd in an app where the aqueous soln of PEG 1000 was percolated through a plug of sulfadiazine supported on a 5/3 sintered glass disc. The percolation was continued until the soln was satd (5 - 6 days). The concn of sulfadiazine was detd spectrophotometrically from a calibration curve using a Uvispek spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (MaCarthy's Ltd, Romford) was a British Pharmacopeia product. It was recrystd twice from a DMF-EtOH mixt (1:3) and dried at 40°C over P_2O_5. Its mp was 254°C (decompn). PEG 1000 was a B.D.H. Laboratory Reagent and was used as received. Tap water once distd from glass was used.

ESTIMATED ERROR:

Soly: nothing specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Elworthy, P. H.; Lipscomb, F. J. *J. Pharm. Pharmac.* 1968, *20*, 790.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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:

Higuchi, T.; Lach, J. L.

J. Amer. Pharm. Assoc., Sci. Ed. 1954, *43*, 349-54.

VARIABLES:

Concentration of caffeine

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Total solubility of sulfadiazine in water containing caffeine at 30°C

Caffeine	Sulfadiazine		Caffeine	Sulfadiazine	
10^2 mol dm^{-3}	10^4 mol dm^{-3}	g dm^{-3} [a]	10^2 mol dm^{-3}	10^4 mol dm^{-3}	g dm^{-3} [a]
0.000	3.64	0.091	10.470	6.47	0.162
1.454	3.80	0.095	10.742	6.36	0.159
1.467	3.77	0.094	12.410	6.64	0.166
3.716	4.51	0.113	12.865	7.04	0.176
3.728	4.50	0.113	14.556	7.69	0.192
5.285	4.84	0.121	14.957	7.51	0.188
5.964	5.04	0.126			
7.356	5.32	0.133			
7.703	5.55	0.139			

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess quantities of sulfadiazine (25 mg) were placed in 125-ml glass-stoppered bottles together with varying but accurately weighed amts of caffeine and 50-ml portion of water. The bottles were placed in a mech shaker in a const temp bath and equilibrated for 8 h at 30°C. Aliquots of the supernatant liquid were analyzed for the sulfadiazine content by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Recrystd sulfadiazine (U.S.P.), mp 255-6°C, recrystd caffeine (U.S.P.), mp 235-7°C and distd water were used.

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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) α-D-Glucopyranoside, β-D-fructofuranosyl- (sucrose); $C_{12}H_{22}O_{11}$; [57-50-1] (3) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Nogami, H.; Nagai, T.; Suzuki, A. *Chem. Pharm. Bull.* 1966, *14(4)*, 339-50.
VARIABLES: Concentration of sucrose	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of sucrose	Solubility of sulfadiazine at 37°C	
mol dm^{-3}	mg/100 ml	10^4 mol dm^{-3} [a]
10^{-3}	10.9	4.35
10^{-2}	11.0	4.39
10^{-1}	12.0	4.79
1	12.9	5.15

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Soly of sulfadiazine was detd from dissoln rate data obtained by the rotating disk method.	**SOURCE AND PURITY OF MATERIALS:** Commercial sulfadiazine J. P. was used. Purity of the remaining materials was not specified.
	ESTIMATED ERROR: Nothing specified.
	REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) Methanol; CH_4O; [67-56-1]	ORIGINAL MEASUREMENTS: Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, 61(1), 97-7.
VARIABLES: Temperature	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^5)
25	19.3
30	22.9
37	29.9

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and methanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

Methanol was a spectrophotometric grade solvent from the Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Methanol; CH_4O; [67-56-1]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.
Alexander, K. S.; Paruta, A. N.
Drug Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^5 X [a]	10^3 mol dm^{-3} [b]
25	1.18	19.3	4.71
30	1.40	22.9	5.59
37	1.82	29.9	7.27

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and methanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Soly was detd from absorbance and previously ascertained Beer's law plots detd on a Cary model 6 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. Methanol was a spectrograde solvent from Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J.W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^5)
25	7.68
30	9.36
37	12.4

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and ethanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

Ethanol was from the U. S. Industrial Chemicals Co.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

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

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^5 X [a]	10^3 mol dm^{-3} [b]
25	0.33	7.68	1.32
30	0.40	9.36	1.60
37	0.53	12.40	2.12

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and ethanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Soly was detd from absorbance and previously ascertained Beer's law plots detd on a Cary Model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. Ethanol was from the U. S. Industrial Chemicals Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N. Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Propanol; C_3H_8O; [71-23-8]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (X 10^5)
25	4.32
30	5.45
37	7.44

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with excess and 1-propanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

1-Propanol was a Baker Analyzed Reagent from J. T. Baker Chemical Co.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Propanol; C_3H_8O; [71-23-8]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr., Alexander, K. S.; Paruta, A. N.

Drug Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^5 X [a]	10^4 mol dm^{-3} [b]
25	0.14	4.32	5.59
30	0.18	5.45	7.19
37	0.25	7.44	9.99

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. 1-Propanol was a Baker Analyzed Reagent (J. T. Baker Chemical Co.). Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (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 sulfadiazine in 2-propanol at 25°C is 0.0430 g/100 cm^3 solution (1.72 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadiazine 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 sulfadiazine was manufd by Squibb 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) 1-Butanol; $C_4H_{10}O$; [71-36-3]	Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.
VARIABLES:	**PREPARED BY:**
Temperature	R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^5)
25	3.18
30	4.09
37	5.66

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-butanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

1-Butanol was from the Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Butanol; $C_4H_{10}O$; [71-36-3]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N.

Drug Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^5 X [a]	10^4 mol dm^{-3} [a]
25	0.087	3.18	3.48
30	0.111	4.09	4.43
37	0.153	5.66	6.11

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. 1-Butanol was from the Mallinckrodt Chemical Works. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzanesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Pentanol; $C_5H_{12}O$; [71-41-0]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	Mole fraction solubility ($\times 10^5$)
25	2.63
30	3.31
37	4.61

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-pentanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

1-Pentanol was from Fisher Scientific Co.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Pentanol; $C_5H_{12}O$; [71-41-0]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^5 X [a]	10^4 mol dm^{-3} [b]
25	0.061	2.63	2.437
30	0.076	3.31	3.036
37	0.106	4.61	4.235

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. 1-Pentanol was from Fisher Scientific Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: 0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, 61(1), 94..

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Octanol; $C_8H_{18}O$; [111-87-5]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^5)
25	1.41
30	1.76
37	2.65

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-octanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet , which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

1-Octanol was from Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Octanol; $C_8H_{18}O$; [111-87-5]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	Solubility		
	mg/ml	10^5 X [a]	10^4 mol dm^{-3} [a]
25	0.022	1.41	0.879
30	0.028	1.76	1.118
37	0.042	2.65	1.678

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. 1-Octanol was from Fisher Scientific Co. Its refractive index and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (2) 1-Decanol; $C_{10}H_{22}O$; [112-30-1]	Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^5)
25	7.40
30	8.04
37	9.47

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadiazine in excess and 1-decanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235 from Eli Lilly and Co.

1-Decanol was from Matheson, Coleman and Bell.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) 1-Decanol; $C_{10}H_{22}O$; [112-30-1]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr. Alexander, K. S.; Paruta, A. N.
Drug Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility mg/ml	Solubility 10^5 X [a]	Solubility 10^4 mol dm^{-3} [a]
25	0.097	7.40	3.875
30	0.105	8.04	4.195
37	0.123	9.47	4.914

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine: lot W02235, Eli Lilly and Co. Its mp agreed with the literature value. 1-Decanol was from Matheson, Coleman and Bell. Its refractive index and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Acetamide, N,N-dimethyl-; C_4H_9NO; [127-19-5]

ORIGINAL MEASUREMENTS:

Sunwoo, C.; Eisen, H.
J. Pharm. Sci. 1971, *60*, 238-44.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfadiazine in N,N-dimethylacetamide at 25°C is 0.0239 (6.57 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by the method reported by Restaino and Martin (1). Sulfadiazine was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 270 nm after diln of a sample with 95% alcohol or water.

SOURCE AND PURITY OF MATERIALS:

A USP sulfadiazine (American Cyanamide) Co., Pearl River, N. Y.) was recrystd from warm acetone. N,N-Dimethylacetamide was of technical grade.

ESTIMATED ERROR:

Temp: ±1.0° (authors).

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

REFERENCES:

1. Restaino, F. A.; Martin, A. N.
J. Pharm. Sci. 1964, *53*, 636.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) Formamide, N,N-dimethyl-; C_3H_7NO; [68-12-2]

ORIGINAL MEASUREMENTS:

Elworthy, P. H.; Worthington, H. E. C.

J. Pharm. Pharmac. 1968, *20*, 830-5.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	Weight %	10^2 mole fraction	mole kg^{-1} water [a]
20	18.0	6.02	0.782
30	18.7	6.29	0.818
40	19.4	6.57	0.962

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Solns were prepd by shaking powd sulfadiazine with DMF for 24 h and transferred to a soly app which was of the percolation type and a modification of that used by Davies and Griffiths (1). The soln was recycled in the app through a sintered-glass filter until satd (7-14 days). Samples were evapd and the residues dried to const wt.

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (B.P. quality) was twice recrystd from an EtOH-DMF mixt (3:1 by vol) and dried over P_2O_5. Its mp was 255°C. Assay by the Pharmacopeial method gave 100.0% purity calcd with reference to the material dried at 105°C.

DMF (May and Baker Ltd) was distd under reduced pressure and gave $n_D^{25} = 1.4283$.

ESTIMATED ERROR:

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

Temp: ±0.05°C (authors).

REFERENCES:

1. Davies, M.; Griffiths, D. M. L. *Trans. Faraday Soc.* 1953, *49*, 1405.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(2) n-Hexane; C_6H_{14}; [110-54-3]

ORIGINAL MEASUREMENTS:

Corby, T. C.; Elworthy, P. H.

J. Pharm. Pharmac. 1971, *23*, Suppl. 39S-48S.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of sulfadiazine in a saturated n-hexane solution at 20°C is 0 millimolal.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly was detd in an app where n-hexane percolated through a plug of sulfadiazine supported on a 5/3 sintered glass disc. The percolation was continued until the soln was satd (5-6 days). The concn of sulfadiazine was detd spectrophotometrically from a calibration curve using a Uvispek spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine (MaCarthy's Ltd, Romford) was a British Pharmacopeia product. It was recrystd twice from a DMF-EtOH mixt (1:3) and dried at 40°C over P_2O_5. Its mp was 254°C (decompn). A spectroscopic grade n-hexane (B.D.H.) was used as received.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Elworthy, P. H.; Lipscomb, F. J. *J. Pharm. Pharmac.* 1968, *20*, 790.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9] (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 sulfadiazine in chloroform at 20°C is 15 mg% (6.0×10^{-4} 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-pyrimidinyl- (sulfadiazine); $C_{10}H_{10}N_4O_2S$; [68-35-9]

(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 sulfadiazine in chloroform at 30°C is 0.49 mmol/L (0.12 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadiazine (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 sulfadiazine 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-4-pyrimidinyl- (4- sulfapyrimidine); $C_{10}H_{10}N_4O_2S$; [599-82-6]

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

ORIGINAL MEASUREMENTS:

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 4-sulfapyrimidine in water at 37°C is 354 mg/100 cm^3 solution (1.41×10^{-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 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 231-2°C (dec, cor), was prepd by the authors. Anal: %C 48.0 (calcd 48.0); %H 3.4 (3.5); %N 20.2 (19.9). 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-pyrimidinyl-; $C_{10}H_{10}N_4O_2S$; [17103-48-9]

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

ORIGINAL MEASUREMENTS:

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

J. Am. Chem. Soc. 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-5-pyrimidinylbenzenesulfonamide in water at 37°C is 9.8 mg/100 cm^3 solution (3.9×10^{-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 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 260-1°C (cor), was prepd by the authors. Anal: %C 48.1 (calcd 48.0); %H 4.2 (4.0); %N 22.5 (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) Aluminum, tris(4-amino-N-2-pyrimidinylbenzenesulfonamidato-N^N, O)- (Al sulfadiazine); $C_{30}H_{27}AlN_{12}O_6S_3$; [71280-76-7]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.
Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg.
1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Al(III) sulfadiazine in water at room temperature (28-30°C)[a] is 6.6 mg% (8.5 x 10^{-5} 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 Al sulfadiazine was prepared in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Cerium, tris(4-amino-*N*-2-pyrimidinylbenzenesulfonamidato-*N*^{N},*O*)- (Ce sulfadiazine); $C_{30}H_{27}CeN_{12}O_6S_3$; [66269-03-2]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.; Stanford, J. W.; Fox, P. L.; *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Ce sulfadiazine in water at room temperature (28-30°C)[a] is 83.0 mg% (9.35×10^{-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 Ce sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

The identity of the Ce sulfadiazine was questioned by Bult and associates (2) (compiler).

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *120*, 537.
2. Bult, A.; Hulsing, N.; Weyland, J. W. *Pharm. Weekblad, Sci. Ed.* 1980, *2*, 190.
   J. Pharm. Pharmacol. 1981, *33*, 171.

COMPONENTS:

(1) Chromium, bis(4-amino-$\underline{N}$-2-pyrimidinylbenzenesulfonamidato-$\underline{N}^{N},\underline{O}$)- (Cr(II) sulfadiazine); $C_{20}H_{18}CrN_8O_4S_2$; [71261-84-2]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L, Jr.; Modak, S.; Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg. 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Cr(II) sulfadiazine in water at room temperature (28-30°C)[a] is 15.5 mg% (2.81 x 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 Cr(II) sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Copper, (4-amino-$\underline{N}$-2-pyrimidinyl-benzenesulfonamidato-$\underline{N}^{N}$,O)- (Cu(I) sulfadiazine); $C_{10}H_9CuN_4O_2S$; [71261-85-3]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.; Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg. 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Cu(I) sulfadiazine in water at room temperature (28-30°C)[a] is 5.8 mg% (1.8×10^{-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 Cu(I) sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Copper, bis(4-amino-$\underline{N}$-2-pyrimidinylbenzenesulfonamidato-$\underline{N}^{N}$,O)- (Cu(II) sulfadiazine); $C_{20}H_{18}CuN_8O_4S_2$; [12171-53-8]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.; Stanford, J . W.; Fox, P.L.
Scand. J. Plast. Reconstr. Surg.
<u>1979</u>, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Cu(II) sulfadiazine in water at room temperature (28-30°C)[a] is 3.7 mg% (6.6×10^{-5} 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 Cu(II) sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS: (1) Cobalt, bis(4-amino-N-2-pyrimidinyl-benzenesulfonamidato-N^N, O)- (Co sulfadiazine); $C_{20}H_{18}CoN_8O_4S_2$; [71280-79-0] (2) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Fox, Ch. L., Jr.; Modak, S; Stanford, J. W.; Fox, P. L. *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.
VARIABLES: One temperature: 28-30°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of Co(II) sulfadiazine in water at room temperature (28-30°C)[a] is 86.9 mg% (1.56×10^{-3} 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 Co sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Iron, tris(4-amino-N-2-pyrimidinylbenzenesulfonamidato-N^N,O)- (Fe(III) sulfadiazine); $C_{30}H_{27}FeN_{12}O_6S_3$; [71261-86-4] (2) Water; H_2O; [7732-18-5]	Fox, Ch. L; Modak, S.; Stanford, J. W. ; Fox, P. L. *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.
VARIABLES:	**PREPARED BY:**
One temperature: 28-30°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of Fe(III) sulfadiazine in water at room temperature (28-30°C)[a] is 6.0 mg% (7.5×10^{-5} 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 Fe(III) sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

The Fe(III) sulfadiazine was prepd by the authors as follows: an inorg Fe(III) salt was reacted with Na salt of sulfadiazine and the ppt was analyzed and characterized. No details were given, however. Purity of the materials was 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-pyrimidinyl-, monosilver (+) salt; (AgSD); $C_{10}H_9AgN_4O_2S$; [22199-08-2]

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

ORIGINAL MEASUREMENTS:

Modak, S. M.; Fox, Ch. L. Jr.

Biochem. Pharmacol. 1973, *22*, 2391-404.

VARIABLES:

One temperature: 28°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of AgSD in water at room temperature (28°C) is 0.5μ mole per 100 ml water (5 x 10^{-6} mol dm^{-3} water, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

According to personal communication of one of the authors (C.L.F.) the following procefure was employed: A satd soln of ^{110m}Ag sulfadiazine of known sp activity was made and left at room temp (28°C) overnight. The supernatant was then taken out and centrifuged at higher speed to remove small floating particles of the solid. Radioactive measurement was done on the aliquot of the clear supernatant and the soly was calcd using the sp activity of ^{110m}AgSD.

SOURCE AND PURITY OF MATERIALS:

$^{110m}AgNO_3$ obtained from the International Chem and Nuclear Corp was reacted with Na sulfadiazine (source and purity not specified) to give ^{110m}AgSD with a sp activity of 1.14 mCi/mmol.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosilver (+) salt; (Ag sulfadiazine); $C_{10}H_9AgN_4O_2S$; [22199-08-2] (2) Water; H_2O; [7732-18-5]	Fox, Ch. L., Jr. Modak, S.; Stanford, J. W.; Fox, P. L. *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.
VARIABLES: One temperature: 28-30°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of Ag sulfadiazine in water at room temperature (28-30°C)[a] is 0.2 mg% (6×10^{-6} mol dm^{-3} solution, compiler).

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

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Nothing 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-pyrimidinyl-, monosilver salt (Ag sulfadiazine); $C_{10}H_9AgN_4O_2S$; [22199-08-2]

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

ORIGINAL MEASUREMENTS:

Bult, A.; Klassen, H. B.
Arch. Pharm. (Weinheim) 1980, *313(12)*, 1016-20.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Ag sulfadiazine in water at 25±0.1°C is 0.34 mg/100 ml (9.5×10^{-6} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Ag sulfadiazine was equilibrated with water at 25±0.1°C for one week in a vial with a parafilm-sheet covered rubber closure and wrapped with Al foil. The vial was rotated during equilibration in a thermostated bath. The satd soln was filtered through 25 mm in diam and 1.2 μm av pore size filters (Selectron-filter, type ST69), Schleicher and Schüll, Dassel, Germany). The filtrate was analyzed for sulfadiazine by uv spectrophotometry (Perkin Elmer 124) and for Ag by atomic absorption spectrophotometry.

SOURCE AND PURITY OF MATERIALS:

Ag sulfadiazine was prepd by the earlier reported method (1). Its purity was not specified.
Doubly distd water was used.

ESTIMATED ERROR:

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

REFERENCES:

1. Fox, Ch. L., Jr.; Modak, S. M. *Antimicrob. Agents Chemother.* 1974, *6*, 562.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosilver salt (Ag sulfadiazine); $C_{10}H_9AgN_4O_2S$; [22199-08-2]

(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. 1977, *66(4)*, 519-22.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Table I

Total molar solubility, S, of Ag sulfadiazine determined by the method of known subtraction and the molar concentration of the silver ion determined by direct potentiometry on identical samples at 25±0.1°C, ionic strength 0.1M, in nitric acid buffers

	pH 2.128		pH 3.851	
	$S \times 10^5$	$[Ag^+] \times 10^5$	$S \times 10^5$	$[Ag^+] \times 10^5$
	59.18	59.11	6.690	6.455
	58.06	57.97	6.690	6.517
	59.35	59.34	6.434	6.517
	58.53	58.42	6.768	6.475
	59.19	60.00	6.586	6.375
	57.30	57.97	6.612	6.455
Mean	58.60	58.80	6.466	6.629

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Mixts of 100 mg of Ag sulfadiazine and 25 ml of the HNO_3-KNO_3 buffer with an ionic strength adjusted to 0.1M with KNO_3 were placed in paraffin-coated vials and rotated end-over-end in a thermostated bath until equilibrium soly was obtained. After filtration, the solns were analyzed at 25±0.1°C in paraffin-coated beakers for the Ag-ion concn using a Ag^+-ion selective electrode (No.94-16, Orion Res., Cambridge, Mass) standardized at 25±0.1 °C and an ionic strength of 0.1M. The electrode displayed a Nernstian response throughout the concn range of $1 \times 10^{-2} - 1.5 \times 10^{-6}$M for the Ag^+ion. The pH was measured with a pH electrode (Corning Sci Instruments, Medfield, Mass) standardized using standard buffers meeting NBS requirements. The total Ag^+ concn was detd by the method of known subtraction (1,2) in the HNO_3-buffered soln to which a sufficient amt of a std soln of KI was added to precipitate approx one-half of the free Ag^+ ion.

SOURCE AND PURITY OF MATERIALS:

All reagents were of anal grade. Ag sulfadiazine was prepd by the method of Braun and Towle (3) and recrystd. Water had a sp cond of $(1\text{-}10) \times 10^{-7}$ ohm^{-1} cm^{-1}.

The source of HNO_3 and KNO_3 was not specified.

ESTIMATED ERROR: Soly: the means in Table I are not statistically different at the 5% level (authors). Std deviation of the mean K_s value in Table II is $\pm 0.12 \times 10^{-12}$ (authors). To be contd.

REFERENCES:

1. Durst, R. A., in *"Ion Selective Electrodes"*, R.A. Durst, Ed., NBS Special Publ No 314, US Govt Printing Office, Washington, DC, 1969, p. 381.
2. *Orion Research Inc Newsletter* 1969, *1*, 25.
3. Braun, E. E.; Towle, J. L. *J. Am. Chem. Soc.* 1941, *63*, 3523.

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

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

J. Pharm. Sci. <u>1977</u>, *66(4)*, 519-22.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Table II

Calculation of solubility product of Ag sulfadiazine[a], K_s, at 25±0.1°C and ionic strength 0.1M.

pH	f_o^b	$[Ag^+]^2$	K_s
2.122	2.688×10^{-5}	2.980×10^{-7}	8.04×10^{-12}
2.373	6.024×10^{-5}	1.352×10^{-7}	8.16×10^{-12}
2.630	1.279×10^{-4}	6.165×10^{-8}	7.90×10^{-12}
2.891	2.583×10^{-4}	3.139×10^{-8}	8.14×10^{-12}
		Mean	$8.06 \times 10^{-12} \pm 0.12 \times 10^{-12}$

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

Continued from previous page

ORIGINAL MEASUREMENTS:

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

J. Pharm. Sci. 1977, *66(4)*, 519-22.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

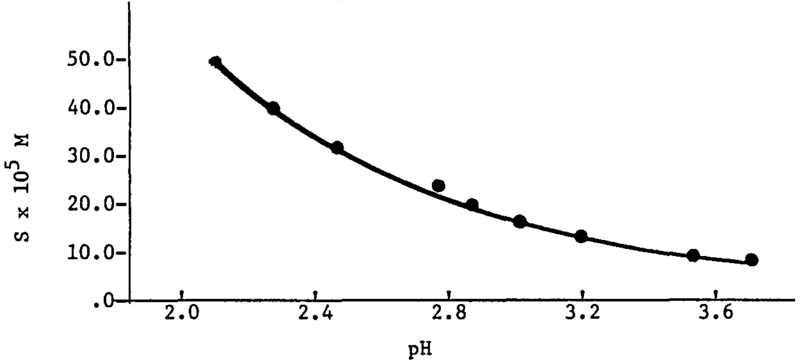
^{a}from equation $K_s = f_o S^2$, where $f_o = \left(1 + \frac{[H_3O^+]}{K_2} + \frac{[H_3O^+]^2}{K_1 K_2} \right)^{-1}$

S is the total molar solubility, and K_1 and K_2 are the ionization constants of the N^4- (amine) and N^1- (amide) hydrogens of sulfadiazine, resp.

$^{b}K_1 = 8.59 \times 10^{-3}$, and $K_2 = 3.82 \times 10^{-7}$.

Figure

Molar solubility, S, of Ag sulfadiazine versus pH at 0.1M ionic strength at 25±0.1°C. Solid circles denote experimental values and open circles denote those calculated from equation $S^2 = [Ag^+]^2 = \frac{[H_3O^+]K_s}{K_1 K_2} + \frac{[H_3O^+]K_s}{K_2}$



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

Temp: ±0.1°C (authors).

pH : accuracy ±0.001 pH unit (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl-, monosilver salt (Ag sulfadiazine); $C_{10}H_9AgN_4O_2S$; [22199-08-2]
(2) 4-Morpholineethanesulfonic acid; $C_6H_{13}NO_4S$; [4432-31-9]
(3) 4-Morpholineethanesulfonic acid, sodium salt; $C_6H_{12}NNaO_4S$; [71119-23-8]
(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. <u>1977</u>, *66(4)*, 519-22.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Molar solubility[a], S, in a 0.05M 4-morpholine-ethanesulfonic acid buffer at 0.1M ionic strength (KNO_3) at 25±0.1°C
6	5.40×10^{-6}
7	3.19×10^{-6}

[a] Estimated by equation, $S^2 = [Ag^+]^2 = \frac{[H_3O^+]K_s}{K_2} + K_s$, where K_s is the solubility product contant, (8.06 ± 0.12) x 10^{-12}, and K_2 is the ionization constant of the N^1 (amido)- hydrogen of sulfadiazine (3.82×10^{-7}).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Mixts of 100 mg of Ag sulfadiazine and 25 ml of 0.05M 4-morpholineethanesulfonic acid buffer were adjusted to an ionic strength of 0.1 M with KNO_3, placed in paraffin-coated vials and rotated in a thermostated bath until equilibrium was obtained. After filtration the solns were analyzed at 25±0.1°C and an ionic stregnth of 0.1M in paraffin-coated beakers for the Ag^+-ion concn using a Ag^+-ion selective electrode standardized using std buffers meeting NBS requirements. The total Ag^+-ion concn was detd by the method of known addn (1); the added reagent was a std soln of $AgNO_3$ representing a 100-fold increase in the free Ag^+ ion present in the sample solns. The pH was measured with triple-purpose pH electrode.

SOURCE AND PURITY OF MATERIALS:

All reagents were of anal grade (source not specified). Ag sulfadiazine was prepd by the method of Braun and Towle(2) and recrystd. The buffer soln was prepd by titrn of the acid with a std NaOH soln. Water had a sp cond.of(1-10) x 10^{-7} ohm^{-1} cm^{-1}.

ESTIMATED ERROR:

Soly: not specified.
Temp: ±0.1°C (authors).
pH : accuracy ±0.001 pH unit (authors).

REFERENCES:

1. *Orion Research Inc Newsletter* <u>1969</u>, *1*, 25.
2. Braun, C. E.; Towle, J. L. *J. Am. Chem. Soc.* <u>1941</u>, *63*, 3523.

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

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

J. Pharm. Sci. 1977, *66(4)* 519-22.

VARIABLES:

pH

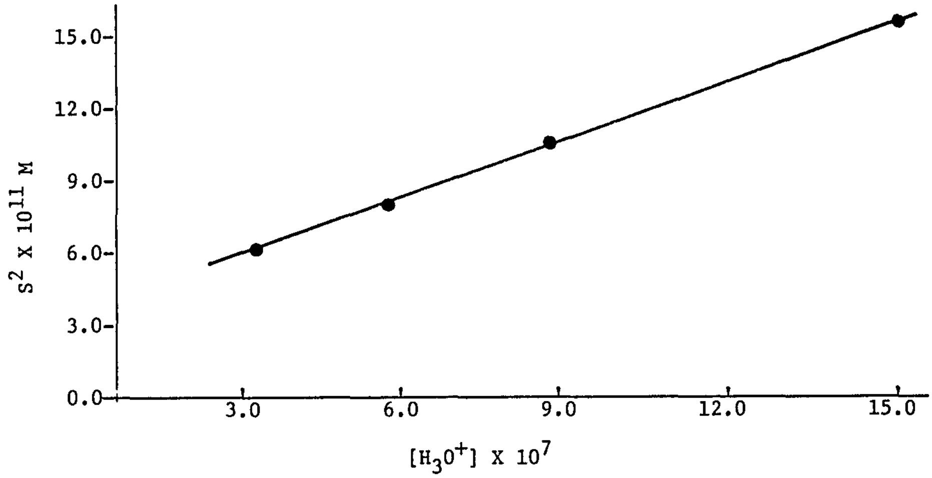
PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Figure

Equilibrium values of S^2 versus $[H_3O^+]$ in 0.05M 4-morpholineethanesulfonic acid buffer at 0.1M ionic strength (KNO_3) at 25±0.1°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

(1) ($\underline{T}$-4)-(4-amino-N-2-pyrimidinylbenzenesulfonamidato-$\underline{N}^N$,O)bis(1H-imidazole-$\underline{N}^3$)-silver (Ag sulfadiazine imidazole); $C_{10}H_9AgN_4O_2S \cdot 2C_3H_4N_2$; [76634-39-4]

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

ORIGINAL MEASUREMENTS:

Bult, A.; Klasen, H. B.
Arch. Pharm. (Weinheim, Ger.) 1980, *313(12)*, 1016-20.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Ag sulfadiazine imidazole in water at 25°C is 3.4 mg/100 ml (6.9×10^{-5} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Ag sulfadiazine imidazole was equilibrated with doubly distd water at 25±0.1°C for one week in a vial with a paraffin coated sheet rubber closure and wrapped with Al foil. The vial was rotated during equilibration in a thermostated bath. The satd soln was filtered through 25 mm in diam and 1.2 μm av pore size filters (Selectron filter type ST69, Schleicher and Schuell, Dassel, Ger.). The filtrate was analyzed for the sulfonamide by uv spectrophotometry (Perkin Elmer 124) and for Ag by atomic absorption spectrophotometry.

SOURCE AND PURITY OF MATERIALS:

The Ag sulfadiazine imidazole was synthesized by the authors. Analysis- Calcd: C 38.9, H 3.47, N 22.7, S 6.5, Ag 21.9% Found: C 39.1, H 3.5, N 23.2, S 6.5, Ag 21.7%. Sulfadiazine by amperometric titrn: 50.3 (lit 50.52).

Doubly distilled water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

REFERENCES:

COMPONENTS: (1) Butanoic acid, 4-oxo-4-[[[4-(2-pyrimidinylamino)sulfonyl]phenyl]amino]-, disilver(1+)salt (Ag succinylsulfadiazine); $C_{14}H_{12}Ag_2N_4O_5S$; [76619-75-5] (2) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Bult, A.; Klasen, H. B. *Arch. Pharm. (Weinheim, Ger.)* 1980, *313(12)*, 1016-20.
VARIABLES: One temperature: 25°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of Ag succinylsulfadiazine in water at 25°C is 0.55 mg/100 ml (9.7×10^{-6} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Ag succinylsulfadiazine was equilibrated with doubly distd water at 25±0.1°C for one week in a vial with a paraffin coated sheet rubber closure and wrapped with Al foil. The vial was rotated during equilibration in a thermostated bath. The satd soln was filtered through 25 mm in diam and 1.2μm av pore size filters (Selectron filter type ST69, Schleicher and Schuell, Dassel, Ger.) The filtrate was analyzed for the sulfonamide by uv spectrophotometry (Perkin Elmer 124) and for Ag by atomic absorption spectrophotometry.

SOURCE AND PURITY OF MATERIALS:

The Ag succinylsulfadiazine was synthesized by the authors. Analysis - Calcd: C 29.8, H 2.32, N 9.9, S 5.7, Ag 38.3%. Found: C 29.0, H 2.1, N 9.7, S 5.5, Ag 37.0%

Doubly distilled water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-2-pyrimidinyl, monosodium salt (sodium sulfadiazine); $C_{10}H_9N_4NaO_2S$; [547-32-0]

(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/°C	Solubility	
	g/100 g water	mol kg^{-1} water[a]
25	50.0	1.84
37	65.0	2.39

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small tinted glass container contg excess Na sulfadiazine 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 sulfadiazine 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-pyrimidinyl-, monosodium salt (sodium sulfadiazine); $C_{10}H_{10}N_4O_2S \cdot Na$; [547-32-0] (2) 2-Propanol; C_3H_8O; [67-63-0]	Burlage, H. M. *J. Am. Pharm. Assoc., Sci. Ed.* 1948, *37*, 345.
VARIABLES:	**PREPARED BY:**
One temperature: 25°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sodium sulfadiazine in 2-propanol at 25°C is 0.1860 g/100 cm^3 solution (6.832×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd soln of sodium sulfadiazine 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 sodium sulfadiazine was of the U. S. P. purity, manufd by Squibb. The source and purity of 2-propanol was 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-pyrimidinyl-, zinc(2+) salt (zinc sulfadiazine); $C_{20}H_{18}N_8O_4S_2Zn$; [66219-86-1]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.; Stanford, J. W.; Fox, P. L. *Scand. J. Plast. Reconstr. Surg.* 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Zn sulfadiazine in water at room temperature (28-30°C)[a] is 56.0 mg% (9.93×10^{-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 sulfadiazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfadiazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

The identity of the Zn sulfadiazine was questioned by Bult and associates (2) (compiler).

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Bratton, A. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *120*, 537.
2. Bult, A.; Hulsing, N.; Weyland, J. W. *Pharm. Weekblad, Sci. Ed.* 1980, *2*, 190; *J. Pharm. Pharmacol.* 1981, *33*, 171.

COMPONENTS:	EVALUATOR:
(1) Acetamide, N-[4-[(2-pyrimidinyl-amino)-sulfonyl]phenyl]- (acetyl sulfapyrimidine) $C_{12}H_{12}N_4O_3S$; [127-74-2] (2) Water	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 acetyl derivative of sulfadiazine in water at 310K has been reported by Roblin et al. (1) and Kikuth (2). The values given were 5.13 x 10^{-4} mol dm^{-3} and 5.75 x 10^{-3}, respectively. Only the former (1) supplied sufficient experimental details. Because of the uncertainty in Kikuth's value only a tentative average value of the solubility in water of 5.44 x 10^{-4} mol dm^{-3} at 310K can be recommended. It should be noted that in this case the acetyl group causes about a ten fold decrease in the equilibrium solubility with respect to the parent compound.

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

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

		10^4 mol dm^{-3}	
Reference	pH	293K	310K
3	5.9	4.52	7.2
4	6.0	7.9	-
3	7.0	28.7	56.8
4	7.0	24.6	-
3	8.0	86.5	-
4	8.0	71.2	-

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

REFERENCES:

(1) Roblin, R. O., Jr.; Williams, J. H.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1940, *62*, 2002-5.

(2) Kikuth, W. *Med. Welt* 1943, *17(26/27)*, 483-6.

(3) Krüger-Thiemer, E. *Arch. Dermatol. Syphilis* 1942, *183* 90-116.

(4) Pulver, R.; Suter, R. *Schweiz. Med. Wochenschr.* 1943, *73(13)*, 403-8.

COMPONENTS: (1) Acetamide, N-[4-[(2-pyrimidinylamino) sulfonyl]phenyl]- (acetyl sulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** 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 fo acetyl sulfapyrimidine in water at 37°C is 15.0 mg/100 cm^3 solution (5.13×10^{-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 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 acetyl sulfapyrimidine, mp 258-9°C, (cor), was prepd by the authors. Anal: %C 49.2 (calcd 49.4); %H 4.1 (4.1); %N 19.2 (19.2). 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) Acetamide, N-[4-[(2-pyrimidinylamino) sulfonyl]phenyl]- (acetyl sulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Kikuth, W. *Med. Welt* 1943, *17(26/27)*, 483-6.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyrimidine in water at 37°C is 168 mg/100 cm^3 solution (5.75×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyrimidine: not specified.
The pH of the water was 7.0.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino) sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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%	10^4 mol dm^{-3} [a]
5.7	23	7.9
6.3	24	8.2

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfadiazine was boiled with water for 1 h in a sealed ampul followed by keeping the ampul at 37°C. Before the assaying, the solute was treated with 2.6N NaOH soln (1) to cleave the acetyl group and sulfadiazine 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-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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.

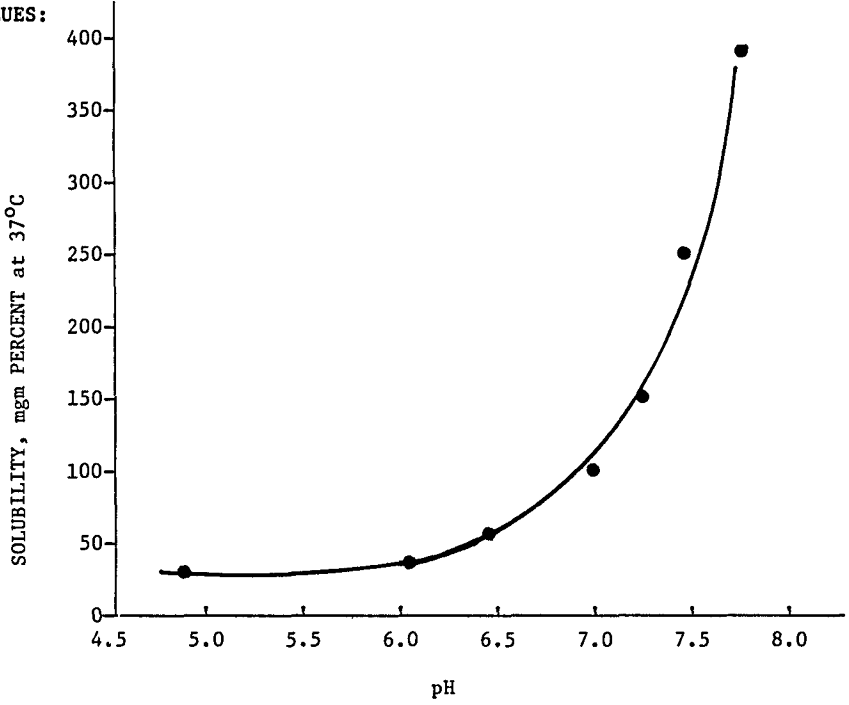
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfadiazine 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 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 drug was then de-acetylated and the concn of sulfadiazine 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 sulfadiazine were not specified.

Water was doubly distilled.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Plummer, M. N.

Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

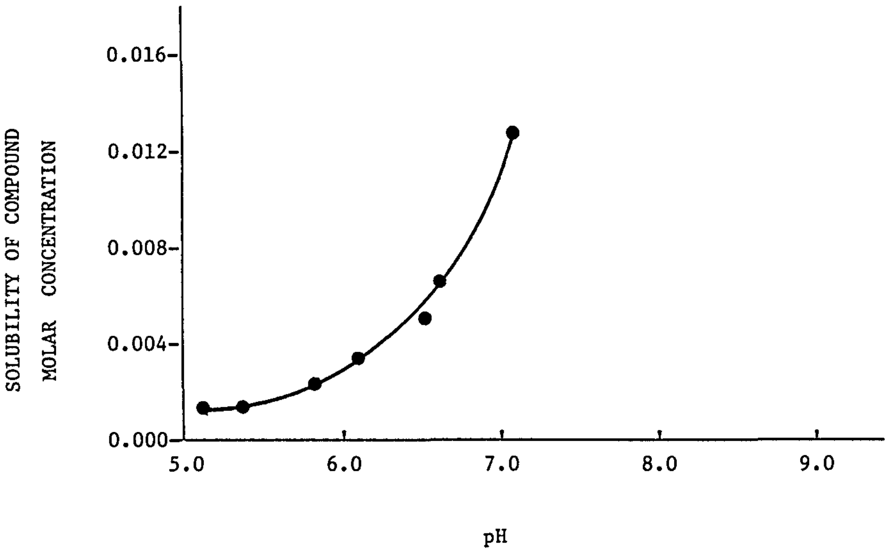
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfadiazine in M/10 Na citrate + NaOH solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfadiazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Garb, S.; Plummer, N. *Proc. Soc. Exp. Biol. Med.* 1943, *52*, 248-50.

VARIABLES:

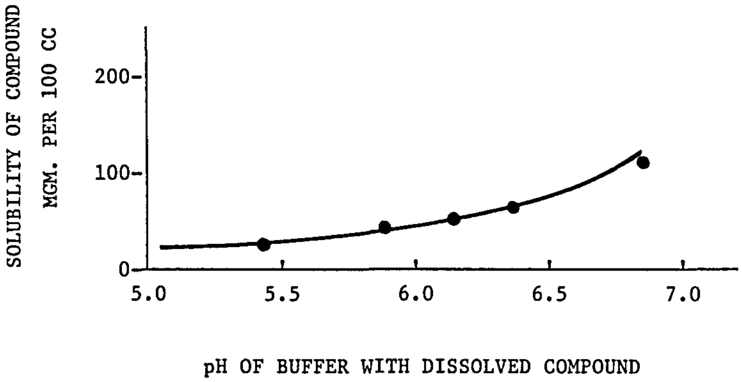
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The curve of sulobility of acetyl sulfadiazine in M/10 citrate plus NaOH buffer solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

NOthing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetylsulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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 acetyl sulfapyrimidine in a 0.735M (10%) KH_2PO_4 solution of pH 4.37 at room temperature (about 20°C) is 0.0072 g% (2.5×10^{-4} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyrimidine (0.5 g) was dissolved in 10 cm^3 of the 0.735M (10%) KH_2PO_4 soln of pH 4.37, 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 sulfapyrimidine) by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph usisng a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyrimidine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyrimidine. 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-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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 temperature: ca 20°C; one pH: 8.74

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyrimidine in a 0.705M (10%) Na_2HPO_4 solution of pH 8.74 at room temperature (about 20°C) is 0.548 g% (1.875×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyrimidine (0.5 g) was dissolved in 10 cm^3 of the 0.705M (10%) Na_2HPO_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 (as sulfapyrimidine) 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 sulfapyrimidine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyrimidine. 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) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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			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	0.0082	0.28	-	-
10.0	90.0	0.91	5.906	0.0132	0.452	0.021	0.72
61.1	38.9	0.93	7.005	0.0840	2.87	0.166	5.68
9.5	0.5	0.733[b]	7.51	0.1810	6.19	-	-
94.7	5.3	0.95	8.018	0.2530	8.65	-	-

[a] Calculated by compiler.

b Molar content; 10% buffer solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfapyrimidine (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 colorimetrically (as sulfapyrimidine) by the Marshall method modified by Kimmig (1) using the Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfapyrimidine (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfapyrimidine. 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-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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]

VARIABLES:

pH

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Garb, S.; Plummer, N.

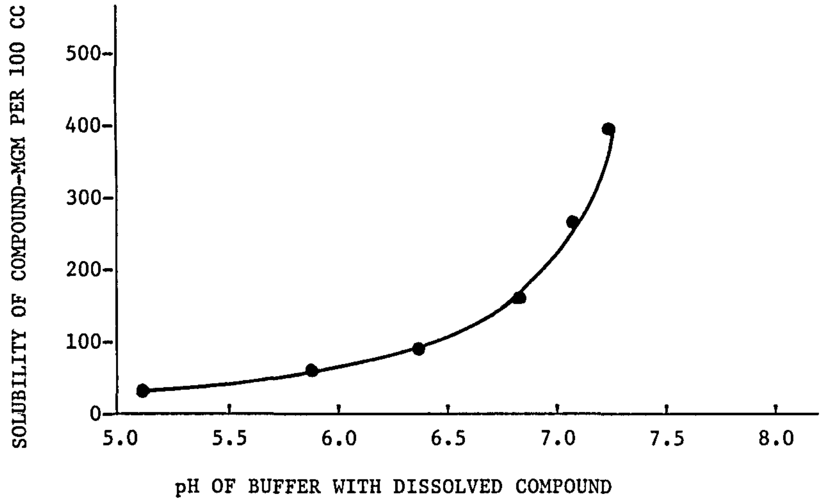
Proc. Soc.. Exp. Biol. Med. <u>1943</u>, *52*, 248-50.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The curve of solubility of acetyl sulfadiazine in M/15 phosphate buffer solutions at 37°C.



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An amt of acetyl sulfadiazine in large excess of that to be dissolved was added to M/15 phosphate buffer solns, shaken for 18 h in a water bath at 37°C and filtered at the same temp. The pH of the filtrate was measured immediately with a Beckmann pH meter and appropraite temp corrections were made. Acetyl sulfadiazine was assayed by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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:

Gilligan, D. R.; Plummer, M. N.
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

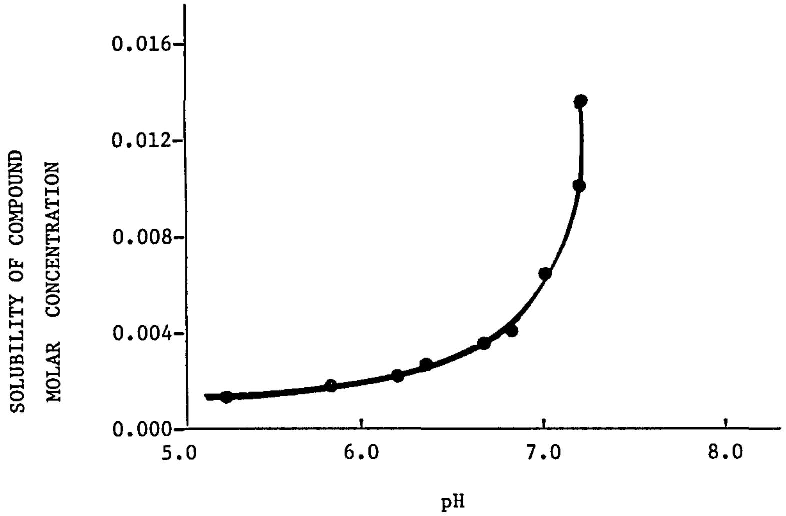
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfadiazine in M/15 phosphate buffer solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfadiazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfadiazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility of acetyl sulfadiazine in M/15 phosphate buffers (according to Sørensen) at 20°C	
	mg%	10^3 mol dm^{-3} [a]
6.0	23	0.79
7.0	72	2.46
8.0	208	7.12

[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-pyrimidinylamino)-sulfonyl]phenyl]- (acetyl sulfapyrimidine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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:

Frisk, A. R.; Hagerman, G.; Helander, S.; Sjögren, B.

Hygiea 1946, *108(12)*, 639-51.

VARIABLES:

One temperature: 37°C; one pH: 6.1

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfapyrimidine in M/30 phosphate buffer of pH 6.1 at 37°C is 35 mg/100 ml solvent (1.2×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfapyrimidine in the phosphate buffer was shaken at 37°C for 24 h. The concn of acetyl sulfapyrimidine was detd by the Bratton and Marshall method (1) using a photoelec colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

ESTIMATED ERROR:

Soly: precision ±4 mg/100 ml (authors).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[(2-pyrimidinylamino)-sulfonyl]phenyl]- (N^4-acetylsulfadiazine); $C_{12}H_{12}N_4O_3S$; [127-74-2]

(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	10^3 mol dm^{-3} [a]
5.5	411	1.41
7.5	1620	5.54

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of N^4-acetylsulfadiazine were prepd in phosphate buffers of pH 5.5 and 7.5 at room temp (25°C). The conc 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 the solute 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:	EVALUATOR:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine) $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water	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:

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

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

	10^3 mol dm^{-3} (*indicates mol kg^{-1})	
Reference	303K	310K
1	-	1.20
2	-	2.50
3	-	0.965*
4	-	1.4
5	0.89	-
6	0.91	-

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

REFERENCES:

(1) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P. *J. Am. Chem. Soc.* 1940, *62*, 2002-5
(2) Kikuth, W. *Med. Welt* 1943, *17(26/27)*, 483-6.
(3) Sapoznikova, N.V.; Postovakii, I. Ya. *Zh. Prikl. Khim.* 1944, *17*, 427-34.
(4) Langecker, H. *Arch. Exptl. Path. Pharmakol.* 1948, *205*, 291-301.
(5) Yamasaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakusaigaku* 1967, *27(1)*, 37-40.
(6) Bhattacharyya, R.; Basu, U.P. *Indian Pharmacist* 1950, *6(3)* 77-8,86.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: 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 sulfamerazine in water at 37°C is 31.8 mg/100 cm^3 solution (1.20×10^{-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 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 235-6°C (dec, cor), was prepd by the authors. Anal: %C 49.6 (calcd 50.0); %H 4.4 (4.6); %N 21.1 (21.2). 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water; H_2O; [7732-18-5]	Kikuth, W. *Med. Welt.* 1943, *17(26/27)*, 483-6.
VARIABLES:	PREPARED BY:
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in water at 37°C is 66.0 mg/100^3 solution (2.50×10^{-3} mol dm^{-3}).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Nothing specified.	Sulfamerazine: not specified. The pH of the water was 7.0.
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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/°C	Solubility	
	Weight%	10^3 mol kg^{-1} water[a]
37	0.0255[b]	0.965
50	0.050	1.89
75	0.172	6.52
99	0.319	12.1

[a] Calculated by compiler

[b] Calculated from the heat of dissolution (10,300 cal mol^{-1})

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamerazine 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 sulfamerazine 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 at 37, 50, and 75°C. At 99°C the accuracy was poor due to evapn of water during sampling (authors). Temp: ±0.05°C (authors).

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Langecker, H. *Arch. Exptl. Path. Pharmakol.* 1948, *205*, 291-301.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility	
	mg%	10^4 mol dm^{-3} [a]
25	21	7.9
37	37	14

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamerazine was boiled with water and left for 24 h in a vessel protected from access of CO_2. The sulfamerazine concn 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water; H_2O; [7732-18-5]	Bhattacharyya, R.; Basu, U. P. *Indian Pharmacist* 1950, *6(3)*, 77-8, 86.
VARIABLES:	PREPARED BY:
One temperature: 30°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in water at 30°C is 24 mg per 100 ml (9.1×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
A weighed sample of sulfamerazine was placed in a clean reagent bottle and a known vol of water was added. The mixt was shaken in a mech shaker at 80-100 strokes/min. After at least 24 h the mixt was filtered through a clean, dried and weighed sintered-glass crucible. At the end of the filtration the crucible was washed with about 1 ml of water, dried at 105°C for 2-3 h, cooled, and weighed to const wt.	Neither source nor purity of the sulfamerazine was specified. Doubly distd water was used. ESTIMATED ERROR: Soly: not specified. Temp: ±0.2°C (authors). REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Water; H_2O; [7732-18-5]	Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.
VARIABLES:	**PREPARED BY:**
One temperature: 30°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in water at 30°C is 0.89 mmol/L (0.24 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamerazine (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 sulfamerazine 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-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

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

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

ORIGINAL MEASUREMENTS:

Holz, E.; Garcia Onandia, T.; Holz, S.

Acta Cient. Venezolana 1955, *6(2)*, 68-73.

VARIABLES:

Concentration of NaOH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of NaOH soln	Volume of the NaOH soln required to dissolve 1 g of sulfamerazine at 26°C	Solubility of sulfamerazine at 26°C
N	cm^3	mol dm^{-3} NaOH soln[a]
1/10	40.9	0.0925
1/4	15.8	0.239
1/2	8.0	0.473
1.00	4.0	0.946
1.25	3.2	1.18
1.30	3.3	1.15
1.40	8.6	0.440
1.50	13.2	0.287
2.00	36.4	0.104
2.50	156	0.0242

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Nothing specified.

SOURCE AND PURITY OF MATERIALS:

Nothing specified. Distd water was used.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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:

Gilligan, D. R.; Plummer, M. N.

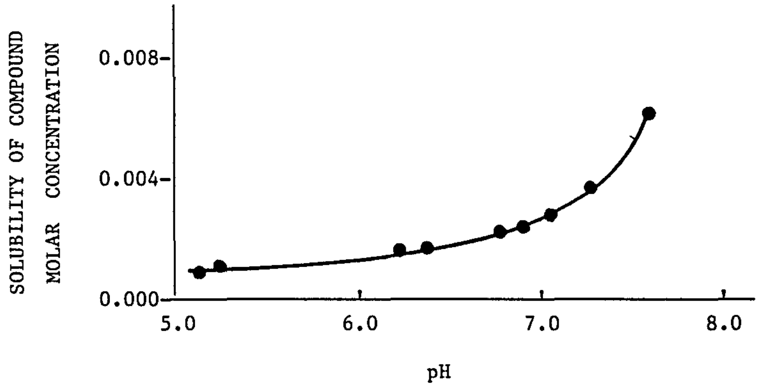
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in M/15 phosphate buffer solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamerazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specifed.

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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:

Frisk, A. R.; Hagerman, G.;
Helander, S.; Sjögren, B.
Hygiea 1946, *108(12)*, 639-51.

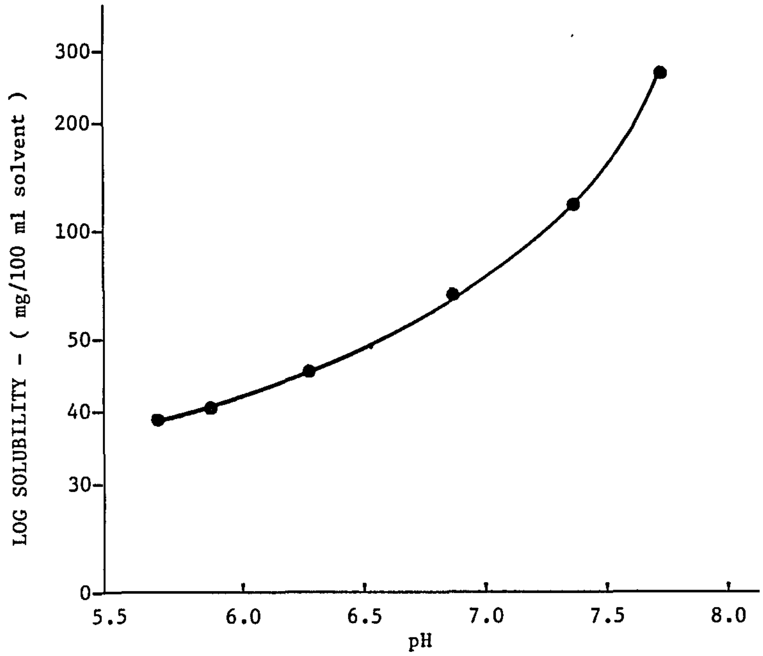
VARIABLES:

One temperature: 37°C; pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



The solubility at pH 6.1 is 40 mg/100 ml solvent (1.5 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethylpyrimidine in the phosphate buffer was shaken at 37°C for 24 h. The concn of the solute was detd by the Bratton and Marshall method (1) using a photoelec colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

ESTIMATED ERROR:

Soly: precision ±3 mg/100 ml (authors).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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	34	1.2
5.9	35	1.3
6.9	86	3.2
7.5	144	5.4

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamerazine was added to a buffer soln and boiled for 1 h in a sealed ampul followed by keeping the ampul at 37°C. The concn of sulfamerazine 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. C.; Marshall, E. K., Jr. *J. Biol. Chem.* 1939, *128*, 537.
2. Havemann, R. *Klin. Wochenschr.* 1940, p. 503.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine)-
$C_{11}H_{12}N_4O_2S$; [127-79-7]

(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 sulfamerazine in M/15 Sörensen buffer solution (pH 7.4) at 20°C is 70 mg% (2.7×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solns of varying pH (7-8) were prepd, satd with sulfamerazine at 20°C, their pH was measured at equilibrium, and the sulfamerazine 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (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]	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 sulfamerazine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 2.45 mmol/L (0.647 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamerazine (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 sulfamerazine 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 and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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, Ch. A.; Vree, T. B.

Antibiotics Chemother. 1982, *31*, 22-118.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^4 mol dm^{-3} [a]
5.5	238	9.00
7.5[b]	840	31.8

[a] Calculated by compiler.

[b] Erroneous pH value of 7.0 is given in the article.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method (1) was used (personal communication). Satd solns of sulfamerazine were prepd in phosphate buffers of pH 5.5 and 7.5 at 25°C. The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a Model 748 column oven and a Pye-Unicam LC-UV spectrophotometric detector.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: the detection limit of the solute by HPLC was 0.5 mg/l (authors).

The errors in temp and pH were not specified.

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Plummer, M. N.

Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

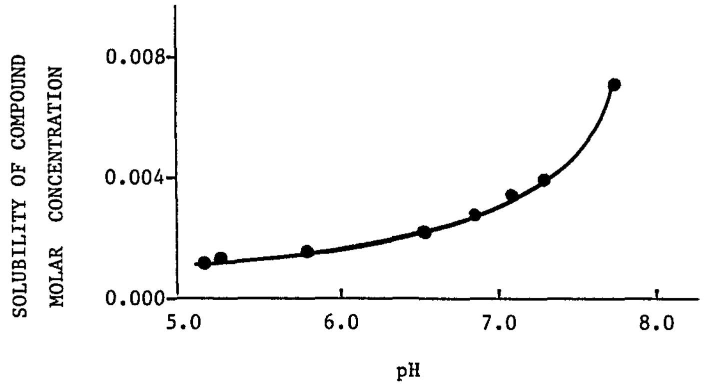
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Benzene, methyl- (toluene); C_7H_8; [108-88-3] (3) Mannitol; $C_6H_{14}O_6$; [87-78-5] (4) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (5) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (6) Sodium chloride; NaCl; [7647-14-5] (7) Water; H_2O; [7732-18-5]	Sonnenberg, H.; Oelert, H.; Baumann, K. *Pflügers Arch. Ges. Physiol.* 1965, *286*, 171-80. PREPARED BY: R. Piekos
VARIABLES: pH	

EXPERIMENTAL VALUES:

Relative lipoid solubility determined on the basis of concentration measurements of sulfamerazine in perfusates[a,b] before (c_i) and after (c_e) equilibration with toluene

pH	$(100 - \frac{100}{c_i} c_e)$
5[a]	8
8[b]	2

[a] Composition of perfusate: 110 mmol/l NaCl, 35 mmol/l mannitol in a phosphate buffer consisting of 98.8 ml of 0.022M KH_2PO_4 and 1.2 of 0.022M Na_2HPO_4.

[b] Composition of perfusate: 68 mmol/l NaCl, 100 mmol/l mannitol in a phosphate buffer consisting of 5.5 ml of 0.022M KH_2PO_4 and 94.5 ml of 0.022M Na_2HPO_4.

AUXILIARY INFORMATION

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(2) Mannitol; $C_6H_{14}O_6$; [87-78-5]

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

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

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

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

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

ORIGINAL MEASUREMENTS:

Sonnenberg, H.; Oelert, H.; Baumann, K.

Pflügers Arch. Ges. Physiol. 1965, *286*, 171-80.

VARIABLES: pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Relative lipoid solubility determined on the basis of concentration measurements of sulfamerazine in perfusates[a,b] before (c_i) and after (c_e) equilibration with chloroform

pH	$(100 - \frac{100\ c_e}{c_i})$
5[a]	72
8[b]	34

[a] Composition of perfusate: 110 mmol/l NaCl, 35 mmol/l mannitol in a phosphate buffer consisting of 98.8 ml of 0.022M KH_2PO_4 and 1.2 ml of 0.022M Na_2HPO_4.

[b] Composition of perfusate: 68 mmol/l NaCl, 100 mmol/l mannitol in a phosphate buffer consisting of 5.5 ml of 0.022M KH_2PO_4 and 94.5 ml of 0.022M Na_2HPO_4.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Lipoid solubilities were detd by shaking equal volumes of the perfusate and $CHCl_3$ for 20 min and measuring the concn of sulfamerazine by the spectrophotometric method of Bratton and Marshall (1) in the aq phase before and after this procedure.

SOURCE AND PURITY OF MATERIALS:

None given.

ESTIMATED ERROR:

None given.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7] (2) Ethanol; C_2H_6O; [64-17-5] (3) 1,2,3-Propanetriol; $C_3H_8O_3$; [56-81-5] (4) Water; H_2O; [7732-18-5]	Dolique, R.; Foucault, J. *Trav. soc. pharm. Montpellier* 1952, *12*, 145-53.
VARIABLES:	PREPARED BY:
One temperature: 26-28°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in a mixture of 1,2,3-propanetriol and 95° ethanol (2:1 by wt) at 26-28°C is 0.45% (1.7 x 10^{-2} mol kg^{-1} solvent, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The sulfamerazine 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-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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]

VARIABLES:

One temperature: 26-28°C

ORIGINAL MEASUREMENTS:

Dolique, R.; Foucault, J.

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

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine 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 0.465% (1.76×10^{-2} mol kg^{-1}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The sulfamerazine 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-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

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

ORIGINAL MEASUREMENTS:

Sekikawa, H.; Nakano, M.; Arita, T.

Chem. Pharm. Bull. 1978, *26(1)*, 118-26.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility[a] 10^3 mol dm^{-3} solution
10	3.57
20	4.46
30	6.32
40	8.99
50	12.8

[a]Original data are presented graphically.

The numerical values are given by the authors.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

After attaining equilibrium, sample solns were removed by a syringe and filtered quickly through a membrane filter (pore size 0.2 μ) and sulfamerazine was assayed spectrophotometrically at 270 nm using a Hitachi Type 200-20 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamerazine, mp 235°C, was obtained from Na sulfamerazine (Tanabe Seiyaku Co.) by addn of HCl_{aq} and recrystn from EtOH. Abs EtOH was obtained by drying and distn of EtOH following the conventional procedures.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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 sulfamerazine in 2-propanol at 25°C is 0.1740 g/100 cm^3 solution (6.583×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfamerazine 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 sulfamerazine was manufd by Sharp and Dohme 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. Pharm. Assoc., Sci. Ed.* 1947, *36(1)*, 16.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(2) Ethanol, 2-ethoxy-; $C_4H_{10}O_2$; [110-80-5]

ORIGINAL MEASUREMENTS:

Sunwoo, C.; Eisen, H.

J. Pharm. Sci. 1971, *60*, 238-44.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfamerazine in 2-ethoxyethanol at 25°C is 0.0109 (3.29 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by the method reported by Restaino and Martin (1). Sulfamerazine was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 270 nm after diln of a sample with 95% ethanol or water.

SOURCE AND PURITY OF MATERIALS:

The USP sulfamerazine (American Cyanamid Co., Pearl River, N.Y.), recrystd from warm alcohol and an industrial grade 2-ethoxyethanol (Cellosolve solvent, Union Carbide, New York, N.Y.) were used.

ESTIMATED ERROR:

Temp: ±1.0° (authors).

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

REFERENCES:

1. Restaino, F. A.; Martin, A. N. *J. Pharm. Sci.* 1964, *53*, 636.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamerazine in chloroform at 20°C is 37 mg% (1.4 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-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(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 sulfamerazine in chloroform at 30°C is 3.08 mmol/L (0.814 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamerazine (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 sulfamerazine 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-(4-methyl-2-pyrimidinyl)- (sulfamerazine); $C_{11}H_{12}N_4O_2S$; [127-79-7]

(2) 2-Pyrrolidinone, 1-ethynyl-,polymers (poly(vinyl pyrrolidone)); $(C_6H_9NO)_x$; [9003-39-8] K-15

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

VARIABLES:

Temperature

ORIGINAL MEASUREMENTS:

Sekikawa, H.; Nakano, M.; Arita, T. *Chem. Pharm. Bull.* 1978, *26(1)*, 118-26.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	M x 10^2 sulfamerazine solubilized by 1M vinyl pyrrolidone equivalent
10.0	0.631
20.0	0.770
30.0	0.950
40.0	1.16
50.0	1.39

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

After attaining equilibrium, sample solns were removed by a syringe and filtered quickly through a membrane filter (pore size 0.2μ) and sulfamerazine was assayed spectrophotometrically at 270 nm using a Hitachi Type 200-20 spectrophotometer. No significant absorbance was found for poly(vinyl pyrrolidone).

SOURCE AND PURITY OF MATERIALS:

Sulfamerazine, mp 235°C, was obtained from Na sulfamerazine (Tanabe Seiyaku Co.) by addn of HCl_{aq} and recrystn from EtOH. Poly(vinyl pyrrolidone) K-15 was from Daiichi Pure Chemicals Co., Tokyo. Abs EtOH was obtained by drying and distn of EtOH following the conventional procedure.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Zinc, bis[4-amino-$\underline{N}$-(4-methyl-2-pyrimidinyl)benzenesulfonamidato-$\underline{N}^N$,O]-
(Zn(II) sulfamerazine); $C_{22}H_{20}N_8O_4S_2Zn$;
[71496-63-4]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.;
Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg. 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Zn(II) sulfamerazine in water at room temperature (28-30°C)[a] is 25.2 mg% (4.24×10^{-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) sulfamerazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfamerazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calcd from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:	EVALUATOR:
(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl- (acetyl sulfamerazine) $C_{13}H_{14}N_4O_3S$; [127-73-1] (2) Water	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:

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

	10^4 mol dm^{-3} (*indicates mol kg^{-1})
Reference	310K
1	9.14
2	37.5
3	7.8*

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

REFERENCES:

(1) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P. *J. Am. Chem. Soc.* 1940, *62*, 2002-5.
(2) Kikuth, W. *Med. Welt* 1943, *17(26/27)*, 483-6.
(3) Sapozhnikova, N.V.; Postovskii, I. Ya. *Zh. Prikl. Khim.* 1944, *17*, 427-34.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1] (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:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamerazine in water at 37°C is 28.0 mg/100 cm^3 solution (9.14×10^{-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 Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfamerazine, mp 248-9°C (cor), was prepd by the authors. Anal: %C 51.0 (calcd 51.0); %H 4.8 (4.6); %N 17.9 (18.3). 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:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1] (2) Water; H_2O; [7732-18-5]	Kikuth, W. *Med. Welt* 1943, *17(26/27)*, 483-6.
VARIABLES:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamerazine in water at 37°C is 115 mg/100 cm^3 solution (3.75×10^{-3} mol dm^{-3} , compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Nothing specified.	Acetyl sulfamerazine: not specified. The pH of the water was 7.8
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1]

(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]
37	0.024	0.78
75	0.170	5.56

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Acetyl sulfamerazine 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 acetyl sulfamerazine 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 (authors).

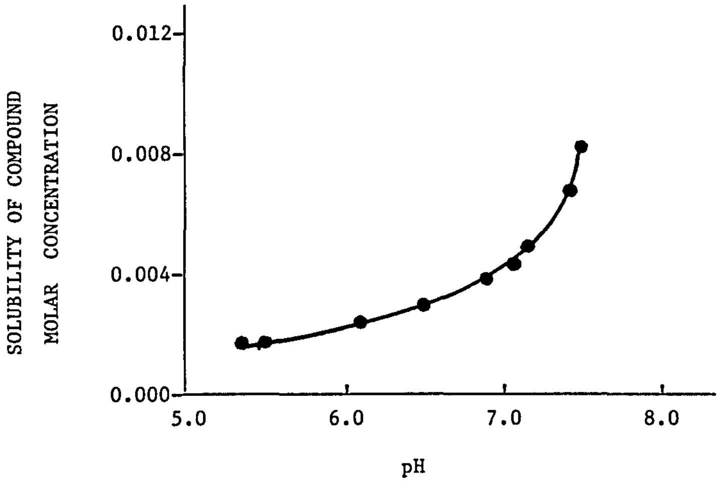
Temp: ±0.05°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Acetamide, N-[4-[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); $C_{13}H_{14}N_4C_3S$; [127-73-1] (2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate); $C_6H_6Na_2O_7$; [144-33-2] (3) Sodium hydroxide; NaOH; [1310-73-2] (4) Water; H_2O; [7732-18-5]	Gilligan, D. R.; Plummer, M. N. *Proc. Soc. Exp. Biol. Med.* 1943, *53*, 142-5.
VARIABLES: pH	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

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



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfamerazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamerazine); $C_{13}H_{14}N_4C_3S$; [127-73-1]

(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:

Gilligan, D. R.; Plummer, M. N.
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

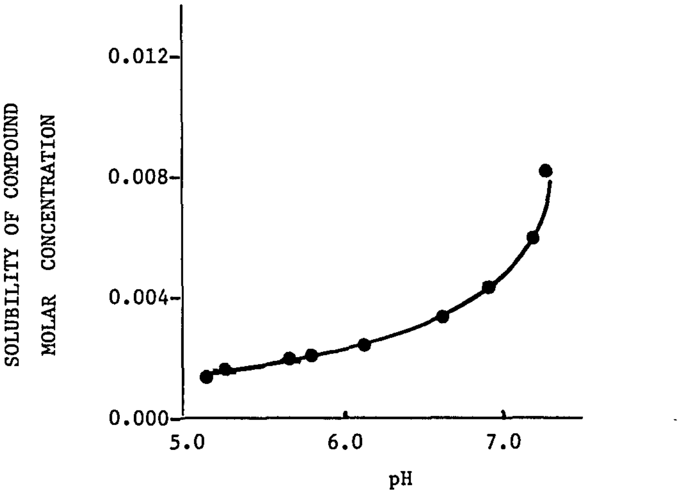
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamerazine in M/15 phosphate buffer solutions at 37°C



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfamerazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfamerazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetyl sulfamethylpyrimidine); $C_{13}H_{14}N_4O_3S$; [127-73-1]

(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:

Frisk, A. R.; Hagerman, G.;
Helander, S.; Sjögren, B.
Hygiea 1946, *108(12)*, 639-51.

VARIABLES:

One temperature: 37°C; one pH: 6.1

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethylpyrimidine in M/30 phosphate buffer of pH 6.1 at 37°C is 53 mg/100 ml solvent (1.7×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfamethylpyrimidine in the phosphate buffer was shaken at 37°C for 24 h. The concn of the solute was detd by the Bratton and Marshall method (1) using a photoelec colorimeter.

SOURCE AND PURITY OF MATERIALS:

Neither source nor purity of the materials was specified.

ESTIMATED ERROR:

Soly: precision ±4 mg/100 ml (authors).

Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (N^4-acetylsulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1]

(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, Ch. A.; Vree, T. B.
Antibiotics Chemother. 1982, *31*, 22-118.

VARIABLES: pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^3 mol dm^{-3} [a]
5.5	585	1.910
7.5[b]	2,300	7.508

[a] Calculated by compiler

[b] Erraneous pH value of 7.0 is given in the article.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method (1) was used (personal communication). Satd solns of N^4-acetylsulfamerazine were prepd in phosphate buffers of pH 5.5 and 7.5 at 25°C. The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a Model 748 column oven and a Pye-Unicam LC-UV spectrophotometric detector.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: the detection limit of the solute by HPLC was 0.5 mg/l (authors).
The errors in temp and pH were not specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]- (acetylsulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1]

(2) Benzene,methyl- (toluene); C_7H_8; [108-88-3]

(3) Mannitol; $C_6H_{14}O_6$; [87-78-5]

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

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

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

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

ORIGINAL MEASUREMENTS:

Sonnenberg,H.; Oelert, H.; Baumann, K. *Pflügers Arch. Ges. Physiol.* 1965, *286*, 171-80.

VARIABLES: - pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Relative lipoid solubility determined on the basis of concentration measurement of acetylsulfamerazine in perfusates [a,b] before (c_i) and after (c_e) equilibration with toluene

pH	$(100 - \frac{100\ c_e}{c_i})$
5^a	8
8^b	0

[a] Composition of perfusate: 110 mmol/l NaCl, 35 mmol/l mannitol in a phosphate buffer consisting of 98.8 ml of 0.022M KH_2PO_4 and 1.2 ml of 0.022M Na_2HPO_4.

[b] Composition of perfusate: 68 mmol/l NaCl, 100 mmol/l mannitol in a phospahte buffer consisting of 5.5 ml of 0.022M KH_2PO_4 and 94.5 ml of 0.022M Na_2HPO_4.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Lipoid solubilities were detd by shaking equal volumes of the aperfusate and toluene with acetylsulfamerazine for 20 min and measuring the concn of acetylsulfamerazine by the spectrophotometric method of Bratton and Marshall (1) in an aq phase before and after this procedure.

SOURCE AND PURITY OF MATERIALS:

None given.

ESTIMATED ERROR:

None given.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4-methyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-(acetylsulfamerazine); $C_{13}H_{14}N_4O_3S$; [127-73-1]
(2) Mannitol; $C_6H_{14}O_6$; [87-78-5]
(3) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]
(4) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]
(5) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]
(6) Sodium chloride; NaCl; [7647-14-5]
(7) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:

Sonnenberg, H.; Oelert, H.; Baumann, K.

Pflügers Arch. Ges. Physiol. 1965, *286*, 171-80.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Relative lipoid solubility determined on the basis of concentration measurements of acetylsulfamerazine in perfusates[a,b] before (c_1) and after (c_e) equilibration with chloroform

pH	$\left(100 - \frac{100\,c_e}{c_1}\right)$
5[a]	42
8[b]	0

[a] Composition of perfusate: 110 mmol/1 NaCl, 35 mmol/1 mannitol in a phosphate buffer conisting of 98.8 ml of 0.022M KH_2PO_4 and 1.2 ml of 0.022M Na_2HPO_4.

[b] Compostion of perfusate: 68 mmol/1 NaCl, 100 mmpl/1 mannitol in a phosphate buffer consisting of 5.5 ml of 0.022M KH_2PO_4 and 94.5 ml of 0.022M Na_2HPO_4.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Lipoid solubilities were detd by shaking equal volumes of the perfusate and chloroform with acetylsulfamerazine for 20 min and measuring the concn of acetylsulfamerazine by the spectrophotometric method of Bratton and Marshall (1) in an aq phase before and after this procedure.

SOURCE AND PURITY OF MATERIALS:

None given.

ESTIMATED ERROR:

None given

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-methoxy-2-pyrimidinyl)-; $C_{11}H_{12}N_4O_3S$; [3213-22-7]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(4-methoxy-2-pyrimidinyl)benzenesulfonamide in water at 37°C is 18.2 mg/100 cm^3 solution (6.49 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 Marshall method (1) using a General Electric recording spectrophotometer for comparing colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 241-2°C, was prepd by the authors. Anal: %C 47.2 (calcd 47.1); %H 4.4 (4.3); %N 19.9 (20.0). 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-methoxy-2-pyrimidinyl)- (sulfamethoxydiazine); $C_{11}H_{12}N_4O_3S$; [651-06-9]

(2) Poly(oxy-1,2,-ethanediyl), α-hydro-ω-hydroxy- (PEG 6000); $(C_2H_4O)_nH_2O$; [25322-68-3] 6000

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

ORIGINAL MEASUREMENTS:

Salib, N. N.; Ebian, A. R.

Pharm. Ind. 1978, *40(3)*, 262-5.

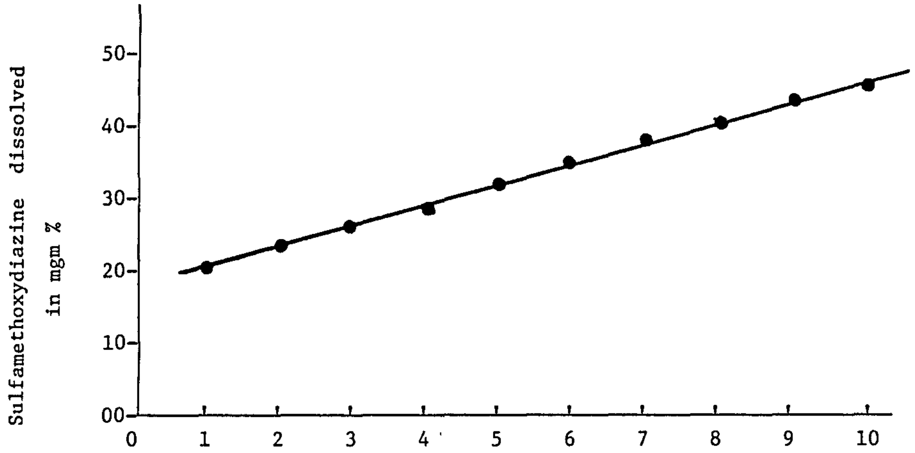
VARIABLES:

Concentration of PEG 6000

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Effect of different concentrations of PEG 6000 on the solubility of sulfamethoxydiazine at 37±1°C .

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxydiazine was added to bottles contg from 0 to 10% PEG 6000 solns. The bottles were rotated at 30 rpm for 24 h in a water bath at 37°C. After equilibrium had been attained, an aliquot was pipetted out, dild with 0.1N HCl, and the solute was assayed spectrophotometrically at 228 nm.

SOURCE AND PURITY OF MATERIALS:

PEG 6000 was a product of Hoechst AG, West Germany. Sulfamethoxydiazine (Bayrena) was supplied by Bayer, Leverkusen. The purity of the materials was not specified.

ESTIMATED ERROR:

Soly: data points are means of 3 detns (authors).

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)- (sulfamethoxydiazine); $C_{11}H_{12}N_4O_3S$; [651-06-9]

(2) Poly(oxy-1,2-ethanediy), α-hydro- ω-hydroxy- PEG (20 000); $(C_2H_4O)_nH_2O$; [25322-68-3] 20 000

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

ORIGINAL MEASUREMENTS:

Salib, N. N.; Ebian, A. R.
Pharm. Ind. 1978, *40(3)*, 262-5.

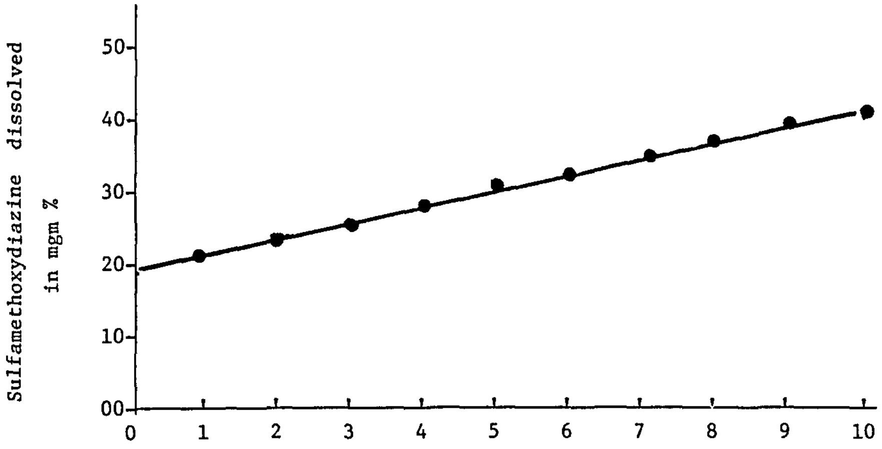
VARIABLES:

Concentration of PEG 20 000

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Effect of different concentrations of PEG 20 000 on the solubility of sulfamethoxydiazine at 37±1°C.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxydiazine was added to bottles contg from 0 to 10% PEG 20 000 solns. The bottles were rotated at 30 rpm for 24 h in a water bath at 37°C. After equilibrium had been attained, an aliquot was pipetted out, dild with 0.1N HCl, and the solute was assayed spectrophotometrically at 228 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxydiazine (Bayrena) was supplied by Bayer, Leverkusen. PEG 20 000 was a product of Hoechst AG, West Germany.
The purity of the materials was not specified.

ESTIMATED ERROR:

Soly: data points are means of 3 detns (authors).

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)- (sulfameter); $C_{11}H_{12}N_4O_3S$; [651-06-9]

(2) Ethanol, 2-Ethoxy-; $C_4H_{10}O_2$; [110-80-5]

ORIGINAL MEASUREMENTS:

Sunwoo, C.; Eisen, H.
J. Pharm. Sci. <u>1971</u>, *60*, 238-44.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfameter in 2-ethoxyethanol at 25°C is 0.0119 (3.61 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by the method reported by Restaino and Martin (1). Sulfameter was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 271 nm after diln of a sample with 95% alcohol or water.

SOURCE AND PURITY OF MATERIALS:

Sulfameter (A. H. Robins Co., Richmond, Va) was recrystd from warm alcohol. 2-ethoxyethanol (Cellosolve solvent, Union Carbide, New York, N. Y.) was of industrial grade.

ESTIMATED ERROR:

Temp: ±1.0°C (authors).

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

REFERENCES:

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

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)- (sulfamonomethoxine, SMM); $C_{11}H_{12}N_4O_3S$; [651-06-9] (2) 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-C-6); $C_{12}H_{24}O_6$; [17455-13-9] (3) Hydrochloric acid; HCl; [7647-01-0] (4) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Takayama, K.; Nambu, B.; Nagai, T. *Chem. Pharm. Bull.* 1978, *26(10)*, 2965-70.
VARIABLES: Temperature	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

t/°C	Saturated concentration of sulfamonomethoxine after decomplexation of its 1:1 complex with 18-C-6 in 0.2N HCl 10^2M
30	0.390
35	0.473
40	0.571

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of the complex was dissolved in 50 ml of 0.2N HCl. The sampling was done by a 1-ml pipet fitted with a G-4 glass filter. The concentratrion of the sulfonamide was detd by uv spectrophotometry after dilg with 0.2N HCl.

SOURCE AND PURITY OF MATERIALS:

SMM (Dai-ichi Pharmaceutical Co) was recrystd from a 30% (V/V) Me_2CO - H_2O system. 18-C-6 was of the reagent grade. The complex was prepd by the authors. Purity of the HCl soln was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2-methoxy-5-pyrimidinyl)-; $C_{11}H_{12}N_4O_3S$; [71119-37-4]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-methoxy-5-pyrimidinyl)benzenesulfonamide in water at 37°C is 9.2 mg/100 cm^3 solution (3.3 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 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 232-4°C (cor), was prepd by the authors. Anal: %C 47.3 (calcd 47.1); %H 4.0 (4.3); %N 20.1 (20.0). 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-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3] (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 sulfamonomethoxine in water at 30°C is 0.17 mmol/L (4.8×10^{-2} g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamonomethoxine (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 sulfamonomethoxine 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-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Ezerskii, M. L.; Per'kova, N. N. *Khim.-Farm. Zh.* 1979, *13(11)*, 87-91.
VARIABLES: Grinding regime	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Specimen of sulfamonomethoxine	Solubility at room temperature	
	g/cm^3	10^4 mol dm^{-3} [a]
Commercial	0.000044	1.6
Commercial, ground in ball mill	0.000058	2.1
Commercial, ground in a jet mill	0.000054	1.9

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns were prepd by prolonged agitation of an excess of sulfamonomethoxine in water at room temp. The solns were then allowed to stand for 12 h and filtered. The concn of sulfamonomethoxine in the filtrate was detd nitritometrically by the method of the State Pharmacopeia X.

SOURCE AND PURITY OF MATERIALS:

Comm, pharmacopeial sulfamonomethoxine was used (source not specified). It was ground in a Pulverisette-5 lab ball mill or in a C-1266-00 jet mill.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3]

(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 sulfamonomethoxine in 0.1N HCl at 37°C is 1.336 mg/ml (4.766×10^{-3} 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 sulfamonomethoxine 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 500-mg uncoated tablets of sulfamonomethoxine were used. Hydrochloric acid was of reagent grade.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3]

(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 sulfamonomethoxine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 2.79 mmol/L (0.782 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamonomethoxine (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 sulfamonomethoxine 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 and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3]

(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:

Takayama, K.; Hasegawa, S.; Sasagawa, S.; Nambu, N.; Nagai, T.
Chem. Pharm. Bull. 1978, *26(1)*, 96-100.

VARIABLES:

One temperature: 30°C; one pH: 7.0

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Saturated concentration of sulfamonomethoxine in a 1/15M phosphate buffer of pH 7.0 at 30°C is 3.47 x 10^{-3}M.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The stationary disk method was employed (1). At appropriate time intervals, 3-ml aliquots of soln were withdrawn, the resultant amt of volume was compensated by adding the dissoln medium of the same temp. The concn was detd by the UV spectrophotometry.

SOURCE AND PURITY OF MATERIALS:

Sulfamonomethoxine (Dai-ichi Pharmaceutical Co.) mp 205°C, was prepd by heating a hydrate (recrystd from 30% (v/v) acetone-water) at 105°C for 4 h according to Japanese Pharmacopeia IX. The identity of the compd was confirmed by X-ray powder diffractometry, IR spectrophotometry and differential scanning calorimetry. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Hamada, Y.; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1975, *23*, 1205.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3]

(2) Benzene; C_6H_6; [71-43-2]

ORIGINAL MEASUREMENTS:

Takayama, K.; Nambu, N.; Nagai, T.
Chem. Pharm. Bull. 1977, *25*, 2608-12.

VARIABLES:

One temperature: 10°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamonomethoxine in benzene at 10°C is 1.45 x 10^{-4} mol dm^{-3} [a].

[a] Numerical value supplied by the authors.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The system was equilibrated in a sealed vial for 72 h at 10°. The satd soln was rapidly filtered through a Toyo filter paper No. 5B, 1 cm^3 of the filtrate was evapd at 40°C and the residue was dissolved in $CHCl_3$ to det the concn in the UV region using a Hitachi 124 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamonomethoxine, m.p. 205°C, was a very pure compd supplied by Dai-ichi Pharmaceutical Co., Ltd.

Purity of the benzene was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3]

(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 sulfamonomethoxine in chloroform at 30°C is 2.63 mmol/L (0.737 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamonomethoxine (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 sulfamonomethoxine 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- (sulfamonomethoxine); $C_{11}H_{12}N_4O_3S$; [1220-83-3] (2) 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6); $C_{12}H_{24}O_6$; [17455-13-9] (3) Benzene; C_6H_6; [71-43-2]	Takayama, K.; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1977, *25*, 2608-12.
VARIABLES:	**PREPARED BY:**
Concentration of 18-Crown-6	R. Piekos

EXPERIMENTAL VALUES:

Concentration of 18-Crown-6 10^3 mol dm^{-3}	Solubility at 10^oC [a] 10^4 mol dm^{-3}
1.0	1.65
2.0	1.99
3.0	2.02
4.0	2.04
5.0	2.05
6.0	1.90
7.0	1.65
8.0	1.68
9.0	1.64
10.0	1.48
12.0	1.55
14.0	1.50
16.0	1.55
18.0	1.56
20.0	1.63

[a] Numerical data supplied by the authors.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The system was equilibrated in a sealed vial for 72 h at 10^oC. The satd soln was rapidly filtered through a Toyo filter paper No. 5B, 1 cm^3 of the filtrate was evapd at 40^oC and the residue was dissolved in $CHCl_3$ to det the concn in the UV region using a Hitachi 124 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamonomethoxine, m. p. 205^oC, was a very pure compd supplied by Dai-ichi Pharmaceutical Co., Ltd.

18-Crown-6 was of the reagent grade.

Purity of the benzene was not specified.

ESTIMATED ERROR:

None specified.

REFERENCES:

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

Takayama, K.; Nambu, N.; Nagai, T.,
Chem. Pharm. Bull. 1977, *25*,
2608-12.

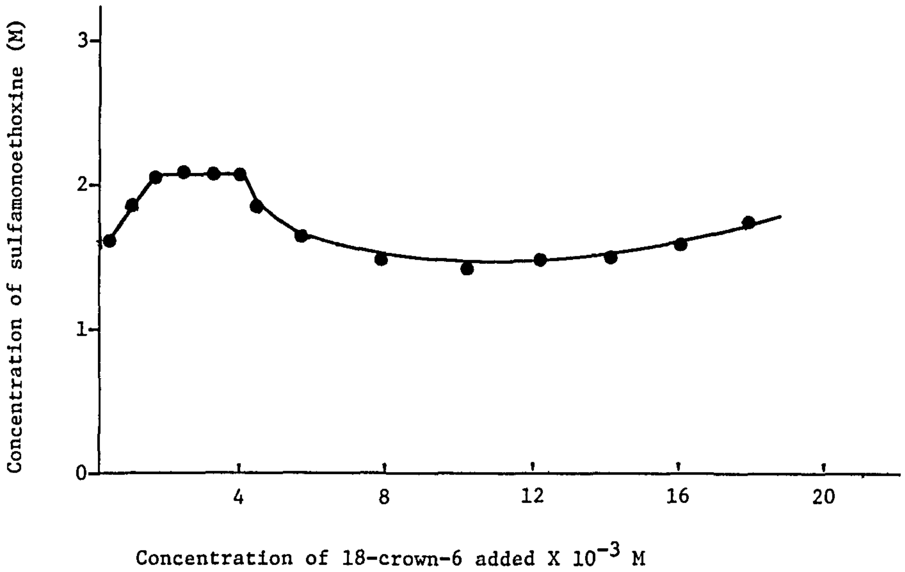
VARIABLES:

Concentration of 18-Crown-6

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Solubility of Sulfamonomethoxine in Benzene as a Function of 18-Crown-6 Added

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(6-methoxy-4-pyrimidinyl)- -1,4,7,10,13,16-Hexaoxacyclooctadecane complex 1:1 (SMM/18-Crown-6-complex); $C_{23}H_{36}N_4O_9S$; [65177-18-6]

(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:

Takayama, K.; Hasegawa, S.; Sasagawa, S.; Nambu, N.; Nagai, T.
Chem. Pharm. Bull. 1978, *26(1)*, 96-100.

VARIABLES:

One temperature: 30°C; one pH: 7.0

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Saturated concentration of the 1:1 SMM/18-Crown-6-complex in a 1/15M phosphate buffer solution of 7.0 is 5.97 x 10^{-3}M.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The stationary disk method was employed (1). At appropraite time intervals, 3-ml aliquots of soln were withdrawn, the resultant amt of vol was compensated by adding the dissoln medium at the same temp. The concn was detd by the UV spectrophotometry.

SOURCE AND PURITY OF MATERIALS:

The complex was prepd by the authors and contained a trace of the starting components. Its identity was confirmed by X-ray diffractometry, IR spectrophotometry, differenctial scanning calorimetry and other methods (2). The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Hamada, Y.; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1975, *23*, 1205.
2. Takayama, K.; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1977, *25*, 2608.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)- - 1,4,7,10,13,16-hexaoxycyclooctadecane complex (1:1) (SMM/18-C-6)); $C_{11}H_{12}N_4O_3S \cdot C_{12}H_{24}O_6$; [65177-18-6]

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

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

ORIGINAL MEASUREMENTS:

Takayama, K.; Nambu, N.; Nagai, T.
Chem. Pharm. Bull. 1978, *26(10)*,
2965-70.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Saturated concentration of the complex in 0.2N HCl 10^2M
30	1.25
35	1.32
40	1.45

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sample powder was dissolved in 50 ml of 0.2N HCl. Sampling was done by a 1-ml pipet fitted with a G-4 glass filter. The concn of SMM in the filtrate was detd by uv spectrophotometry after dilg with 0.2N HCl.

SOURCE AND PURITY OF MATERIALS:

The complex was prepd by sealing 4 g of SMM anhydrate (Dai-ichi Pharmaceutical Co.) with 6 g of reagent-grade 18-C-6 and 100 ml of benzene in a flask and stiring well for 10 days at 10°C. Purity of the HCl soln was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4-ethoxy-2-pyrimidinyl)-; $C_{12}H_{14}N_4O_3S$; [71138-72-2]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S. English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(4-ethoxy-2-pyrimidinyl)benzenesulfonamide in water at 37°C is 5.3 mg/100 cm^3 solution (1.8×10^{-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 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 255-6°C (cor), was prepd by the authors. Anal: %C 48.6 (calcd 49.0); %H 4.7 (4.8); %N 19.4 (19.0). 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-(5-chloro-2-pyrimidinyl)-; $C_{10}H_9ClN_4O_2S$; [4482-46-6]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(5-chloro-2-pyrimidinyl)benzenesulfonamide in water at 37°C is 1.8 mg/100 cm^3 solution (6.3 x 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 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 246-7°C (cor), was prepd by the authors. Anal: %C 42.2 (calcd 42.2). Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2-chloro-5-pyrimidinyl)-; $C_{10}H_9ClN_4O_2S$; [17103-49-0] (2) Water; H_2O; [7732-18-5]	Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.
VARIABLES:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-chloro-5-pyrimidinyl)benzenesulfonamide in water at 37°C is 32.1 mg/100 cm^3 solution (1.13×10^{-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 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 206-7°C (cor), was prepd by the authors. Anal: %C 42.3 (calcd 42.2); %H 3.2 (3.2); %N 19.8 (19.7) 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-(4-amino-2-pyrimidinyl)-; $C_{10}H_{11}N_5O_2S$; [16806-00-1]

(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-(4-amino-2-pyrimidinyl)benzenesulfonamide in water at 37°C is 186 mg/100 cm^{-3} solution (7.01 x 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 271-2°C, was prepd by the authors. Anal: %C 45.7 (calcd 54.3); %H 4.6 (4.2); %N 26.5 (26.4).
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-(2-amino-5-pyrimidinyl)-; $C_{10}H_{11}N_5O_2S$; [71119-38-5]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-amino-5-pyrimidinyl)benzenesulfonamide in water at 37°C is 8.3 mg/100 cm^3 solution (3.1×10^{-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 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 293-8°C (cor), was prepd by the authors. Anal: %C 45.3 (calcd 45.3); %H 4.0 (4.1); %N 26.2 (26.4). 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-[4-(diethylamino)-2-pyrimidinyl]-; $C_{14}H_{19}N_5O_2S$; [71119-24-9]

(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-[4-(diethylamino)-2-pyrimidinyl]benzenesulfonamide in water at 37°C is 4.2 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. 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 > 300°C (cor), was prepd by the authors. Anal: %C 52.5 (calcd 52.3); %H 5.8 (5.9); %N 21.7 (21.8).
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-(4, 5-dimethyl-2-pyrimidinyl)-; $C_{12}H_{14}N_4O_2S$; [4462-43-5]

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

ORIGINAL MEASUREMENTS:

Caldwell, W. T.; Kornfeld, E. C.; Donnell, C. K. *J. Am. Soc. Chem.* 1941, *63*, 2188-90.

VARIABLES:

One temperature: 29°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(4,5-dimethyl-2-pyrimidinyl)benzenesulfonamide in water at 29°C is 20 mg/100 ml solution (7×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by weighing the residue obtained by evapg to dryness a known volume of soln satd at 29°C.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 225-7-6.3°C (cor, recrystd from aq dioxane), was prepd by condensing 2-amino-4,5-dimethyl pyrimidine with acetylsulfanilyl chloride followed by hydrolysis with aq NaOH and pptn at pH 6. Anal: %N 20.09 (calcd 20.13). Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-
(sulfadimezine) $C_{12}H_{14}N_4O_2S$
[57-68-1]

(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:

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

Table I: Solubility of Sulfadimezine in water at 293K

	10^3 mol dm^{-3} (*indicates mol kg^{-1})
Reference	293K
1	1.2*
2	1.2
3	3.3*
4	1.671*

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

REFERENCES:

(1) Gusyakov, V.P.; Likhol'ot, N.M. *Farm. Zh. (kiev)* 1960, *15(3)*, 21-4.
(2) Likhol'ot, N.M. *Farm. Zh. (Kiev)* 1965, *20(5)*, 44-6.
(3) Shkadova, A.I. *Farm. Zh. (Kiev)* 1969, *24(3)*, 39-41.
(4) Gerencsér-Németh, M.; Harvath, M. *Gyógyszerészet* 1973, *17*, 417-21.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Caldwell, W. T.; Kornfeld, E. C.; Donnell, C. K. *J. Am. Chem. Soc.* 1941, *63*, 2188-90.

VARIABLES:

One temperature: 29°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in water at 29°C is 150 mg/100 ml solution (5.39×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by weighing the residue obtained by evapg to dryness a known volume of soln satd at 29°C.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine, mp 178-80°C (cor, recrystd from water), was prepd by condensing 2-amino-4,6-dimethylpyrimidine with acetylsulfanilyl chloride followed by hydrolysis with aq NaOH and pptn at pH 6. Anal: %C 51.78 (calcd 51.78), %H 4.83 (5.07), %N 20.03, 20.17 (20.13). Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Roblin, R. O., Jr.; Winnek, P. S.; English, J. P. *J. Am. Chem. Soc.* 1942, *64*, 567-70.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in water at 37°C is 75 mg/100 cm^3 solution[a] (2.7×10^{-3} mol dm^{-3}, compiler).

[a] The compound tends to remain supersaturated indefinitely in the presence of excess solid. The value represents approximate equilibrium when approached from low side (authors).

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

SOURCE AND PURITY OF MATERIALS:

Sulfadiazine, mp 198-9°C (cor), was prepd by the authors. Anal: %C 52.0 (calcd 51.8); %H 5.1 (5.0); %N 20.0 (20.1). 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-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Gusyakov, V. P.; Likhol'ot, N. M.

Farm. Zh. (Kiev) 1960, *15(3)*, 21-4.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in water at 20°C is 0.033 g/100 g water

(1.2 x 10^{-3} mol kg^{-1}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small excess of sulfadimezine was equilibrated for 8 h in a 50-ml test tube with 20 ml of water. Aliquots were taken with a pipet fitted with a filter. Sulfadimezine was detd at 285 nm using a SF-4 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was carefully washed with water, alcohol, and dried. Its purity conformed to the requirements of the State Pharmacopeia VIII.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: the accuracy corresponded to that of the colorimentric detns (authors:

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Likhol'ot, N. M.; *Farm. Zh. (Kiev)* 1965, *20(5)*, 44-6.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in water at 20°C is 0.033 g/100 ml (1.2 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An earlier described method was employed (1) whereby a small excess of sulfadimezine was equilibrated with 20 ml of water for 8 h in a 50-ml test tube. Aliquots were withdrawn through a filter and sulfadimezine was assayed bromatometrically.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

REFERENCES:

1. Gusyakov, V. P.; Likhol'ot, N. M. *Farm. Zh. (Kiev)* 1960, *15(8)*, 21.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Shkadova, A. I.

Farm. Zh. (Kiev) 1969, *24(3)*, 39-41.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in water at 20°C is 0.33×10^{-2} mol/kg (9.2×10^{-2} g/100 g, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A satd soln of sulfadimezine was equilibrated in a water thermostat at 20±0.1°C. The concn of sulfadimezine was detd by alkalimetric titrn.

SOURCE AND PURITY OF MATERIALS:

Purity of sulfadimezine conformed to the requirements of the State Pharmacopeia IX. Distd water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (author).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Gerencsér-Németh, M.; Horváth, M.
Gyógyszerészet 1973, *17*, 417-21.

VARIABLES:

One temperature: 20°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimidine in water at 20°C is 0.0465 g/100 g solution (1.67 x 10^{-3} mol kg^{-1} water, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A weighed excess of sulfadimidine was shaken with water in a shaker at 120 rpm for 6 h. The soln was then filtered, the residue was washed with the filtrate and finally with a small amt of distd water, dried and weighed.

SOURCE AND PURITY OF MATERIALS:

Sulfadimidine (source and purity not specified) was dried at 100°C for 3 h or over concn H_2SO_4 for 72 h. Its mp was 196.5-8°C. Distd water was used.

ESTIMATED ERROR:

Soly: precision ±0.0003 g/100 g (2 detns)- compiler.

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine; sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Nasipuri, R. N.; Khalil, S. A. H.
J. Pharm. Sci. 1973, *62(3)*, 473-5.

VARIABLES:

One temperature: 24°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Equilibrium solubility of sulfamethazine in water[a] at 24°C is 1.424 mmol/l (0.3963 g dm^{-3}, compiler).

[a] The pH of the saturated aqueous solution was 5.6

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamethazine was assayed spectrophotometrically at 230 nm in a 0.05M HCl soln using a Unicam SP 500 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was a BP grade sulfadimidine (Imperial Chemical Industries, England). The purity of water was not specified.

ESTIMATED ERROR:

Soly: ±1.9% (not stated accuracy or reproducibility - authors).

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Abdel Hadi, I.; Mezősi, J.; Kedvessy, G.; Morvay, J.
Pharmazie 1977, *32*, 791-3.

VARIABLES:

One temperature: 22°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of cyrstalline forms I and II of sulfadimidine in water at 22°C is equal and amounts to 0.35 mg/ml water (1.3×10^{-3} mol dm^{-3}, compiler)

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd as described by Martin (1). The system was equilibrated at 22°C for 48 h.

SOURCE AND PURITY OF MATERIALS:

Sulfadimidine was a comm product (Reanal, Hungary). Cryst. forms I and II, obtained by crystn from MeOH and EtOH resp, had both the mp of 197-8°C. Their identity was confirmed by IR spectroscopy, differential thermal analysis and X-ray diffraction patterns. Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Martin, A. N. *Physical Pharmacy*, Lea and Febiger, Philadelphia 1962, p. 340.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Ezerskii, M. L.; Per'kova, N. M.
Khim.-Farm. Zh. 1979, *13(11)*, 87-91.

VARIABLES:

Grinding regime

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Specimen of sulfadiazine	Solubility at room temperature	
	g/cm^3	10^3 mol dm^{-3} [a]
Commercial	0.00036	1.3
Commercial, ground in a ball mill	0.00036	1.3
Commercial, ground in a jet mill	0.00038	1.4

[a] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns were prepd by prolonged agitation of an excess of sulfadimezine in water at room temp. The solns were then allowed to stand for 12 h and filtered. The concn of sulfadimezine in the filtrate was detd nitritometrically by the method of the State Pharmacopeia X.

SOURCE AND PURITY OF MATERIALS:

Comm, pharmacopeial sulfadimezine was used (source not specified). It was ground in a Pulverisette-5 lab ball mill or in a C-1266-00 jet mill.

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Lithium chloride; LiCl; [7447-41-8]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.
Med. Prom. SSSR 1963, *17(5)*, 28-31.

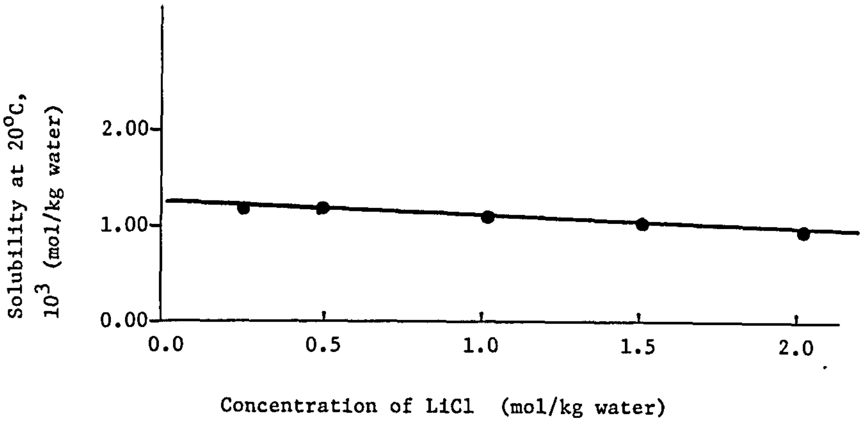
VARIABLES:

Concentration of LiCl

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a LiCl soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was purified by recrystn. Its purity was 98.5%. LiCl was purified by a recommended procedure (1).
Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR 1963, *17(5)*, 28-31.

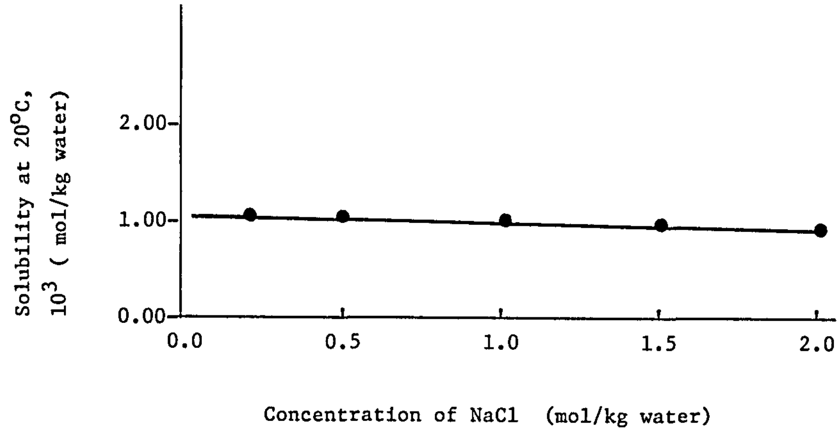
VARIABLES:

Concentration of NaCl

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50 ml tightly closed ampuls in which 20 ml of a NaCl soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. NaCl was purified by a recommended procedure.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repreated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4 dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

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

ORIGINAL MEASUREMENTS:

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

VARIABLES:

Concentration of KCl

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of KCl	Solubility at 20°C	
Weight %	g/100 g water	10^3 mol kg^{-1} [a]
0.74	0.031	1.11
1.82	0.030	1.01
3.59	0.033	1.19
6.93	0.032	1.15
12.97	0.025	0.90

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small excess of sulfadimezine was equilibrated for 8 h in a 50-ml test tube with 20 ml of aqueous KCl soln. Aliquots were taken with a pipet fitted with a filter. Sulfadimezine was detd in the filtrate at 285 nm using a SF-4 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was carefully washed with water, alcohol, and dried. Its purity conformed to the requirements of the State Pharmacopeia VIII.

KCl was doubly crystd. Purity of the water was not specified.

ESTIMATED ERROR:

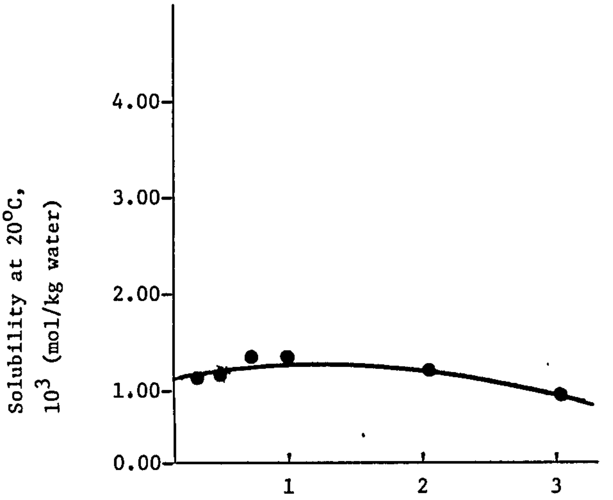
Soly: the accuracy corresponded to that of colorimetric detns. (authors)

Temp: not specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4,6 - dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Potassium chloride: KCl; [7447-40-7] (3) Water; H_2O; [7732-18-5]	Likholet, N. M.; Gusyakov, V. P. *Med. Prom. SSSR* 1963, *17(5)*, 28-31.
VARIABLES:	PREPARED BY:
Concentration of KCl	R. Piekos

EXPERIMENTAL VALUES:



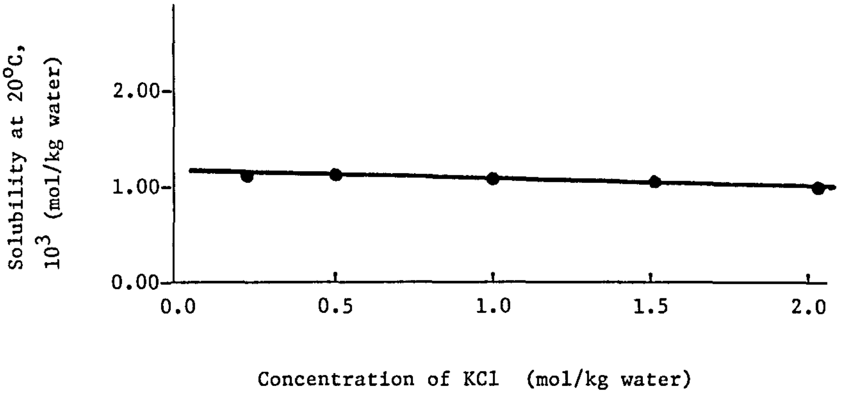
Concentration of KCl (mol/kg water)

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a KCl soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.	Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. KCl was purified by a recommended procedure (1). Purity of the water was not specified.
	ESTIMATED ERROR:
	Soly: measurements were repeated several times (authors). Temp: ±0.1°C (authors).
	REFERENCES:
	1. Karyakin, Ya. V.; Angelov, I. I. *Chistye khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:	ORIGINAL MEASUREMENTS:
Continued from previous page	Likholet, N. M.; Gusyakov, V. P. *Med. Prom. SSSR* 1963, *17(5)*, 28-31.
VARIABLES: Concentration of KCl	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
	ESTIMATED ERROR:
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Potassium bromide; KBr; [7758-02-3] (3) Water; H_2O; [7732-18-5]	Gusyakov, V. P.; Likhol'ot, N. M. *Farm. Zh. (Kiev)* 1960, *15(3)*, 21-4.
VARIABLES: Concentration of KBr	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of KBr	Solubility at 20°C	
Weight %	g/100 g water	10^3 mol kg^{-1} [a]
1.17	0.037	1.33
2.88	0.041	1.47
5.61	0.047	1.69
10.63	0.046	1.65
19.22	0.044	1.58

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small excess of sulfadimezine was equilibrated for 8 h in a 50-ml test tube with 20 ml of aqueous KBr soln. Aliquots were taken with a pipet fitted with a filter. Sulfadimezine was detd in the filtrate at 285 nm using a SF-4 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was carefully washed with water, alcohol, and dried. Its purity conformed to the requirements of the State Pharmacopeia VIII. KBr was doubly crystd. Purity of the water was not specified.

ESTIMATED ERROR:

Soly: the accuracy corresponded to that of colorimetric detns (authors).

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Potassium bromide; KBr; [7758-02-3]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR 1963, *17(5)*, 28-31.

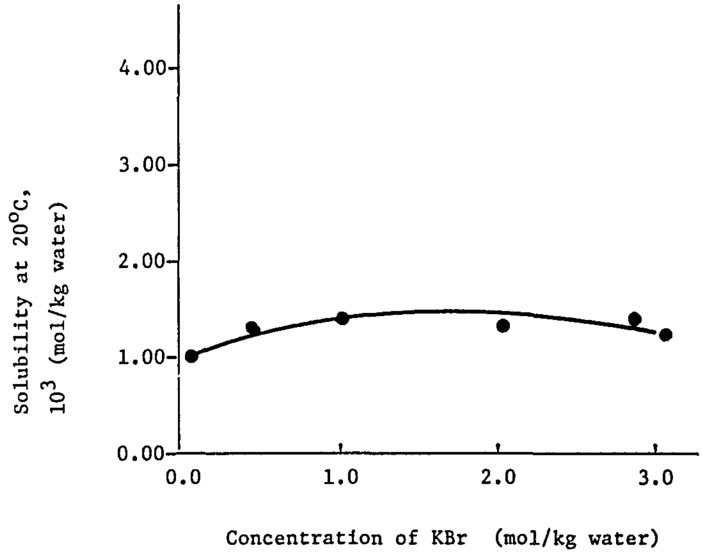
VARIABLES:

Concentration of KBr

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a KBr soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SP-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. KBr was purified by a recommended procedure (1).

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Potassium iodide; KI; [7681-11-0] (3) Water; H_2O; [7732-18-5]	Gusyakov, V. P.; Likhol'ot, N. M *Farm. Zh. (Kiev)* 1960, *15(3)*, 21-4.
VARIABLES: Concentration of KI	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of KI	Solubility at 20°C	
Weight %	g/100 g water	10^3 mol kg^{-1} [a]
1.63	0.039	1.40
3.98	0.038	1.36
7.66	0.048	1.72
14.23	0.053	1.90

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A small excess of sulfadimezine was equilibrated for 8 h in a 50-ml test tube with 20 ml aqueous KI soln. Aliquots were taken with a pipet fitted with a filter. Sulfadimezine was detd in the filtrate at 285 nm using a SF-4 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was carefully washed with water, alcohol, and dried. Its purity conformed to the requirements of the State Pharmacopeia VIII. KI was doubly crystd. Purity of the water was not specified.

ESTIMATED ERROR:

Soly: the accuracy corresponded to that of colorimetric detns (authors).

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Potassium iodide; KI; [7681-11-0]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR 1963, *17(5)*, 28-31.

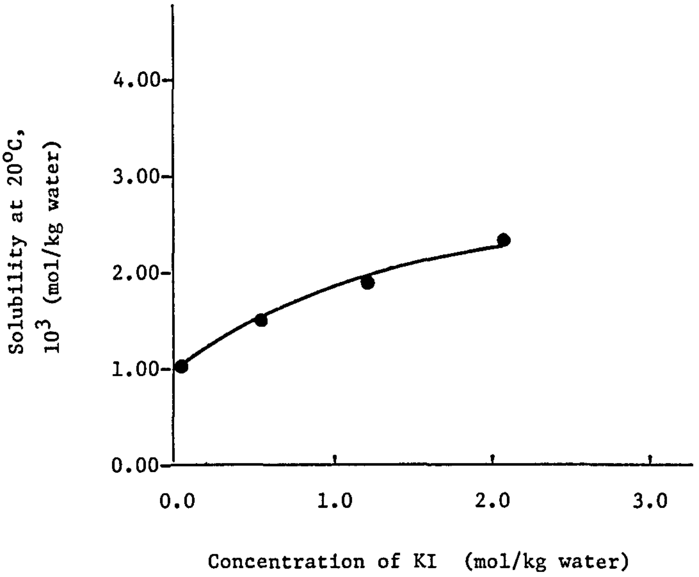
VARIABLES:

Concentration of KI

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a KI soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. KI was purified by a recommended procedure (1).

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye Khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Potassium thiocyanate; KSCN; [333-20-0] (3) Water; H_2O; [7732-18-5]	Gusyakov, V. P.; Likhol'ot, N. M. *Farm. Zh. (Kiev)* 1960, *15(3)*, 21-4.
VARIABLES:	PREPARED BY:
Concentration of KSCN	R. Piekos

EXPERIMENTAL VALUES:

Concentration of KSCN	Solubility at 20°C	
Weight %	g/100 g water	10^3 mol kg^{-1} [a]
0.96	0.036	1.2
2.37	0.039	1.4
4.63	0.047	1.6
8.85	0.064	2.3

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A samll excess of sulfadimezine was equilibrated for 8 h in a 50-ml test tube with 20 ml of aqueous KSCN soln. Aliquots were taken with a pipet fitted with a filter. Sulfadimezine was detd in the filtrate at 285 nm using a SF-4 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine was carefully washed with water, alcohol, and dried. Its purity conformed to the requirements of the State Pharmacopeia VIII. KSCN was doubly cyrstd. Purity of the water was not specified.

ESTIMATED ERROR:

Soly: the accuracy corresponded to that of colorimetric detns (authors).

Temp: not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Potassium thiocyanate; KCNS; [333-20-0]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR. 1963, *17(5)*, 28-31.

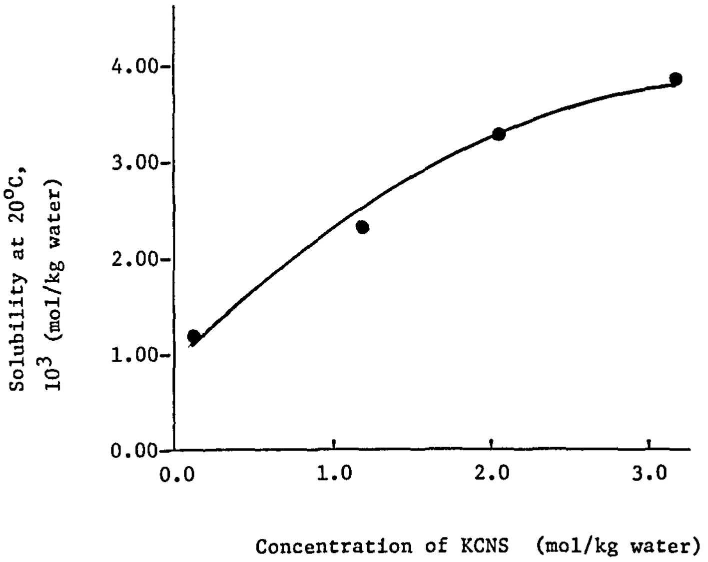
VARIABLES:

Concentration of KCNS

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a KCNS soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%.

KCNS was purified by a recommended procedure (1).

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

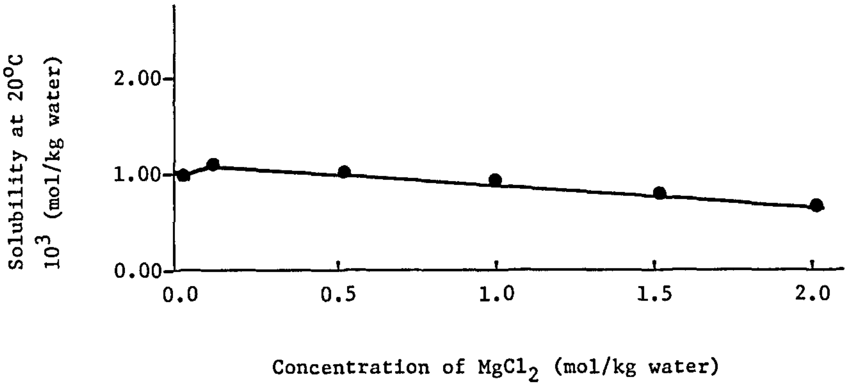
Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye Khimicheskye reaktivy,* Moscow, 1955.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine; $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Magnesium chloride; $MgCl_2$; [7786-30-3] (3) Water; H_2O; [7732-18-5]	Likholet, N. M.; Gusyakov, V. P. *Med. Prom. SSSR* 1963, *17(5)*, 28-31.
VARIABLES:	**PREPARED BY:**
Concentration of $MgCl_2$	R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a $MgCl_2$ soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. $MgCl_2$ was purified by a recommended procedure.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye Khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Barium chloride; $BaCl_2$; [10361-37-2]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR. 1963, *17(5)*, 28-31.

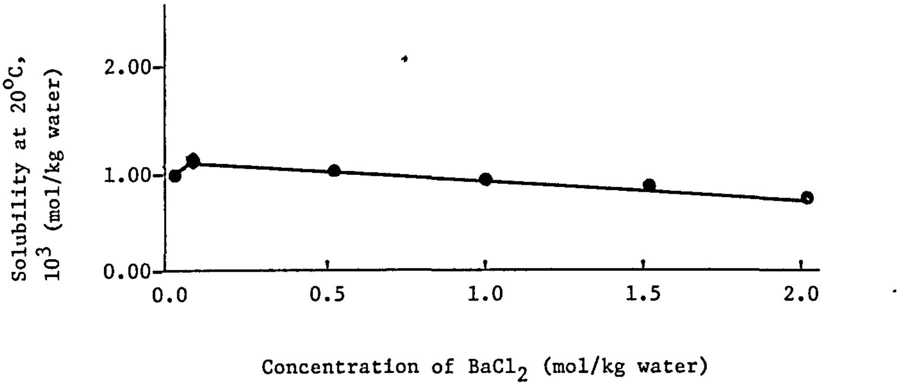
VARIABLES:

Concentration of $BaCl_2$

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a $BaCl_2$ soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. $BaCl_2$ was purified by a recommended procedure (1).

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye khimicheskye reaktivy,* Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Ammonium chloride; NH_4Cl; [12125-02-9]

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.
Med. Prom. SSSR 1963, *17(5)*, 28-31.

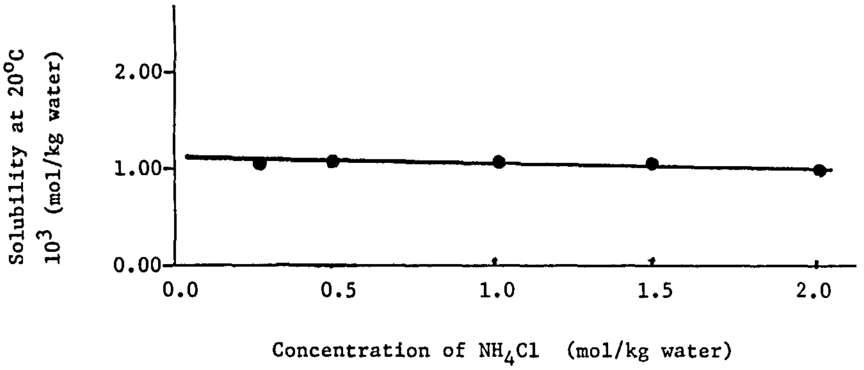
VARIABLES:

Concentration of NH_4Cl

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a NH_4Cl soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by crystn. Its purity was 98.5%. NH_4Cl was purified by a recommended procedure.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye Khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimeththyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

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

ORIGINAL MEASUREMENTS:

Likholet, N. M.; Gusyakov, V. P.

Med. Prom. SSSR 1963, *17(5)*, 28-31.

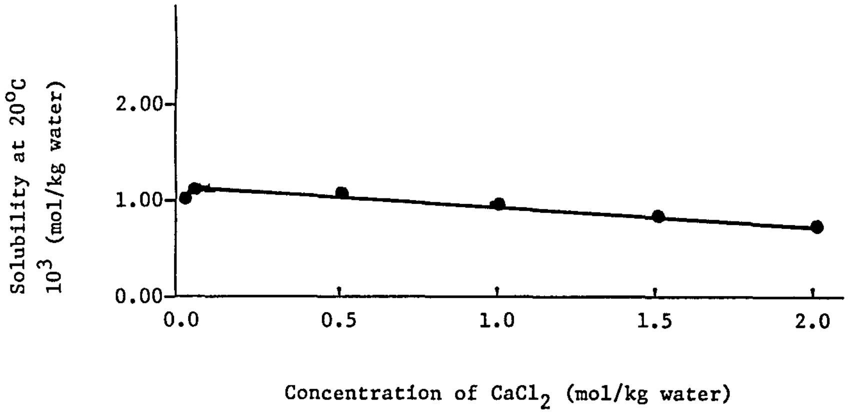
VARIABLES:

Concentration of $CaCl_2$

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimezine were prepd in 50-ml tightly closed ampuls in which 20 ml of a $CaCl_2$ soln was placed and a small excess of sulfadimezine. The mixts were equilibrated for 18 h at 20°C. Aliquots were pipetted out through a filter, dild, and assayed spectrophotometrically at 285 nm on a SF-IV spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) was purified by recrystn. Its purity was 98.5%. $CaCl_2$ was purified by a recommended procedure (1).

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: measurements were repeated several times (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Karyakin, Ya. V.; Angelov, I. I. *Chistye Khimicheskye reaktivy*, Moscow, 1955.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4, 6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

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

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

ORIGINAL MEASUREMENTS:

Portnov, M. A.; Zasosov, V. A.; Veselitskaya, T. A.; Mikhalev, V. A. *Med. Prom. SSSR* 1964, *18(2)*, 36-9.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 20°C	
	g/100 g solution	10^2 mol kg^{-1} [a]
1.1	0.65	2.33
1.5	0.15	0.54

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A test tube with an excess of sulfadimezine in a buffer soln was agitated for 6 h in a TS-15M thermostat and allowed to stand for 2 h. If, after 30 min of agitation, the pH differed from the required value, it was readjusted by the addn of a NaOH or HCl soln. A sample was withdrawn through a tube fitted with a filter and the sulfadimezine concn was detd by diazotization with potentiometric end point detection.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) conformed to the requirements of the State Pharmacopeia IX. The buffer solns were prepd from chemically pure reagents. Purity of the water was not specified.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±0.2°C (authors).

REFERENCES:

1. Portnov, M. A.; Veselitskaya, T. A.; Mikhalev, V. A. *Med. Prom. SSSR* 1962, *16(12)*, 27.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine); $C_{12}H_{12}N_4O_2S$; [57-68-1]

(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:

Gilligan, D. R.; Plummer, M. N.
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

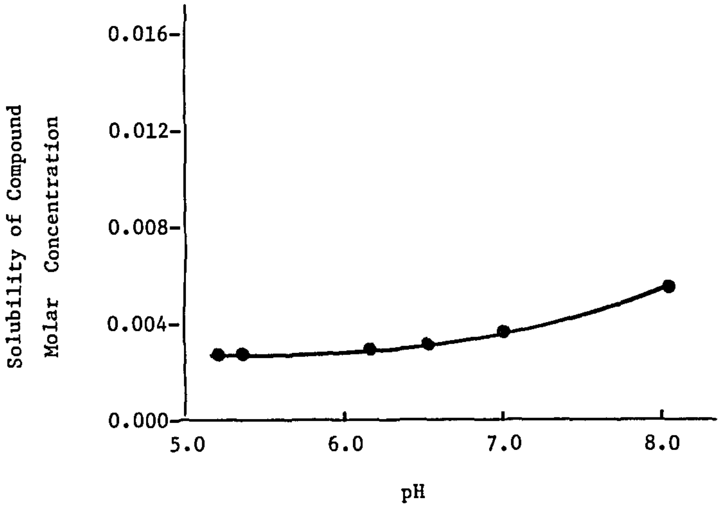
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethazine in M/15 phosphate buffer solutions



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were 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-(4,6-dimethyl-2-pyrimidinyl)- (Elkosin); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(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:

Meier, R.; Allemann, O.; von Meyenburg, H. *Schweiz. Med. Wochenschr.* 1944, *74(42)*, 1091-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility of Elkosin in phosphate buffers at 37°C	
	mg%	10^3 mol dm^{-3} [a]
5.5	191.0	6.862
6.5	209.0	7.509
7.5	297.0	10.67

[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) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (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 sulfadimidine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 60 mg %(2.2 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfadimidine at 20°C, their pH was measured at equilibrium, and the sulfadimidine 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-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(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.

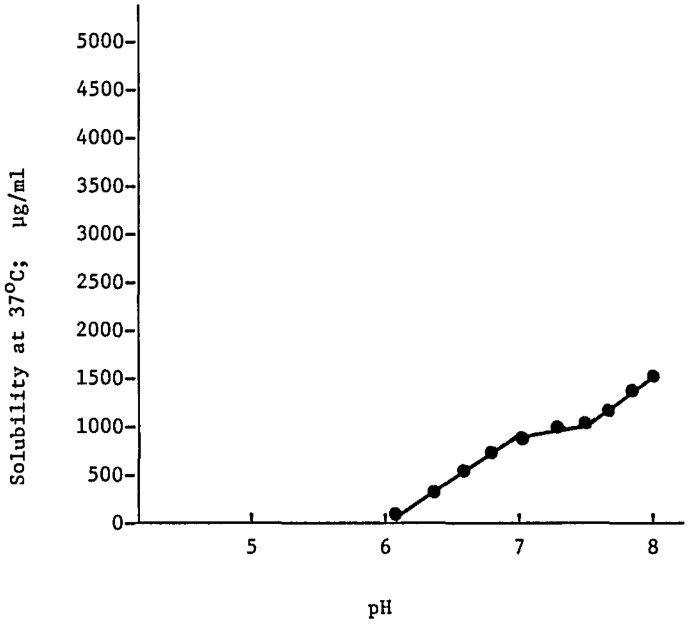
VARIABLES:

pH

PREPARED BY:

R. Piekoś

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly of sulfamethazine 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-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

(3) Phosphoric acid, monosodium salt; NaH_2PO_4; [7558-80-7]

(4) Water; H_2O; [7732-1805]

VARIABLES:

pH

ORIGINAL MEASUREMENTS:

Portnov, M. A.; Zasosov, V. A.; Veselitskaya, T. A.; Mikhalev, V. A.

Med. Prom. SSSR 1963, *18(2)*, 36-9.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH of phosphate buffer	Solubility at 20°C	
	g/100 g solution	10^2 mol kg^{-1} [a]
0.7	0.05	0.2
1.5	0.03	0.1
8.5	0.28	1.0

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A test tube with an excess of sulfadimezine in a buffer soln was agitated for 6 h in a TS-15M thermostat and allowed to stand for 2 h. If, after 30 min of agitation, the pH differed from the required value, it was readjusted by addn of a NaOH or HCl soln. A sample was withdrawn through a tube fitted with a filter and the sulfadimezine concn was detd by diazotization with potentiometric end point detection (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine (source not specified) conformed to the requirements of the State Pharmacopeia IX. The buffer solns were prepd from chemically pure H_3PO_4 and NaOH. Purity of the water was not specified.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±0.2°C (authors).

REFERENCES:

1. Portnov, M. A.; Veselitskaya, T. A.; Mikhalev, V. A. *Med. Prom. SSSR* 1962, *16(12)*, 27.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(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	10^2 mol dm^{-3} [a]
5.5	438	0.157
7.5	7000	2.515

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of sulfadimidine were prepd in phosphate buffers of pH 5.5 and 7.5 at room temp (25°C). The concn of sulfadimidine 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 sulfadimidine 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 were not specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate); $C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Plummer, M. N.

Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

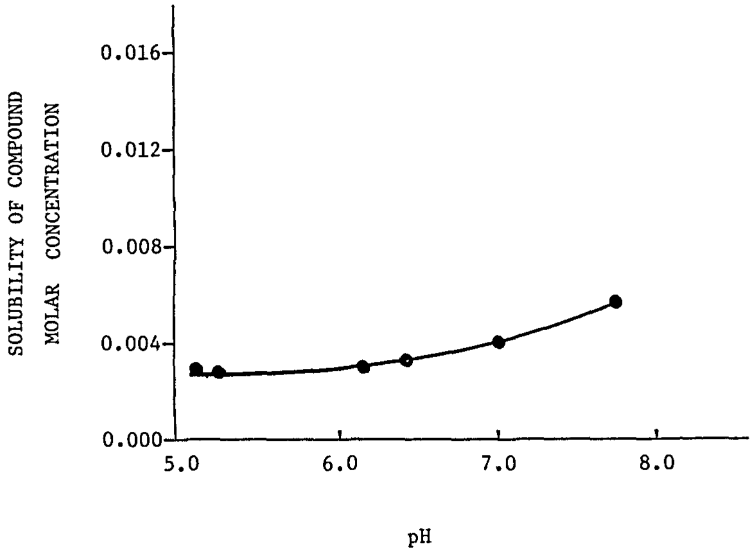
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were 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-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(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:

Likhol'ot, N. M. *Farm. Zh. (Kiev)* 1965, *20(5)*, 44-6.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH of McIllvaine's buffer solution	Solubility at 20°C g/100 ml	Solubility at 20°C 10^3 mol dm^{-3} [a]
4.1	0.034	1.2
5.1	0.037	1.3
5.9	0.039	1.4
6.5	0.045	1.6
6.9	0.054	1.9
7.5	0.093	3.3

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An earlier described method was employed (1) whereby a small excess of sulfadimezine was equilibrated with 20 ml of the McIlvaine's buffer soln for 8 h in a 50-ml test tube. Aliquots were withdrawn through a filter and sulfadimezine was assayed bromatometrically.

SOURCE AND PURITY OF MATERIALS:

Sulfadimezine: not specified.

McIlvaine's buffer solns were prepd from a 0.2M Na_2HPO_4 and a 0.1M citric acid solns. Source and purity of the buffer components were not specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (authors).

pH : not specified.

REFERENCES:

1. Gusyakov, V. P.; Likhol'ot, N. M. *Farm. Zh. (Kiev)* 1960, *15(8)*, 21.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine; sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Benzoic acid; $C_7H_6O_2$; [65-85-0]

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

ORIGINAL MEASUREMENTS:

Nasipuri, R. N.; Khalil, S. A. H.

J. Pharm. Sci. 1973, *62(3)*; 473-5.

VARIABLES:

Sulfamethazine concentration, benzoic acid concentration.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Sulfamethazine concentration	Equilibrium solubility of sulfamethazine at fixed benzoic acid concentration of 8.18 mmoles/l, at 24°C	
mmoles/l	mmoles/l	g dm^{-3} [a]
2.16	0.076	0.0211
3.60	0.083	0.0231
7.20	0.173	0.0481
10.80	1.400	0.3897
14.40	1.442	0.4013
36.00	1.417	0.3944
72.00	1.457	0.4055
144.00	1.424	0.3963
360.00	1.421	0.3955

Initial benzoic acid concentration	Solubility of sulfamethazine[b]	
mg%	mg%	10^3mol dm^{-3}solution[a]
20	38.8	1.39
40	38.2	1.37
60	36.1	1.30
80	13.0	0.467
100	4.8	0.17

[a] Calculated by compiler.

[b] Initial sulfamethazine concentration = 0.2 g%

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The concn of both benzoic acid and sulfamerazine were detd in a filtrate spectrophotometrically by applying equations of Tinker and McBay (1) for two-component systems. Measurements were made using a Unicam SP 500 spectrophotometer at 230 and 300 nm (in 0.05N HCl). The validity of the eqns was tested by assaying known mixts of sulfamethazine and benzoic acid.

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was a BP grade sulfadimidine (Imperial Chemical Industries, England). Benzoic acid was of BP quality (British Drug Houses, England). Purity of the water was not specified.

ESTIMATED ERROR:

Soly: sulfamethazine and benzoic acid ±1.9 and ±2.3%, resp. (not stated accuracy or reproducibility - authors).

Temp: ±0.2°C (authors).

REFERENCES:

1. Tinker, R. B.; McBay, A. J. *J. Amer. Pharm. Assoc., Sci. Ed.* 1954, *43*, 315.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

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

ORIGINAL MEASUREMENTS:

Shkadova, A. I.

Farm. Zh. (Kiev) 1969, *24(3)*, 39-41.

VARIABLES:

Concentration of ethanol

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadimezine was equilibrated with the solvent in a water thermostat at 20±0.1°C. The concn of sulfadimezine was detd by alkalimetric titration.

SOURCE AND PURITY OF MATERIALS:

Purity of sulfadimezine conformed to the requirements of the State Pharmacopiea IX. The EtOH - water mixts were prepd from abs EtOH (purity and source not specified) and distd water.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.1°C (author).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Sorbitan monooleate, polyoxyethylene derivatives (Tween 80); [9005-65-6]

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

ORIGINAL MEASUREMENTS:

Gerencsér-Németh, M.; Horbáth, M.

Gyógyszerészet 1973, *17*, 417-21.

VARIABLES:

Concentration of Tween 80

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Concentration of Tween 80 Weight %	Solubility at 20°C	
	g/100 g soln[a]	10^3 mol kg^{-1} soln[b]
1	0.0530	1.90
	0.0518	1.86
3	0.0734	2.64
	0.0706	2.54
5	0.0922	3.31
	0.0914	3.28
8	0.1078	3.873
	0.1142	4.103

[a] Numerical values supplied by the authors.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfadimidine in an aq Tween 80 soln was shaken in a lab shaker at 120 rpm for 6 h. The soln was then filtered, the residue was washed first with the filtrate and finally with a small amt of water, dried and weighed.

SOURCE AND PURITY OF MATERIALS:

Sulfadimidine (source and purity not specified) was dried at 100°C for 3 h or over concd H_2SO_4 for 72 h. Its mp was 196.5-8°C. Distd water was used. Source and purity of Tween 80 were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine; sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) 2-Pyrrolidinone, 1-ethenyl-, polymers (PVP); $(C_6H_9NO)_x$; [9003-39-8]

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

ORIGINAL MEASUREMENTS:

Nasipuri, R. N.; Khalil, S. A. H.
J. Pharm. Sci. 1973, *62(3)*, 473-5.

VARIABLES:

One temperature: 24°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethazine in an aqueous solution of PVP containing 5 mg% PVP, at 24°C, is 40.1 mg% (1.44×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfamethazine was assayed spectrophotometrically at 230 nm in a 0.05N HCl soln using a Unicam SP 500 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was a BP grade sulfadimidine (Imperial Chemical Industries, England).
PVP was a sample having an av mol wt of 40,000 (Plasdone k 29-32, GAF Corp., New York, N. Y.)
Purity of the water was not specified.

ESTIMATED ERROR:

Soly: ±1.9% (not stated accuracy or reproducibility - authors).

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine; sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Benzoic acid; $C_7H_6O_2$; [65-85-0]

(3) 2-Pyrrolidinone, 1-ethenyl-, polymers (PVP); $(C_6H_9NO)_x$; [9003-39-8]

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

ORIGINAL MEASUREMENTS:

Nasipuri, R. N.; Khalil, S. A. H.

J. Pharm. Sci. 1973, *62(3)*, 473-5.

VARIABLES:

Initial benzoic acid concentration

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Initial benzoic acid concentration	Solubility of sulfamethazine at 24°C in a solution containing 5 mg% of PVP	
mg%	mg%	10^3 mol dm^{-3} solution[a]
20	39.9	1.43
40	40.4	1.45
60	40.2	1.44
80	39.8	1.43
100	39.9	1.43

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The concn of both benzoic acid and sulfamerazine were detd in a filtrate spectrophotometrically by applying equations of Tinker and McBay (1) for two-component systems. Measurements were made using a Unicam SP 500 spectrophotometer at 230 and 300 nm (in 0.05N HCl). The validity of the eqns was tested by assaying known mixts of sulfamethazine and benzoic acid.

SOURCE AND PURITY OF MATERIALS:

Sulfamethazine was a BP grade sulfadimidine (Imperial Chemical Industries, England). Benzoic acid was of BP quality (British Drug Houses, England). PVP (Plasdone k 29-32, GAF Corp., New York, N. Y.) was a sample having an av mol wt of 40,000. Purity of the water was not specified.

ESTIMATED ERROR:

Soly: sulfamethazine and benzoic acid ±1.9 and ±2.3%, resp. (not stated accuracy or reproducibility - authors).

Temp: ±0.2°C (authors).

REFERENCES:

1. Tinker, R. B.; McBay, A. J. *J. Amer. Pharm. Assoc., Sci. Ed.* 1954, *43*, 315.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

(2) Ethanol, 2-ethoxy-; $C_4H_{10}O_2$; [110-80-5]

ORIGINAL MEASUREMENTS:

Sunwoo, C.; Eisen, H.
J. Pharm. Sci. <u>1971,</u> *60,* 238-44.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfamethazine in 2-ethoxyethanol at 25°C is 0.0184 mol/dm^3. (5.47 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by the method reported by Restaino and Martin (1). Sulfamethazine was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 270 nm after diln of a sample with 95% ethanol or water.

SOURCE AND PURITY OF MATERIALS:

The USP sulfamethazine (American Cyanamid Co., Pearl River, N.Y.), recrystd from warm alcohol and an industrial grade 2-ethoxyethanol (Cellosolve solvent, Union Carbide, New York, N. Y.) were used.

ESTIMATED ERROR:

Temp: ±1.0°C (authors).

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

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- (sulfamethazine); $C_{12}H_{14}N_4O_2S$; [57-68-1]

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

ORIGINAL MEASUREMENTS:

Gutierrrez, 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	4.481	4.288	36.502	131.1	9.39	22.31	27.66
5	4.601	4.397	37.213	133.7	9.59	21.73	26.86
10	4.701	4.489	37.741	135.6	9.80	21.27	26.49
15	4.959	4.724	39.528	142.0	10.35	20.16	25.29
20	5.269	5.005	41.688	149.8	10.99	18.98	23.98
25	5.406	5.128	42.448	152.5	11.28	18.49	23.56
30	5.684	5.377	44.295	159.1	11.86	17.59	22.57
35	6.002	5.651	46.413	166.7	12.52	16.66	21.54
40	6.597	6.188	50.625	181.9	13.76	15.19	19.75
45	7.486	6.964	56.998	204.8	15.62	13.36	17.54
50	8.759	8.053	66.174	237.3	18.27	11.42	15.11

$^a G = \frac{p\ 100}{P - p}$, 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 dissolved 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 was confirmed by procedures of the German Pharmacopeia VI and Spanish Pharmacopeia VIII.

The purity of sulfamethazine 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-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimidine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (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 sulfadimidine in chloroform at 20°C is 240 mg% (8.62×10^{-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-(4,6-dimethyl-2-pyrimidinyl)- (sulfadimezine); $C_{12}H_{14}N_4O_2S$; [57-68-1] (2) Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (PEG 400); $(C_2H_4O)_nH_2O$; [25322-68-3] 400	ORIGINAL MEASUREMENTS: Gusyakov, V. P.; Likhol'ot, N. M.; Kutna, I. M. *Farm. Zh. (Kiev)* 1968, *23(6)*, 56-61.
VARIABLES: One temperature: 21-25°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimezine in α-hydro-ω -hydroxypoly(oxy-1,2-ethanediyl) 400 at room temperature (21-25°C) is 10.4% by weight (0.417 mol kg^{-1} PEG 400, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: Small quantities (2-4 mg) of sulfadimezine were added to a known quantity of PEG 400 under stirring until satn was attained.	SOURCE AND PURITY OF MATERIALS: Sulfadimezine: neither source nor purity was specified. PEG 400: source not specified; sp gr 1.127 g cm^{-3}; temp of solidification approx 6°C; refractive index 1.466 (temp not indicated).
	ESTIMATED ERROR: Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)- hemihydrate (sulfamethazine hemihydrate); $C_{12}H_{14}N_4O_2S \cdot 1/2H_2O$; [82537-68-6]

(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.

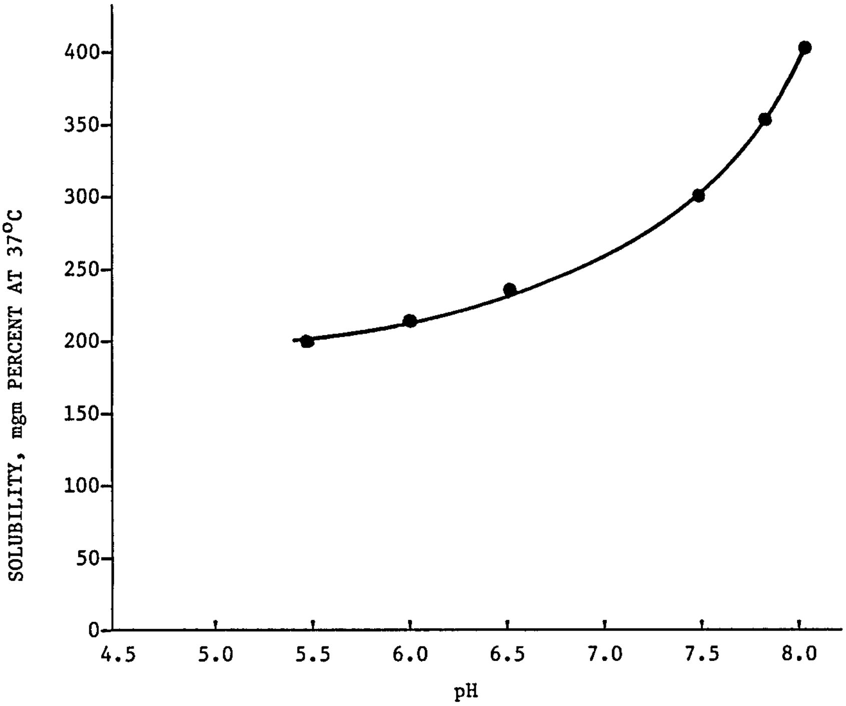
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethazine hemihydrate 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 sulfamethazine hemihydrate 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 sulfamethazine hemihydrate and of NaOH were not specified. Water was doubly distilled.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Cobalt, bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-N^N,O]-, hydrate; $C_{24}H_{26}CoN_8O_4S_2 \cdot nH_2O$; [86729-24-0]

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

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

ORIGINAL MEASUREMENTS:

Tskitishvili, M. G.; Mikadze, I. I.
Soobshch. Akad. Nauk Gruz. SSR
1978, *89(3)*, 589-92.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

K_{so} over the HCl concentration range $2.5 \times 10^{-2} - 2.5 \times 10^{-5}$ mol dm^{-3}, at 25°C, is 3.35×10^{-13}.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

In a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute was placed and shaken for 6 h in a water thermostat at 25°C. After attaining equilibrium, the pH of the soln was measured and the Co^{2+} and S content was detd to calculate K_{so}.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-methoxy-2-pyrimidinyl)- (sulfamethoxydiazine); $C_{11}H_{12}N_4O_3S$; [651-06-9]

(2) Poly(oxy-1,2-ethanediy) ,α -hydro- ω -hydroxy- PEG (20 000); $(C_2H_4O)_nH_2O$; [25322-68-3] 20 000

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

ORIGINAL MEASUREMENTS:

Salib, N. N.; Ebian, A. R.

Pharm. Ind. 1978, *40(3)*, 262-5.

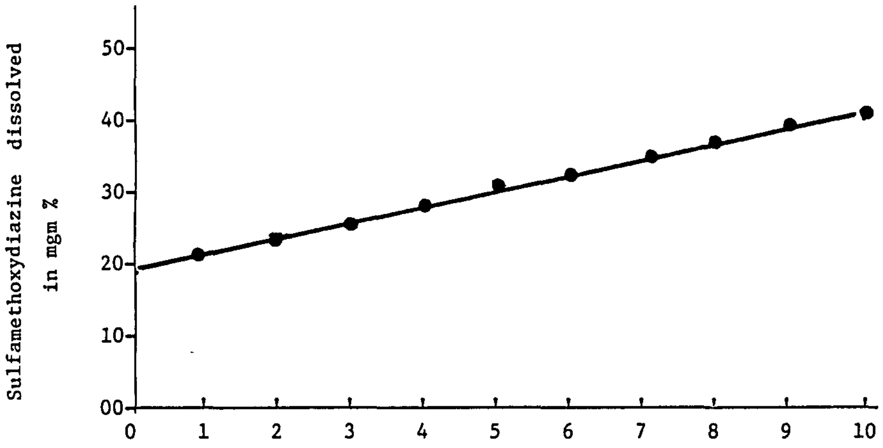
VARIABLES:

Concentration of PEG 20 000

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Effect of different concentrations of PEG 20 000 on the solubility of sulfamethoxydiazine at 37±1°C.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxydiazine was added to bottles contg from 0 to 10% PEG 20 000 solns. The bottles were rotated at 30 rpm for 24 h in a water bath at 37°C. After equilibrium had been attained, an aliquot was pipetted out, dild with 0.1N HCl, and the solute was assayed spectrophotometrically at 228 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxydiazine (Bayrena) was supplied by Bayer, Leverkusen. PEG 20 000 was a product of Hoechst AG, West Germany.
The purity of the materials was not specified.

ESTIMATED ERROR:

Soly: data points are means of 3 detns (authors).

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Copper, bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-N^{N},O]-, hydrate; $C_{24}H_{26}CuN_8O_4S_2 \cdot nH_2O$; [86729-23-9]

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

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

ORIGINAL MEASUREMENTS:

Tskitishvili, M. G.; Mikadze, I. I.
Soobshch. Akad. Nauk Gruz. SSR
1978, *89(3)*, 589-92.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

K_{so} over the HCl concentration range 2.5×10^{-2} - 2.5×10^{-5} mol dm^{-3}, at 25°C, is 1.77×10^{-16}.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

In a glass vessel, a mixt of 100 ml of HCl of appropriate concn and the solute was placed and shaken for 6 h in a water thermostat at 25°C. After attaining equilibrium , the pH of the soln was measured and the Cu^{2+} and S content was detd to calculate K_{so}.

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Manganese, bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-N^N,O]-hydrate; $C_{24}H_{26}MnN_8O_4S_2\cdot nH_2O$; [84812-75-9]

(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	10^9 K_{so} at 25°C
1.0×10^{-2}	6.40	7.91
5.0×10^{-3}	6.77	7.94
2.5×10^{-3}	6.96	7.91
1.0×10^{-3}	7.54	7.92
5.0×10^{-4}	7.82	7.90
2.5×10^{-4}	7.90	7.92
1.0×10^{-4}	8.10	7.94
5.0×10^{-5}	8.12	7.97
1.5×10^{-5}	8.15	8.00
	Mean	7.94

To be continued on the next page.

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 solutions of chem pure $Mn(OAc)_2$, monosodium salt of sulfadimezine, HCl as well as doubly distd water were used. The source of the materials was no specified.

ESTIMATED ERROR:

K_{so} : std deviation 3×10^{-11} (compiler).
Temp and pH: not specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Nickel,bis[4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-N^N,O]-dihydrate; $C_{24}H_{26}N_8NiO_4S_2 \cdot 2H_2O$; [84812-74-8] (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: pH	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of HCl (mol/l)	pH	10^{14} K_{so} at 25°C
2.5×10^{-2}	6.08	1.61
1.0×10^{-2}	6.50	1.63
5.0×10^{-3}	7.37	1.66
2.5×10^{-3}	8.29	1.60
1.0×10^{-3}	8.85	1.60
5.0×10^{-4}	9.10	1.66
2.5×10^{-4}	9.25	1.64
1.0×10^{-4}	9.34	1.67
5.0×10^{-5}	9.35	1.67
2.5×10^{-5}	9.37	1.63
	Mean	1.64

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 sulfadimezine, 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^{-16} (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) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, monosilver salt (Ag sulfamethazine); $C_{12}H_{13}AgN_4O_2S$; [53081-02-0]

(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 Sulfamethazine 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 2.186		pH 3.970	
	$S \times 10^3$	$[Ag^+] \times 10^3$	$S \times 10^4$	$[Ag^+] \times 10^4$
	1.194	1.185	0.9920	1.028
	1.191	1.185	0.9689	1.003
	1.191	1.171	0.9813	1.041
	1.218	1.194	1.1010	1.170
	1.194	1.157	0.9945	1.053
	1.204	1.166	-	-
Mean	1.198	1.176	1.0100	1.059

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Mixts of 100 mg Ag sulfamethazine 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 themostated 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 used were anal or USP grade.

Ag sulfamethazine was prepd by the method of Rosenzweig and Fuchs (1) and recrystd from ammonia (2). Water had a sp cond of (1-10) x 10^{-7} ohm^{-1} cm^{-1}.

The source of the reagents was not specified.

ESTIMATED ERROR:

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

REFERENCES:

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-(4,6-dimethyl-2-pyrimidinyl)-, monosilver salt (Ag sulfamethazine); $C_{12}H_{13}AgN_4O_2S$; [53081-02-0]

(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:

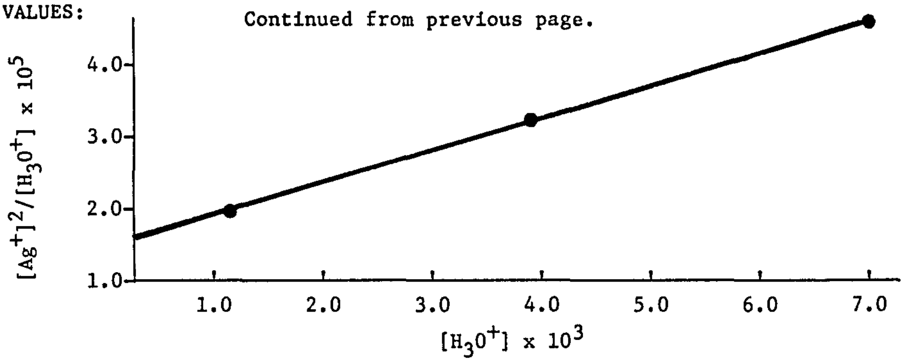
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Continued from previous page.



Equilibrium values of $[Ag^+]^2/[H_3O^+]$ versus $[H_3O^+]$ for silver sulfamethazine in nitric acid buffer at 0.1M ionic strength and 25 ± 0.1°

Calculation of the solubility product of Ag sulfamethazine[a], K_s, at 25 ± 0.1°C and 0.1M ionic strength.

[a] from eq. $K_s = f_oS^2$, where $f_o = \left(1 + \frac{[H_3O^+]}{K_2} + \frac{[H_3O^+]^2}{K_1K_2}\right)^{-1}$

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 sulfamethazine, respectively.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

Continued from previous page.

ORIGINAL MEASUREMENTS:

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

J. Pharm. Sci. 1977, *66(4)*, 519-22.

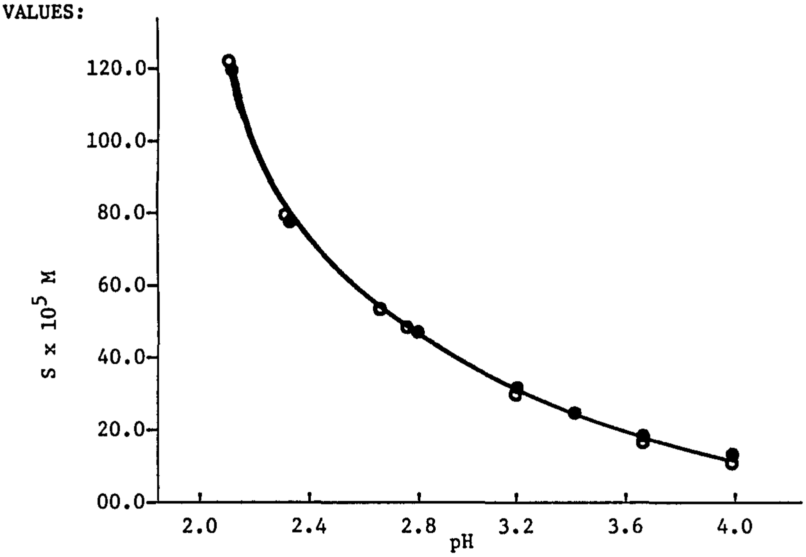
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



Molar solubility, S, of silver sulfamethazine versus pH at 0.1M ionic strength and 25 ± 0.1°. Key: o, calculated from Eq. 7, and ●, experimental values.

Eq. 7: $$S^2 = [Ag^+]^2 = \frac{[H_3O^+]^2K_s}{K_1\ \ K_2} + \frac{[H_3O^+]K_s}{K_2}$$

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

Temp: ±0.1° (authors).

pH : accuracy ±0.001 pH unit (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
Continued from previous page.	Nesbitt, R. U., Jr.; Sandmann, B. J. *J. Pharm. Sci.* 1978, *67(7)*, 1012-17.
VARIABLES:	PREPARED BY:
pH	R. Piekos

EXPERIMENTAL VALUES:

pH	f_o	S^2	$K_s{}^a$
2.174	2.551×10^{-6}	1.477×10^{-6}	3.77×10^{-12}
2.421	6.323×10^{-6}	5.897×10^{-7}	3.72×10^{-12}
2.668	1.455×10^{-5}	2.606×10^{-7}	3.79×10^{-12}
2.934	3.265×10^{-5}	1.151×10^{-7}	3.76×10^{-12}
		Mean	$(3.76 \pm 0.03)10^{-12}$

[a] K_s reported as mean ± SD.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-, monosilver salt (Ag sulfamethazine); $C_{12}H_{13}AgN_4O_2S$; [53081-02-0]

(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:

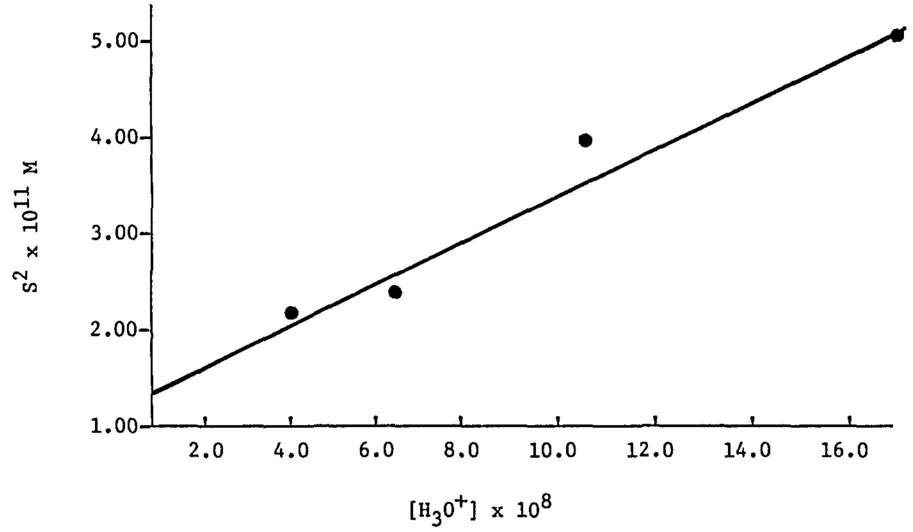
Hydronium-ion concentration

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Equilibrium values of S^2 (S = total molar solubility) versus $[H_3O^+]$ for Ag sulfamethazine 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 Ag sulfamethazine 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 sulfamethazine was prepd by the method of Rosenzweig and Fuchs (1) and recrystd from 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° (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) Zinc, (*T*-4)-bis[4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamidato-N^N,O]-
(Zn(II) sulfamethazine);
$C_{24}H_{24}N_8O_4S_2Zn$; [71261-83-1]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.;
Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg.
1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Zn(II) sulfamethazine in water at room temperature (28-30°C)[a] is 8.6 mg% (1.4×10^{-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) sulfamethazine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfamethazine content using the colorimetric method of Bratton and Marshall (1). The soly value was then calcd from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-(acetyl sulfamethazine); $C_{14}H_{16}N_4O_3S$; [100-90-3]

(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:

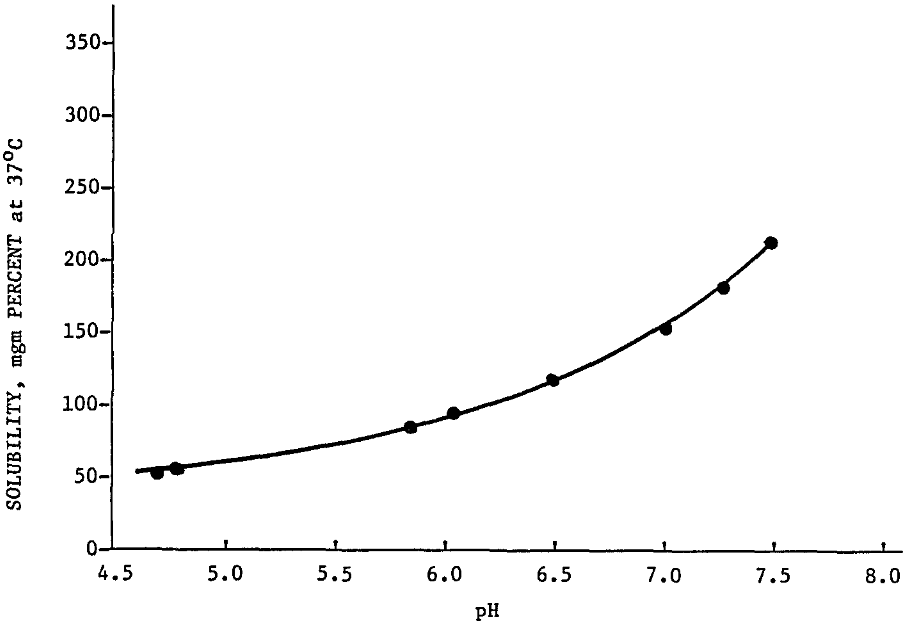
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility at pH 6.5, at 37°C, was 117 mg/100 cm^3 (3.65×10^{-3} mol dm^{-3}, compiler).



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfamethazine 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 drug was then de-acetylated and the concn of sulfamethazine 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 sulfamethazine and of NaOH was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-(acetyl sulfamethazine); $C_{14}H_{16}N_4O_3S$; [100-90-3]

(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:

Gilligan, D. R.; Plummer, M. N.

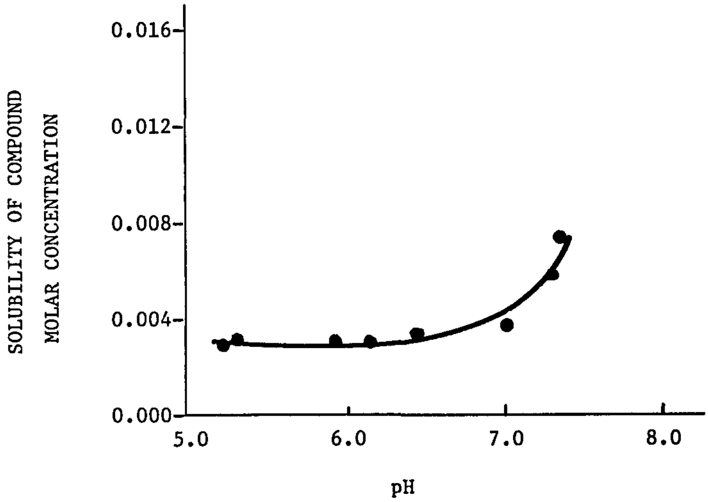
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethazine in M/15 phosphate buffer solutions



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of acetyl sulfamethazine was shaken in M/15 phosphate buffer solns of various pH values for 18 h in a water bath at 37°C, and filtered in an incubator room at this temp. The pH of the filtrate was measured immediately at room temp with a Beckmann glass electrode pH meter and appropriate corrections for the differences between room temp and 37°C were applied. The amt of dissolved compd was measured by the method of Bratton and Marshall (1).

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfamethazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-(acetyl Elkosin); $C_{14}H_{16}N_4O_3S$; [100-90-3]

(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:

Meier, R; Allemann, O., von Meyenburg, H. *Schweiz. Med. Wochenschr.* 1944, *74(42)*, 1091-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility of acetyl Elkosin in phosphate buffers at 37°C	
	mg%	10^3 mol dm^{-3} [a]
5.5	115.0	3.590
6.5	117.0	3.652
7.5	176.0	5.494

[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-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-(N^4-acetylsulfadimidine); $C_{14}H_{16}N_4O_3S$; [100-90-3]

(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:

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	10^3 mol dm^{-3} a
5.5	752	2.35
7.5	1340	4.18

a Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Satd solns of N^4- acetylsulfadimidine 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 the solute 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) Acetamide, N-[4-[[(4,6-dimethyl-2-pyrimidinyl)amino]sulfonyl]phenyl]-
$C_{14}H_{16}N_4O_3S$; [100-90-3]

(2) 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, disodium salt (Na citrate)
$C_6H_6Na_2O_7$; [144-33-2]

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

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

ORIGINAL MEASUREMENTS:

Gilligan, D. R.; Plummer, M. N.
Proc. Soc. Exp. Biol. Med. 1943, *53*, 142-5.

VARIABLES:

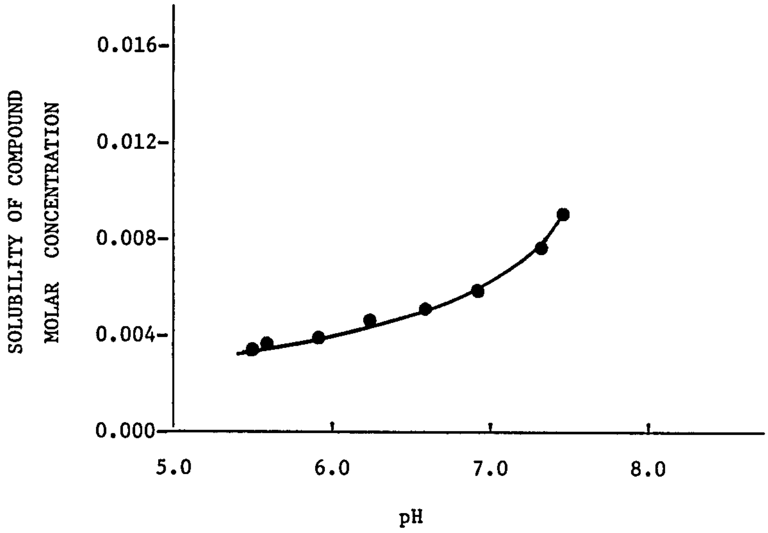
pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

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



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Acetyl sulfamethazine was supplied by Lederle Labs, Inc. The source and purity of the remaining materials were not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[[4-(acetylamino)phenyl]-sulfonyl]-N-(4,6-dimethyl-2-pyrimidinyl)- (N^1, N^4-diacetylsulfamidine); $C_{16}H_{18}N_4O_4S$; [59224-69-0]

(2) Phosphoric acdi, 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:

Hekster, Ch. A.; Vree, T. B.
Antibiotics Chemother. 1982, *31*, 22-118.

PREPARED BY:
R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^5 mol dm^{-3} [a]
5.5	11.8	3.25
7.5[b]	9.3	2.6

[a] Calculated by compiler

[b] Erroneous pH value of 7.0 is given in the article.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method (1) was used (personal communication). Satd solns of N^1,N^4-diacetylsulfadimidine were prepd in phosphate buffers of pH 5.5 and 7.5 at 25°C. The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a Model 748 column oven and a Pye-Unicam LC-UV spectrophotometric detector.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: the detection limit of the solute by HPLC was 0.5 mg/l (authors).

The errors in temp and pH were not specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(4-methyl-5-n-pentyl-2-pyrimidinyl)-; $C_{16}H_{22}N_4O_2S$; [71119-35-2] (2) Water; H_2O; [7732-18-5]	Caldwell, W. T.; Kornfeld, E. C.; Donnell, C. K. *J. Am. Chem. Soc.* 1941, *63*, 2188-90.
VARIABLES:	PREPARED BY:
One temperature: 29°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(4-methyl-5-n-pentyl-2-pyrimidinyl)benzenesulfonamide in water at 29°C is 2.8 mg/100 ml solution (8.4×10^{-5} mol dm^{-3} - compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Soly was detd by weighing the residue obtained by evapg to dryness a known volume of soln satd at 29°C.	The sulfonamide, mp 188-90°C (cor, recrystd from aq EtOH), was prepd by condensing 2-amino-4-methyl-5-n-pentylpyrimidine with acetylsulfanilyl chloride followed by hydrolysis with aq NaOH and pptn at pH 6. Anal: %N 16.67 (calcd 16.75). Purity of the water was not specified.
	ESTIMATED ERROR:
	Nothing specified.
	REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(4,6-dimethoxy-2-pyrimidinyl)- (sulfadimethoxypyrimidine); $C_{12}H_{14}N_4O_4S$; [155-91-9]

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

(3) 1,2,3-Propanetricaboxylic 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.

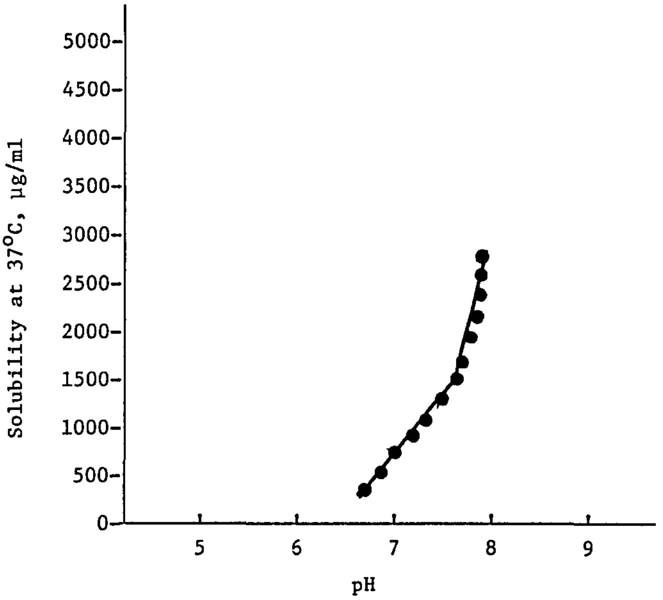
VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The soly of sulfadimethoxypyrimidine 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-(2-methyl-4-pyrimidinyl)-; $C_{11}H_{12}N_4O_2S$; [599-84-8]

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

ORIGINAL MEASUREMENTS:

Roblin, R. O., Jr.; Winnek, P. S.; English, J. P.; *J. Am. Chem. Soc.* 1942, *64*, 567-70.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of 4-amino-N-(2-methyl-4-pyrimidinyl)benzenesulfonamide in water at 37°C is 623 mg/100 cm^3 solution (2.36×10^{-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 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 207-8°C (cor), was prepd by the authors. Anal: %C 50.2 (calcd 50.0); %H 4.6 (4.6); %N 21.4 (21.2).

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:	EVALUATOR:
(1) Benzenesulfonamide, 4-amino-N-(2-6-dimethyl-4-pyrimidinyl)- (sulfasomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Water	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 value of 6.86 x 10^{-3} mol dm^{-3} at 310K as given by Kaneniwa et al. (1) is based on 3-5 days equilibration and accurate spectrophotometric analytical method. The temperature variation was well controlled, ±0.05K. Five years later, Goto et al. (2), also using several days of equilibration and a spectrophotometric analysis provided a value of 6.75 x 10^{-3} mol dm^{-3}, in good agreement with the earlier one. The recommended value is given as 6.80 x 10^{-3} mol dm^{-3} in water at 310K.

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

REFERENCES:

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

(2) Goto, S.; Komatsu, M.; Tagawa, K.; Kawata, M. *Chem. Pharm. Bull.* 1983, *31(1)*, 256-61.

(3) Mauger, J.W.; Paruta, A.N.; Gerraughty, R.J.; *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

(4) Martin, A.; Miralles, M.J. *J. Pharm. Sci.* 1982, *71(4)*, 439-42.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(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 sulfisomidine in water at 30°C is 5.65 mmol/L (1.57 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfisomidine (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 sulfisomidine 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-(2,6-dimethyl -4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Water; H_2O; [7732-18-5]	**ORIGINAL MEASUREMENTS:** Kaneniwa, N.; Watari, N.; Iijima, H. *Chem. Pharm. Bull.* 1978, *26(9)*, 2603-14.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomidine in water at 37°C is 1.91 mg/ml solution (6.86 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: An excess of sulfisomidine was placed in a flask contg 25 ml of water. The flask was shaken (2 strokes/s at the amplitude of 3 cm) in a thermostatically controlled water bath at 37°C. One-ml sample was withdrawn every 6 h (total equilibration period was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically (1).	**SOURCE AND PURITY OF MATERIALS:** Commercial sulfisomidine of the Japanese Pharmacopeia grade and distd water were used. **ESTIMATED ERROR:** Soly: not specified. Temp: ±0.05°C (authors). **REFERENCES:** 1. Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1974, *22*, 1699.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

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

ORIGINAL MEASUREMENTS:

Goto, S.; Komatsu, M.; Tagawa, K.; Kawata, M.
Chem. Pharm. Bull. 1983, *31(1)*, 256-61.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility	
	g/l	10^3 mol dm^{-3} [a]
37	1.88	6.75
55	3.35	12.0

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A 3 g sample of sulfisomidine powder was accurately weighed into a 20-ml ampul and 10 ml of water was added. The ampul was sealed, placed in a const temp (37° or 55°C) bath and allowed to stand for several days. The equilibrium concn of the solute was measured spectrophotometrically at 538 nm after diazotization with the 0.1% Tsuda reagent (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine had mp 245-9°C (decomp). The purity of water was not specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

1. Tsuda, K.; Matsunaga, S. *Yakugaku Zasshi* 1942, *62*, 362.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(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 sulfisomidine in 0.1N HCl at 37°C is 49.418 mg/ml (0.17755 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 sulfisomidine 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 500-mg uncoated tablets of sulfisomidine were used.

Hydrochloric acid was of reagent grade.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) Carbonic acid, monosodium salt; $NaHCO_3$; [144-55-8]

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.
Tsuchiya, S.; Hiura, M.
Chem. Pharm. Bull. 1973, *21(7)*,
1440-5.

VARIABLES:

One temperature: 37°C; one pH: 8.4

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomidine in a $NaHCO_3$ solution (1.680 g $NaHCO_3$/100 ml water) of pH 8.4 at 37°C is 9.32 mg/ml solution[a] (3.35×10^{-2} mol dm^{-3} solution, compiler).

[a] Numerical value to the graphical data given by one of the authors (S. T.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the $NaHCO_3$ solution were placed in glass-stoppered flask with excess of sulfisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfisomidine was of pharmaceutical grade. The source and purity of $NaHCO_3$ were not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Carbonic acid, disodium salt; Na_2CO_3; [497-19-8] (3) Water; H_2O; [7732-18-5]	Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.
VARIABLES:	PREPARED BY:
One temperature: 37°C; one pH: 11.3	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomidine in a Na_2CO_3 solution (2.210 g Na_2CO_3/100 ml water) of pH 11.3 at 37°C is 37.38 mg/ml solution[a] (0.1343 mol dm^{-3} solution, compiler).

[a] Numerical value to the graphical data was given by one of the author (S. T.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the Na_2CO_3 soln were placed in glass-stoppered flasks with excess of sulfisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supenatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfisomidine was of pharmaceutical grade. The source and purity of Na_2CO_3 were not specified.
Distd water was used.

ESTIMATED ERROR:

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

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) Carbonic acid, disodium salt; Na_2CO_3; [497-19-8]

(3) Carbonic acid, monosodium salt; $NaHCO_3$; [144-55-8]

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M.

Chem. Pharm. Bull. 1973, *21(7)*, 1440-5.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Na_2CO_3	$NaHCO_3$	pH	Solubility at 37°C	
g/100 ml water	g/100 ml water		mg/ml soln[a]	10 mol dm^{-3} soln[b]
0.212	1.512	9.1	11.82	0.4247
0.848	1.008	9.8	25.70	0.9234
1.908	0.168	10.7	34.36	1.2345

[a] Numerical values to the graphical data were given by one of the authors (S. T.) in personal communication.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the carbonate buffer solns were placed in glass-stoppered flasks with excess of sulfisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfisomidine was of pharmaceutical grade. The source and purity of Na_2CO_3 and $NaHCO_3$ were not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfaisodimidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(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. 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 sulfaisodimidine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 190 mg% (6.83×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfaisodimidine at 20°C, their pH was measured at equilibrium, and the sulfaisodimidine was assayed colorimetrically. The measured pH values were then plotted against concn, and the soly at pH 7.4 was detd by interpolation (personal communication).

SOURCE AND PURITY OF MATERIALS:

Nothing specified.

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (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]	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 sulfisomidine in a phosphate buffer solution of pH 7.4 ($\mu = 0.17$) at 30°C is 8.53 mmol/L (2.37 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Sulfisomidine (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 sulfisomidine was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.	Nothing specified. ESTIMATED ERROR: Soly and pH: not specified. Temp: ±1°C (authors). REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (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:** Hekster, Ch. A.; Vree, T. B. *Antibiotics Chemother.* 1982, *31*, 22-118.
VARIABLES: pH	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^3 mol dm^{-3} [a]
5.5	1,580	5.677
7.5[b]	2,480	8.910

[a] Calculated by compiler

[b] Erroneous pH value of 7.0 is given in the article.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method (1) was used (personal communication). Satd solns of sulfisomidine were prepd in phosphate buffers of pH 5.5 and 7.5 at 25°C. The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a Model 748 column oven and a Pye-Unicam LC-UV spectrophotometric detector.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: the detection limit of the solute by HPLC was 0.5 mg/l (authors).

The errors in temp and pH were not specified.

REFERENCES:

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

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (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]	Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M. *Chem. Pharm. Bull.* 1973, *21(7)*, 1440-5.
VARIABLES:	PREPARED BY:
pH	R. Piekos

EXPERIMENTAL VALUES:

Citric acid	Na_2HPO_4	pH	Solubility at 37°C	
g/100 ml water	g/100 ml water		mg/ml soln[a]	10^2 mol dm^{-3} soln[b]
1.680	0.572	3.1	2.98	1.071
1.260	1.144	4.2	1.92	0.690
0.840	1.716	5.8	1.48	0.532
0.420	2.228	6.8	1.81	0.650

[a] Numerical values to the graphical data were given by one of the authors (S. T.) in personal communication.

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the buffer soln were placed in glass-stoppered flasks with excess of sulfisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported method (1).

SOURCE AND PURITY OF MATERIALS:

The sulfisomidine was of pharmaceutical grade. The source and purity of the citric acid and Na_2HPO_4 were not specified. Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, T.; Tsuchiya, S.; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

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

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

ORIGINAL MEASUREMENTS:

Takubo, T.; Matsumaru, H.; Tsuchiya, S.; Hiura, M.

Chem. Pharm. Bull. 1973, *21(7)*, 1440-5.

VARIABLES:

One temperature: 37°C; one pH: 2.1

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomidine in a citric acid solution (2.100 g citric acid per 100 ml water) of pH 2.1 at 37°C is 6.21 mg/ml solution[a] (2.23×10^{-2} mol dm^{-3} solution, compiler).

[a] Numerical value to the graphical data given by one of the authors (S. T.) in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Aliquots of the citric acid soln were placed in glass-stoppered flasks with excess of sulfisomidine. The flasks were allowed to stand at 37±1°C and shaken vigorously for 4 h until equilibrium was established. One ml of the supernatant was removed by means of a filter pipet and sulfisomidine was assayed by the previously reported procedure (1).

SOURCE AND PURITY OF MATERIALS:

The sulfisomidine was of pharmaceutical grade. The source and purity of the citric acid were not specified.

Distd water was used.

ESTIMATED ERROR:

Soly and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

1. Takubo, M; Tsuchiya, S; Hiura, M. *Yakuzaigaku* 1971, *31*, 298.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

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

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

ORIGINAL MEASUREMENTS:

Martin, A,; Miralles, M. J.
J. Pharm. Sci. 1982, *71(4)*, 439-42.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Mole fraction solubility of sulfisomidine in 94.94% (v/v) ethanol at 25°C is 0.001110 (numerical value given in personal communication to compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

About 20 ml of 95% (label) ethanol was introduced into screw-capped vials contg an excess of sulfisomidine. The vials were agitated for 72 h in a shaker bath maintained at 25±0.2°C. After equilibrium was obtained, a filtered aliquot was pipetted, using an automatic micropipet, into a volumetric flask and appropriately dild with MeOH. The solns were analyzed in a Beckmann Model 25 spectrophotometer at 281.5 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine, mp 515.6 K, was from Sigma Chemical, St. Louis, Mo. The 94.94% (v/v) ethanol (labeled 95%), d = 0.8139 g cm^{-3} at 25°C, was from Fisher Scientific, Fair Lawn, N. J. Its purity was not specified.

ESTIMATED ERROR:

Soly: detns were run in triplicate (authors).
Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

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

(3) Formic acid; H_2CO_2; [64-18-6]

(4) Sodium formate; $HCNaO_2$; [141-53-7]

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

ORIGINAL MEASUREMENTS:

Martin, A.; Miralles, M. J.

J. Pharm. Sci. 1982, *71(4)*, 439-42.

VARIABLES:

Concentration of ethanol

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

% Ethanol in aqueous buffer[a]	Mole fraction solubility[b] at 25°C
95	0.001320
90	0.001460
80	0.001660
50	0.000858

[a] The buffer solution was prepared by mixing together 29.9107 g HCO_2H, 2.0500 g NaOH, and 470.0393 g distilled water. Its pH was 2.59 (personal communication to compiler).

[b] Numerical values given in personal communication to compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

About 20 ml of the solvent mixt was introduced into screw-capped vials contg an excess of sulfisomidine. The vials were agitated for 72 h in a shaker bath maintained at 25±0.2°C. After equilibrium was obtained, a filtered aliquot was pipetted, using an automatic micropipette, into a volumetric flask and appropriately dild with MeOH. The solns were analyzed in a Beckmann Model 25 spectrophotometer at 281.5 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine, mp 515,6 K, was from Sigma Chemicals, St. Louis, Mo. Ethanol (94.94% v/v) and NaOH were from Fisher Scientific, Fair Lawn, N. J.

The source and purity of formic acid were not specified.

Distilled water was used.

ESTIMATED ERROR:

Soly: detns were run in triplicate (authors).

TEmp: ±0.2°C (authors).

REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Methanol; CH_4O; [67-56-1]	ORIGINAL MEASUREMENTS: Mauger, J. W.; Paruta, A.N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.
VARIABLES: Temperature	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	11.2
30	12.7
37	16.5

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and methanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

Methanol: spectrophotometric grade solvent, Mallinckdrodt Chem Works.

ESTIMATED ERROR:

Soly: av values of 3 detns are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) Methanol; CH_4O; [67-56-1]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug. Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^3 X [a]	10^2 mol dm^{-3} [b]
25	7.64	1.12	2.74
30	8.67	1.27	3.15
37	11.2	1.65	4.02

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. Methanol was a spectrograde solvent from the Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av of at least 3 detn is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

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

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^{\circ}C$	Mole fraction solubility (x 10^4)
25	5.53
30	6.38
37	8.20

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and ethanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

Ethanol was from the U. S. Industrial Chemicals Co. (purity not specified).

ESTIMATED ERROR:

Soly: av values of 3 detns are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Ethanol; C_2H_6O; [64-17-5]	Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.
VARIABLES:	**PREPARED BY:**
Temperature	R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^4 X [a]	10^2 mol dm^{-3} [b]
25	2.63	5.53	0.945
30	3.02	6.38	1.08
37	3.86	8.20	1.39

[a] X = mole fraction

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. Ethanol was from the U.S. Industrial Chemicals Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Ethanol; C_2H_6O; [64-17-5]	ORIGINAL MEASUREMENTS: Martin, A.; Miralles, M. J. *J. Pharm. Sci.* 1982, *71(4)*, 439-42.
VARIABLES: One temperature: 25°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Mole fraction solubility of sulfisomidine in absolute ethanol at 25°C is 0.000557 (numerical value given in personal communication to compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

About 20 ml of abs ethanol was introduced into screw-capped vials contg an excess of sulfisomidine. The vials were agitated for 72 h in a shaker bath maintained at 25±0.2°C. After equilibrium was obtained, a filtered aliquot was pipetted, using an automatic micropipette, into a volumetric flask and appropriately dild with MeOH. The solns were analyzed in a Beckmann Model 25 spectrophotometer at 281.5 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine, mp 515.6 K, was from Sigma Chemicals, St. Louis, Mo., and abs ethanol was from Commercial Solvent, Terre Haute, Ind., and contained 0.57% (v/v) water. The reagents were tested for identity and purity.

ESTIMATED ERROR:

Soly: detns were run in triplicate (authors).

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) Ethanol, 2-ethoxy-, $C_4H_{10}O_2$; [110-80-5]

ORIGINAL MEASUREMENTS:

Sunwoo, C.; Eisen, H.

J. Pharm. Sci. 1971, *60*, 238-44.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfisomidine in 2-ethoxyethanol at 25°C is 0.0111 (3.35 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Soly was detd by the method reported by Restaino and Martin (1). Sulfisomidine was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 270 nm after diln of a sample with 95% alcohol or water.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine (Ciba Pharmaceutical Co., Summit, N. J.) was recrystd from warm alcohol. 2-Ethoxyethanol was of industrial grade (Cellosolve solvent, Union Carbide, New York, N. Y.).

ESTIMATED ERROR:

Temp: ±1.0°C (authors).

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

REFERENCES:

1. Restaino, F. A.; Martin, A. N. *J. Pharm. Sci.* 1964, *53*, 636.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) 1-Propanol; C_3H_8O; [71-23-8]	**ORIGINAL MEASUREMENTS:** Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	4.23
30	4.89
37	6.48

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and 1-propanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

1-Propanol was a Baker Analyzed Reagent, J. T. Baker Chemical Co.

ESTIMATED ERROR:

Soly: av values of 3 detns are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Propanol; C_3H_8O; [71-23-8]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr. Alexander, K. S.; Paruta, A. N. *Drug. Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	$10^4 x^a$	10^3 mol dm^{-3} ^{b}
25	1.57	4.23	5.64
30	1.81	4.89	6.50
37	2.39	6.48	8.59

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. 1-Propanol was Baker Analyzed Reagent (J.T. Baker Chemical Co.). Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Butanol; $C_4H_{10}O$; [71-36-3]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	3.44
30	4.17
37	5.56

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and 1-butanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predtd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

1-Butanol was from the Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) 1-Butanol; $C_4H_{10}O$; [71-36-3]	**ORIGINAL MEASUREMENTS:** Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^4 X^a	10^3 mol dm^{-3} ^{b}
25	1.04	3.44	3.74
30	1.26	4.17	4.53
37	1.67	5.56	6.00

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot 2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. 1-Butanol was from the Mallinckrodt Chemical Works. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Pentanol; $C_5H_{12}O$; [71-41-0]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	2.84
30	3.43
37	4.54

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and 1-pentanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

1-Pentanol was from Fisher Scientific Co.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Pentanol; $C_5H_{12}O$; [71-41-0]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N.
Drug. Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

$t/^\circ C$	Solubility		
	mg/ml	10^4 X^a	10^3 mol dm^{-3} ^{b}
25	0.73	2.84	2.62
30	0.88	3.43	3.16
37	1.16	4.54	4.17

^{a} X = mole fraction

^{b} Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. 1-Pentanol was from Fisher Scientific Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Octanol; $C_8H_{18}O$; [111-87-5]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	1.36
30	1.83
37	2.44

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and 1-octanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

1-Pentanol was from Fisher Scientific Cp.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Octanol; $C_8H_{18}O$; [111-87-5]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N.
Drug Dev. Ind. Pharm. 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^4 X^a	10^3 mol dm^{-3} ^{b}
25	0.24	1.36	0.86
30	0.32	1.83	1.15
37	0.43	2.44	1.55

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. 1-Octanol was from Fisher Scientific Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

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

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_4S$; [515-64-0] (2) 1-Decanol; $C_{10}H_{22}O$ [112-30-1]	**ORIGINAL MEASUREMENTS:** Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J.; *J. Pharm. Sci.* 1972, *61(1)*, 94-7.
VARIABLES: Temperature	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	1.80
30	2.04
37	2.53

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfisomidine in excess and 1-decanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498 from Ciba Pharmaceutical Co.

1-Decanol was from Matheson, Coleman and Bell.

ESTIMATED ERROR:

Soly: av values of 3 runs are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) 1-Decanol; $C_{10}H_{22}O$; [112-30-1]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^4 X^a	10^3 mol dm^{-3} a
25	0.26	1.80	0.93
30	0.30	2.04	1.08
37	0.37	2.53	1.33

[a] X = mole fraction

[b] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine: lot E2498, Ciba Pharmaceutical Co. Its mp agreed with the literature value. 1-Decanol was from Matheson, Coleman and Bell. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0]

(2) n-Hexane; C_6H_{14}; [110-54-3]

ORIGINAL MEASUREMENTS:

Martin, A.; Miralles, M. J.
J. Pharm. Sci. 1982, *71(4)*, 439-42.

VARIABLES:

One temperature: 25°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Mole fraction solubility of sulfisomidine in n-hexane at 25°C is 0.000038 (numerical value given in personal communication - compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

About 20 ml of n-hexane was introduced into screw-capped vials contg an excess of sulfisomidine. The vials were agitated for 72 h in a shaker bath maintained at 25±0.2°C. After equilibrium was obtained, a filtered aliquot was pipetted, using an automatic micropipette, into a volumetric flask and appropriately dild with MeOH. The solns were analyzed in a Beckmann Model 25 spectrophotometer at 281.5 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine, mp 515.6 K, was from Sigma Chemicals, St. Louis, Mo., and n-hexane was from Aldrich Chemical, Milwaukee, Wis. They were tested for identity and purity.

ESTIMATED ERROR:

Soly: the detn was made in triplicate (authors).

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfaisodimidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	Riess, W. *Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart* 1963, *1*, 627-32.
VARIABLES:	PREPARED BY:
One temperature: 20°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfaisodimidine in chloroform at 20°C is 38 mg%

(1.4 x 10^{-3} 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:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.
VARIABLES:	PREPARED BY:
One temperature: 30°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomidine in chloroform at 30°C is 1.63 mmol/L (0.454 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Sulfisomidine (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 sulfisomidine was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.	Nothing specified. ESTIMATED ERROR: Soly: not specified. Temp: ±1°C (authors). REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethyl-4-pyrimidinyl)- (sulfisomidine); $C_{12}H_{14}N_4O_2S$; [515-64-0] (2) Ethanol; C_2H_6O; [64-17-5] (3) n-Hexane; C_6H_{14}; [110-54-3]	Martin, A.; Miralles, M. J. *J. Pharm. Sci.* 1982, *71(4)*, 439-42.
VARIABLES:	**PREPARED BY:**
Concentration of n-hexane	R. Piekos

EXPERIMENTAL VALUES:

% n-Hexane	Mole fraction solubility[a] at 25°C
75	0.000037
60	0.000088
40	0.000207
20	0.000392
10	0.000473

[a]Numerical values given in personal communication to compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

About 20 ml of the solvent mixt was introduced into screw-capped vials contg an excess of sulfisomidine. The vials were agitated for 72 h in a shaker bath maintained at 25±0.2°C. After equilibrium was obtained, a filtered aliquot was pipetted, using an automatic micropipette, into a volumetric flask and appropriately dild with MeOH. The solns were analyzed in a Beckmann Model 25 spectrophotometer at 281.5 nm.

SOURCE AND PURITY OF MATERIALS:

Sulfisomidine, mp 515.6 K, was from Sigma Chemicals, St. Louis, Mo., and abs ethanol was from Commercial Solvent, Terre Haute, Ind., and contained 0.57% (v/v) water, n-Hexane was from Aldrich Chemical, Milwaukee, Wis. The reagents were tested for identity and purity.

ESTIMATED ERROR:

Soly: detns were made in triplicate (authors).

Temp: ±0.2°C (authors).

REFERENCES:

COMPONENTS:

(1) Zinc, ($\underline{T}$-4)-bis[4-amino-$\underline{N}$-(2,6-dimethyl-4-pyrimidinyl)benzenesulfonamidato-$\underline{N}^{N}$,$\underline{O}$]-
(Zn(II) sulfisomidine);
$C_{24}H_{24}N_8O_4S_2Zn$; [71261-88-6]

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

ORIGINAL MEASUREMENTS:

Fox, Ch. L., Jr.; Modak, S.;
Stanford, J. W.; Fox, P. L.
Scand. J. Plast. Reconstr. Surg. 1979, *13(1)*, 89-94.

VARIABLES:

One temperature: 28-30°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of Zn(II) sulfisomidine in water at room temperature (28-30°C)[a] is 171.0 mg% (2.758×10^{-3} 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) sulfisomidine was prepd in water and after 24 h aliquots from the clear supernatant were assayed for sulfisomidine content using the colorimetric method of Bratton and Marshall (1). The soly was then calculated from the molecular formula.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

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

COMPONENTS:

(1) Acetamide, N-[4-[[(2,6-dimethyl-4-pyrimidinyl)amino]sulfonyl]phenyl]-(N^4-acetylsulfisomidine); $C_{14}H_{16}N_4O_3S$; [3163-31-3]

(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:

Hekster, Ch. A.; Vree, T. B.
Antibiotics Chemother. 1982, *31*, 22-118.

VARIABLES:

pH

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^4 mol dm^{-3} [a]
5.5	53	1.65
7.5[b]	128	3.99

[a] Calculated by compiler.

[b] Erraneous pH vaue of 7.0 is given in the article.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier developed method (1) was used (personal communication). Satd solns of N^4-acetylsulfisomidine were prepd in phosphate buffers of pH 5.5 and 7.5 at 25°C. The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a Model 748 column oven and a Pye-Unicam LC-UV spectrophotometric detector.

SOURCE AND PURITY OF MATERIALS:

Neither source nor the purity of the materials was specified.

ESTIMATED ERROR:

Soly: the detection limit of the solute by HPLC was 0.5 mg/l (authors).
The errors in temp and pH were not specified.

REFERENCES:

1. Hekster, Y. A.; Vree, T. B.; Damsma, J. E.; Friesen, W. T. *J. Anitmicrob. Chemother.* 1981, *8*, 133.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2-6-dimethoxy-4-pyrimidinyl) (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2] (2) Water or Aqueous HCl	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 sulfadimethoxine in water at 310K was reported by Watari, Hanano and Kaneniwa in two different journals (1,2); the determined value of the solubility for sulfadimethoxine given as 1.49 x 10^{-4} mol dm^{-3}. Except for the source of the material all experimental conditions were identical. With the assumption that the commercial grade (1), purified by crystallization, was equivalent to the pharmacopeial grade (2), the recommended value of solubility in water at 310K is 1.49 x 10^{-4} mol dm^{-3}.

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

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

(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 sulfadimethoxine in water at 30°C is 0.10 mmol/L (3.1×10^{-2} g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadimethoxine (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 sulfadimethoxine 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-(2,6-dimethoxy-4-pyrimidinyl)-
(sulfadimethoxine); $C_{12}H_{14}N_4O_4S$;
[122-11-2]

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

ORIGINAL MEASUREMENTS:

Watari, N.; Hanano, M.; Kaneniwa, N.
Chem. Pharm. Bull. 1980, *28(7)*,
2221-5.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimethoxine in water at 37°C is 4.63 mg/100 ml
(1.49×10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier reported app and procedure was employed (1): an excess of sulfadimethoxine, required to saturate the medium, was placed in a flask contg 25 ml of water. The flask was shaken (2 strokes/s) at the amplitude of 3 cm in a thermostatically controlled water bath at 37±0.05°C. One-ml sample was removed every 6 h (total equilibration period was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300), and the filtrate was dild with water and assayed spectrophotometrically.

SOURCE AND PURITY OF MATERIALS:

Comm sulfadimethoxine was recrystd from EtOAc and sieved through a Ro-Tap testing sieve shaker.

Distd water was used.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Kaneniwa, N.; Watari, N.
Chem. Pharm. Bull. 1974, *22*,
1699.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2] (2) Water; H_2O; [7732-18-5]	ORIGINAL MEASUREMENTS: Watari, N.; Kaneniwa, N.; Hanano, M. *Int. J. Pharm.* 1980, *6(2)*, 155-66.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimethoxine in water at 37°C is 4.63 mg/100 ml (1.49 x 10^{-4} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE: The earlier developed method was employed (1), whereby an excess of sulfadimethoxine, required to saturate medium, was placed in a flask contg 25 ml of water. The flask was stroken (2 strokes/s) at an amplitude of 3 cm, in a thermostatically controlled bath. One-ml sample was removed every 6 h (total equilibration time was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically.	SOURCE AND PURITY OF MATERIALS: Sulfadimethoxine was of the Japanese Pharmacopeia grade. Distilled water was used. ESTIMATED ERROR: Soly: not specified. Temp: ±0.05°C (authors). REFERENCES: 1. Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1974, *22*, 1699.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxime); $C_{12}H_{14}N_4O_4S$; [122-11-2] (2) Hydrochloric acid; HCl; [7647-01-0] (3) Water; H_2O; [7732-18-5]	Ogata, H. ; Shibazaki, T.; Inoue, T.; Ejima, A. *Chem. Pharm. Bull.* 1979, *27(6)*, 1281-6.
VARIABLES:	PREPARED BY:
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimethoxine in 0.1N HCl at 37°C is 0.606 mg/ml (1.95×10^{-3} 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 sulfadimethoxine 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 μ m), and the procedure was repeated until a const concn was obtained.

SOURCE AND PURITY OF MATERIALS:

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

ESTIMATED ERROR:

Nothing specified.

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

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

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

ORIGINAL MEASUREMENTS:

Watari, N.; Hanano, M.; Kaneniwa, N.; *Chem. Pharm. Bull.* 1980, *28(7)*, 2221-5.

VARIABLES:

One temperature: 37°C

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfadimethoxine in 0.1N HCl solution at 37°C is 24.6 mg/100 ml (7.93×10^{-4} mol dm^{-3} - compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The earlier reported app and procedure was employed (1): an excess of sulfadimethoxine, required to saturate the medium, was placed in a flask contg 25 ml of 0.1N HCl soln. The flask was shaken (2 strokes/s) at the amplitude of 3 cm in a thermostatically controlled water bath at 37±0.05°C. One-ml sample was removed every 6 h (total equilibration period was 3-5 days) using a warmed Millipore filter syringe with a filter pore size of 0.45 μ (Millipore HAWP 01300), and the filtrate was dild with water and assayed spectrophotometrically.

SOURCE AND PURITY OF MATERIALS:

Comm sulfadimethoxine was recrystd from EtOAc and sieved through a Ro-Tap testing sieve shaker.

Source and purity of the 0.1N HCl soln were not specified.

ESTIMATED ERROR:

Soly: not specified.

Temp: ±0.05°C (authors).

REFERENCES:

1. Kaneniwa, N.; Watari, N. *Chem. Pharm. Bull.* 1974, *22*, 1699.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

(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:

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 sulfadimethoxine in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 28 mg% (9.0×10^{-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 sulfadimethoxine at 20°C, their pH was measured at equilibrium, and the sulfadimethoxine 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-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

(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 sulfadimethoxine in a phosphate buffer solution of pH 7.4 (μ = 0.17) at 30°C is 1.73 mmol/L (0.537 g dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfadimethoxine (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 sulfadimethoxine 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 and pH: not specified.

Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

(2) Methanol; CH_4O; [67-56-1]

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*,

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	11.6
30	13.9
37	17.7

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadimethoxine and methanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadimethoxine: lot 203057, Hoffmann-La Roche, Inc.

Methanol: spectrophotometric grade solvent, Mallinckrodt Chem Works.

ESTIMATED ERROR:

Soly: av values of 3 detns are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2] (2) Methanol; CH_4O; [67-56-1]	Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* <u>1977,</u> *3(2),* 163-83.
VARIABLES:	**PREPARED BY:**
Temperature	R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^3 X [a]	10^2 mol dm^{-3} [b]
25	8.84	1.16	2.85
30	10.5	1.39	3.38
37	13.4	1.77	4.32

[a] X = mole fraction

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadimethoxine: lot 203027, Hoffman-La Roche, Inc. Its mp agreed with the literature value. Methanol was a spectrograde solvent from the Mallinckrodt Chemical Works.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

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

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

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

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94-7.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Mole fraction solubility (x 10^4)
25	7.14
30	8.58
37	11.00

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A const temp bath contg screw-capped bottles with sulfadimethoxine in excess and ethanol was rotated for 24 h. Samples were withdrawn through a pledget of glass wool into a pipet, which was wiped clean and allowed to drain into a volumetric flask. Solute concns were detd by spectrophotometric assay at predetd wavelengths using a Cary model 16 spectrophotometer (1).

SOURCE AND PURITY OF MATERIALS:

Sulfadimethoxine: lot 203057, Hoffmann - La Roche, Inc.

Ethanol (purity not specified) was from U.S. Industrial Chemicals Co.

ESTIMATED ERROR:

Soly: av values of 3 detns are given (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Paruta, A. N.; Mauger, J. W. *J. Pharm. Sci.* 1971, *60*, 432.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)- (sulfadimethoxine); $C_{12}H_{14}N_4O_4S$; [122-11-2]

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

ORIGINAL MEASUREMENTS:

Mauger, J. W.; Petersen, H., Jr.; Alexander, K. S.; Paruta, A. N. *Drug Dev. Ind. Pharm.* 1977, *3(2)*, 163-83.

VARIABLES:

Temperature

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

t/°C	Solubility		
	mg/ml	10^4 X [a]	10^2 mol dm^{-3} [b]
25	3.78	7.14	1.22
30	4.52	8.58	1.46
37	5.74	11.00	1.85

[a] X = mole fraction

[b] Calculated by compiler.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

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

SOURCE AND PURITY OF MATERIALS:

Sulfadimethoxine: lot 203027, Hoffmann La Roche, Inc. Its mp agreed with the literature value. Ethanol was from the U. S. Industrial Chemicals Co. Its refractive index value and density agreed with literature values.

ESTIMATED ERROR:

Soly: av of at least 3 detns is reported (authors).

Temp: ±0.1°C (authors).

REFERENCES:

1. Mauger, J. W.; Paruta, A. N.; Gerraughty, R. J. *J. Pharm. Sci.* 1972, *61(1)*, 94.