

<p>COMPONENTS:</p> <p>(1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-(sulfamethylthiadiazole); $C_9H_{10}N_4O_2S_2$; [144-82-1]</p> <p>(2) Water</p>	<p>EVALUATOR:</p> <p>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</p>
<p>CRITICAL EVALUATION:</p> <p>At 310K, three values were available (1-3) for the aqueous solubility of this compound: Durel and Allinne (1) reported a value of $3.25 \times 10^{-3} \text{ mol dm}^{-3}$. Kaneniwa and Watari (2) gave a value of $3.27 \times 10^{-3} \text{ mol dm}^{-3}$, a value of $3.27 \times 10^{-3} \text{ mol dm}^{-3}$ in 1978 (3) and in 1980 (4) with Hanano a value of $3.27 \times 10^{-3} \text{ mol dm}^{-3}$ was given. Since all these values were produced by the same workers (2-4) using identical methodologies, the value given was only considered once. The simple average of the two values (1) and (2-4) were taken and a recommended value of $3.26 \times 10^{-3} \text{ mol dm}^{-3}$ is given in water at 310K.</p> <p>REFERENCES:</p> <p>(1) Durel, M.P.; Allinne, M. <i>Bull. Soc. Med. Hop. Paris III</i> <u>1941</u>, 251-9. (2) Watari, N.; Kaneniwa, N. <i>Chem. Pharm. Bull.</i> <u>1976</u>, <i>24(11)</i>, 2577-84. (3) Kaneniwa, N.; Watari, N. <i>Chem. Pharm. Bull.</i> <u>1978</u>, <i>26(3)</i>, 813-26. (4) Watari N.; Kaneniwa, N.; Hanano, M. <i>Int. J. Pharm.</i> <u>1980</u>, <i>6(2)</i>, 155-66.</p>	

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Watari, N.; Kaneniwa, N. <i>Chem. Pharm. Bull.</i> <u>1976</u> , <i>24(11)</i> , 2577-84.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: <p style="text-align: center;">Total solubility of sulfamethizole in water at 37°C is 0.884 mg/ml solution ($3.27 \times 10^{-3} \text{ mol dm}^{-3}$, compiler).</p>	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: An excess of sulfamethizole, 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 sulfamethizole of the Japanese Pharmacopeia grade and distd water were used. ESTIMATED ERROR: Soly: not specified Temp: $\pm 0.05^\circ\text{C}$ (authors). REFERENCES: 1. Kaneniwa, N.; Watari, N. <i>Chem. Pharm. Bull.</i> <u>1974</u> , <i>22</i> , 1699.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-(sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Watari, N.; Kaneniwa, N.; Hanano, M. <i>Int. J. Pharm.</i> <u>1980</u> , <i>6(2)</i> , 155-66.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: <p style="text-align: center;">Solubility of sulfamethizole in water at 37°C is 88.4 mg/100 ml (3.27×10^{-3} mol dm⁻³, compiler).</p>	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: The earlier developed method was employed (1), whereby an excess of sulfamethizole, required to saturate medium, was placed in a flask contg 25 ml of water. The flask was shaken (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 soze pf 0.45 μ (Millipore HAWP 01300) and the filtrate was dild with water and assayed spectrophotometrically.	SOURCE AND PURITY OF MATERIALS: Sulfamethizole 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. <i>Chem. Pharm. Bull.</i> <u>1974</u> , <i>22</i> , 1699.

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Goto, S.; Komatsu, M.; Tagawa, K.; Kawata, M. <i>Chem. Pharm. Bull.</i> <u>1983</u> , <i>31(1)</i> , 256-61.											
VARIABLES: Temperature	PREPARED BY: R. Piekos											
EXPERIMENTAL VALUES: <table border="1" data-bbox="395 661 875 903"> <thead> <tr> <th rowspan="2">t/°C</th> <th colspan="2">Solubility</th> </tr> <tr> <th>g/l</th> <th>$10^3 \text{ mol dm}^{-3} \text{ a}$</th> </tr> </thead> <tbody> <tr> <td>37</td> <td>0.87</td> <td>3.22</td> </tr> <tr> <td>55</td> <td>2.10</td> <td>7.77</td> </tr> </tbody> </table> <p data-bbox="454 943 751 973" style="text-align: center;">^a Calculated by compiler</p>		t/°C	Solubility		g/l	$10^3 \text{ mol dm}^{-3} \text{ a}$	37	0.87	3.22	55	2.10	7.77
t/°C	Solubility											
	g/l	$10^3 \text{ mol dm}^{-3} \text{ a}$										
37	0.87	3.22										
55	2.10	7.77										
AUXILIARY INFORMATION												
METHOD/APPARATUS/PROCEDURE: A 3 g sample of sulfamethizole 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 542 nm after diazotization with the 0.1% Tsuda reagent (1).	SOURCE AND PURITY OF MATERIALS: Sulfamethizole had mp 207-11°C. The purity of water was not specified. ESTIMATED ERROR: Nothing specified. REFERENCES: 1. Tsuda, K.; Matsunaga, S. <i>Yakugaku Zasshi</i> <u>1942</u> , <i>62</i> , 362.											

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Hydrochloric acid; HCl; [7647-01-0] (3) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Ogata, H.; Shibasaki, T.; Inoue, T.; Ejima, A. <i>Chem. Pharm. Bull.</i> <u>1979</u> , <i>27(6)</i> , 1281-6.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: Solubility of sulfamethizole in 0.1N HCl at 37°C is 9.172 mg/ml (3.393×10^{-2} mol dm^{-3} , compiler).	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: A centrifuge tube contg 30 ml of 0.1N HCl and 0.5-3.0 g of the sulfamethizole powder was tightly sealed and shaken at 37°C. The concn of the dissolved drug was detd spectrophotometrically following filtration through a Millipore filter (type EH, pore size 0.5 μm), and the procedure was repeated every 24 h until a const concn was obtained.	SOURCE AND PURITY OF MATERIALS: Comm available 250-mg uncoated tablets of sulfamethizole were used. Hydrochloric acid was of reagent grade. ESTIMATED ERROR: Nothing specified REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-(sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Hydrochloric acid; HCl; [7647-01-0] (3) Sodium chloride; NaCl; [7647-14-5] (4) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Nicklasson, M.; Brodin, A.; Nyqvist, H. <i>Acta Pharm. Suec.</i> <u>1981</u> , <i>18</i> , 119-28.
VARIABLES: One temperature: 37°C; one pH: 1.20	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: <p style="text-align: center;">Solubility of sulfamethizole in a HCl - NaCl buffer solution of pH 1.20 (ionic strength 0.2) at 37°C is 5.62 mg/ml^a (2.08×10^{-2} mol dm⁻³, compiler).</p> <p>^aNumerical value given by one of the authors (M. N.)</p>	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: Sulfamethizole, taken in excess of a quantity required for satn, was added to the HCl-NaCl buffer soln of pH 1.20. The suspension was equilibrated at 37°C for 18-24 h using a magnetic stirrer. No degradation of the drug was observed at the pH indicated. Five-ml samples were filtered through 0.1- μ m polycarbonate filters (Nuclepore [®] Co.), and dild to suitable concn for spectrophotometry. Concns were determined using a Pye Unicam SP8-100 spectrophotometer. Samples were assayed at wavelengths of max absorption, taking into consideration changes in spectra due to ionization.	SOURCE AND PURITY OF MATERIALS: Sulfamethizole of commercial grade was used (source not specified). HCl and NaCl were anal grade reagents (source not specified). Purity of the water was not specified. ESTIMATED ERROR: Soly: mean of 2 detns is given (authors). pH : precision ± 0.01 pH unit (authors). Temp: $\pm 0.5^\circ C$ (authors). REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethylthiadiazole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Phosphoric acid, disodium salt; Na_2HPO_4 ; [7558-94-4] (3) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Krüger-Thiemer, E. <i>Arch. Dermatol. Syphilis</i> <u>1942</u> , <u>183</u> , 90-116.
VARIABLES: One temperature: ca 20°C; one pH: 8.74	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: Solubility of sulfamethylthiadiazole in a 0.705 M (10%) Na_2HPO_4 solution of pH 8.74, at room temperature (about 20°C), is 1.625 g% (6.011×10^{-2} mol dm^{-3} solution, compiler).	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: Sulfamethylthiadiazole (0.5 g) was dissolved in 10 cm^3 of the 0.705 M (10%) Na_2HPO_4 solution of pH 8.74, 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 2N HCl, and the sulfonamide content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.	SOURCE AND PURITY OF MATERIALS: Sulfamethylthiadiazole was the product manufd by Schering under the name Tetracid. The source and purity of the remaining materials was not specified. ESTIMATED ERROR: Soly: precision $\pm 5\%$ (author). Temp: not specified. pH : ± 0.05 pH unit (author). REFERENCES: 1. Kimmig, J. <i>Arch. Dermatol.</i> <u>1938</u> , <u>176</u> , <u>722</u> ; <i>Erg. Hyg.</i> <u>1941</u> , <u>24</u> , <u>398</u> .

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazole-2-yl)- (sulfamethylthiadiazol); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Phosphoric acid, monopotassium salt; KH_2PO_4 ; [7778-77-0] (3) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Krüger-Thiemer, E. <i>Arch. Dermatol. Syphilis</i> <u>1942</u> , <i>183</i> , 90-116.
VARIABLES: One temperature: ca 20°C; one pH: 4.37	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: Solubility of sulfamethylthiadiazole in a 0.735 M (10%) KH_2PO_4 solution of pH 4.37, at room temperature (about 20°C), is 0.027 g% (9.99×10^{-2} mol dm^{-3} solution, compiler).	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: Sulfamethylthiadiazole (0.5 g) was dissolved in 10 cm^3 of the 0.735 M (10%) KH_2PO_4 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 2N HCl, and the sulfonamide content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultragraph using a glass electrode.	SOURCE AND PURITY OF MATERIALS: Sulfamethylthiadiazole was the product manufd by Schering under the name Tetracid. The source and purity of the remaining reagents were not specified.
	ESTIMATED ERROR: Soly: precision $\pm 5\%$ (author) Temp: not specified pH : ± 0.05 pH unit (author)
	REFERENCES: 1. Kimmig, J. <i>Arch. Dermatol.</i> <u>1938</u> , <i>176</i> , 722; <i>Erg. Hyg.</i> <u>1941</u> , <i>24</i> , 398.

COMPOSITION OF 1/15 M PHOSPHATE BUFFER SOLUTIONS				SOLUBILITY			
Na ₂ HPO ₄	KH ₂ PO ₄	%Content	pH	Room temp (ca 20°C)		37°C	
				g%	10 ² mol dm ⁻³ solution	g%	10 ² mol dm ⁻³ solution ^a
1.0	99.0	0.91	4.944	0.058	0.214	-	-
10.0	90.0	0.91	5.906	0.155	0.573	0.212	0.784
61.1	38.9	0.93	7.005	0.823	3.044	0.913	3.377
9.5	0.5	0.733 ^b	7.51	1.235	4.569	-	-
94.7	5.3	0.95	8.018	1.232	4.557	-	-

^a Calculated by compiler

^b Molar content; 10% buffer solution

COMPONENTS:
 (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazole-2-yl)- (sulfamethylthiadiazole); C₉H₁₀N₄O₂S₂; [144-82-1]
 (2) Phosphoric acid, disodium salt; Na₂HPO₄; [7558-94-4]
 (3) Phosphoric acid, monopotassium salt; KH₂PO₄; [7778-77-0]
 (4) Water; H₂O; [7732-18-5]

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

VARIABLES:
 Temperature, pH

PREPARED BY:
 R. Piekos

EXPERIMENTAL VALUES:

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
 Sulfamethylthiadiazole (0.5 g) was dissolved in 10 cm³ of a buffer soln, shaken for 2 h at 20°C (or left for 48 h at 37°C), and filtered at respective temp. A 1-cm³ aliquot of the filtrate was then withdrawn, cooled (dild for expts at 37°C), acidified with 1 cm³ of 2N HCl, and the sulfonamide content was detd colorimetrically by the method of Marshall modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

SOURCE AND PURITY OF MATERIALS:
 Sulfamethylthiadiazole was the product manufd by Schering under the name Tetracid. 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-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethylthiadiazole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (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: Bandelin, F. J.; Malesh, W. <i>J. Am. Pharm. Assoc. Sci. Ed.</i> <u>1959</u> , 48, 177-81.																										
VARIABLES: <p style="text-align: center;">pH</p>	PREPARED BY: <p style="text-align: center;">R. Piekos</p>																										
EXPERIMENTAL VALUES: <p style="text-align: center;">Solubility of sulfamethylthiadiazole in buffers of varying mixtures of $Na_2HPO_4 \cdot 7H_2O$ (71.6 g/l distilled water; 0.27 mol dm^{-3}, compiler) and KH_2PO_4 (36.3 g/l distilled water; 0.27 mol dm^{-3}, compiler) at 37°C.</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">Initial pH</th> <th colspan="2">Solubility</th> </tr> <tr> <th>mg/100 ml</th> <th>10^2 mol dm^{-3} a</th> </tr> </thead> <tbody> <tr><td>4.5</td><td>105</td><td>0.388</td></tr> <tr><td>5.0</td><td>125</td><td>0.462</td></tr> <tr><td>5.5</td><td>200</td><td>0.739</td></tr> <tr><td>6.0</td><td>470</td><td>1.738</td></tr> <tr><td>6.5</td><td>1000</td><td>3.699</td></tr> <tr><td>7.0</td><td>1990</td><td>7.361</td></tr> <tr><td>8.0</td><td>9250</td><td>34.218</td></tr> </tbody> </table> <p style="text-align: center;">^a Calculated by compiler</p>		Initial pH	Solubility		mg/100 ml	10^2 mol dm^{-3} a	4.5	105	0.388	5.0	125	0.462	5.5	200	0.739	6.0	470	1.738	6.5	1000	3.699	7.0	1990	7.361	8.0	9250	34.218
Initial pH	Solubility																										
	mg/100 ml	10^2 mol dm^{-3} a																									
4.5	105	0.388																									
5.0	125	0.462																									
5.5	200	0.739																									
6.0	470	1.738																									
6.5	1000	3.699																									
7.0	1990	7.361																									
8.0	9250	34.218																									
AUXILIARY INFORMATION																											
METHOD/APPARATUS/PROCEDURE: Solns were prepd by adding an excess of sulfamethylthiadiazole to 10 ml of buffer soln at each pH level in 18 x 150-mm test tubes, stoppering the tubes and placing them in a water bath at 37°C with gentle agitation for 24 h. The mixt was then filtered and a 1-ml aliquot was accurately pipetted into a volumetric flask for diln and analysis. The balance was retained for pH detn to ascertain any change in pH value. The sulfonamide was assayed colorimetrically by the method of Bratton and Marshall as described in detail by Biamonte and Schneller (1). A standard curve was prepd using accurately prepd standard solutions.	SOURCE AND PURITY OF MATERIALS: Neither source nor purity of the reagents were specified. Distilled water was used.																										
ESTIMATED ERROR: Soly: av values of duplicate runs are reported (authors). Temp and pH: not specified.																											
REFERENCES: 1. Biamonte, A. R.; Schneller, G. E. <i>J. Am. Pharm. Assoc. Sci. Ed.</i> ; <u>1952</u> , 41, 341.																											

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (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.; <i>J. Antimicrob. Chemother.</i> 1981, 8, 133-44.											
VARIABLES: <p style="text-align: center;">pH</p>	PREPARED BY: <p style="text-align: center;">R. Piekos</p>											
EXPERIMENTAL VALUES: <table style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">pH</th> <th colspan="2">Solubility at 25°C</th> </tr> <tr> <th>mg/l</th> <th>$10^3 \text{ mol dm}^{-3} \text{ a}$</th> </tr> </thead> <tbody> <tr> <td>5.5</td> <td>1555</td> <td>5.752</td> </tr> <tr> <td>7.5</td> <td>5022</td> <td>18.578</td> </tr> </tbody> </table> <p style="text-align: center;">^aCalculated by compiler</p>		pH	Solubility at 25°C		mg/l	$10^3 \text{ mol dm}^{-3} \text{ a}$	5.5	1555	5.752	7.5	5022	18.578
pH	Solubility at 25°C											
	mg/l	$10^3 \text{ mol dm}^{-3} \text{ a}$										
5.5	1555	5.752										
7.5	5022	18.578										
AUXILIARY INFORMATION												
METHOD/APPARATUS/PROCEDURE: Satd solns of sulfamethizole 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 sulfamethizole 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-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Phosphoric acid; H_3PO_4 ; [7664-38-2] (3) Phosphoric acid; monosodium salt; NaH_2PO_4 ; [7558-80-7] (4) Sodium chloride; $NaCl$; [7647-14-5] (5) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Nicklasson, M.; Brodin, A.; Nyqvist, H. <i>Acta Pharm. Suec.</i> 1981, 18, 119-28.											
VARIABLES: pH	PREPARED BY: R. Piekos											
EXPERIMENTAL VALUES: <table style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">pH</th> <th colspan="2">Solubility in a $H_3PO_4 - NaH_2PO_4 - NaCl$ buffer solution (ionic strength 0.2) at 37°C^a</th> </tr> <tr> <th>mg/ml</th> <th>10^3 mol dm^{-3} ^b</th> </tr> </thead> <tbody> <tr> <td>1.93</td> <td>1.73</td> <td>6.40</td> </tr> <tr> <td>3.15</td> <td>0.76</td> <td>2.81</td> </tr> </tbody> </table> <p style="text-align: center;"> ^a Numerical values given by one of the authors (M.N.) ^b Calculated by compiler </p>		pH	Solubility in a $H_3PO_4 - NaH_2PO_4 - NaCl$ buffer solution (ionic strength 0.2) at 37°C ^a		mg/ml	10^3 mol dm^{-3} ^b	1.93	1.73	6.40	3.15	0.76	2.81
pH	Solubility in a $H_3PO_4 - NaH_2PO_4 - NaCl$ buffer solution (ionic strength 0.2) at 37°C ^a											
	mg/ml	10^3 mol dm^{-3} ^b										
1.93	1.73	6.40										
3.15	0.76	2.81										
AUXILIARY INFORMATION												
METHOD/APPARATUS/PROCEDURE: Sulfamethizole, taken in excess of a quantity required for satn, was added to the $H_3PO_4 - NaH_2PO_4 - NaCl$ buffer soln and the suspension was equilibrated at 37°C for 18-24 h using a magnetic stirrer. No degradation of the drug was observed at the pH values indicated. Five-ml samples were filtered through 0.1- μm polycarbonate filters (Nuclepore [®] Co.), and dild to suitable concn for spectrophotometry. Concns were determined using a Pye Unicam SP8-100 spectrophotometer. Samples were assayed at wavelengths of max absorption, taking into consideration changes in spectra due to ionization.	SOURCE AND PURITY OF MATERIALS: Sulfamethizole of commercial grade was used (source not specified). The remaining materials were anal grade reagents (source not specified). Purity of the water was not specified.											
	ESTIMATED ERROR: Soly: mean of 2 detns is given (authors). pH : precision ± 0.01 pH unit (authors). Temp: $\pm 0.5^\circ\text{C}$ (authors).											
	REFERENCES:											

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Phosphoric acid, disodium salt; Na_2HPO_4 ; [7558-94-4] (3) 1,2,3-Propanecarboxylic acid, 2-hydroxy- (citric acid); $C_6H_8O_7$; [77-92-9] (4) Sodium chloride; NaCl; [7647-14-5] (5) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Nicklasson, M.; Brodin, A.; Nyqvist, H. <i>Acta Pharm. Suec.</i> <u>1981</u> , <i>18</i> , 119-28.															
VARIABLES: <p style="text-align: center;">pH</p>	PREPARED BY: <p style="text-align: center;">R. Piekos</p>															
EXPERIMENTAL VALUES: <p style="text-align: center;">Solubility in a citric acid - Na_2HPO_4- NaCl buffer solution (ionic strength 0.2) at 37°C^a</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th style="text-align: center;">pH</th> <th style="text-align: center;">mg/ml</th> <th style="text-align: center;">mol dm⁻³ b</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">4.50</td> <td style="text-align: center;">0.77</td> <td style="text-align: center;">2.85×10^{-3}</td> </tr> <tr> <td style="text-align: center;">5.32</td> <td style="text-align: center;">1.66</td> <td style="text-align: center;">6.14×10^{-3}</td> </tr> <tr> <td style="text-align: center;">6.10</td> <td style="text-align: center;">9.55</td> <td style="text-align: center;">3.53×10^{-2}</td> </tr> <tr> <td style="text-align: center;">7.38</td> <td style="text-align: center;">134.9</td> <td style="text-align: center;">0.4990</td> </tr> </tbody> </table> <p>^aNumerical values given by one of the authors (M.N.). ^bCalculated by compiler.</p>		pH	mg/ml	mol dm ⁻³ b	4.50	0.77	2.85×10^{-3}	5.32	1.66	6.14×10^{-3}	6.10	9.55	3.53×10^{-2}	7.38	134.9	0.4990
pH	mg/ml	mol dm ⁻³ b														
4.50	0.77	2.85×10^{-3}														
5.32	1.66	6.14×10^{-3}														
6.10	9.55	3.53×10^{-2}														
7.38	134.9	0.4990														
AUXILIARY INFORMATION																
METHOD/APPARATUS/PROCEDURE: Sulfamethizole, taken in excess of a quantity required for satn, was added to the citric acid- Na_2HPO_4 -NaCl buffer soln and the suspension was equilibrated at 37°C for 18-24 h using magnetic stirrer. No degradation of the drug was observed at the pH values indicated. Five-ml samples were filtered through 0.1- μ m polycarbonate filters (Nuclepore [®] Co.), and dild to suitable concn for spectrophotometry. Concns were determined using a Pye Unicam SP8-100 spectrophotometer. Samples were assayed at wavelengths of max absorption, taking into consideration changes in spectra due to ionization.	SOURCE AND PURITY OF MATERIALS: Sulfamethizole of commercial grade was used (source not specified). The remaining materials were anal grade reagents (source not specified). Purity of the water was not specified.															
ESTIMATED ERROR: Soly: mean of 2 detns is given (authors). pH : precision ± 0.01 pH unit (authors). Temp: $\pm 0.5^\circ C$ (authors).																
REFERENCES:																

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethylthiadiazole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (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: Alric, R.; Puech, R. <i>J. Pharmacol. (Paris)</i> <u>1971</u> , 2(2), 141-54.
VARIABLES: One temperature: 37°C; one pH: 4	PREPARED BY: R. Piekos
EXPERIMENTAL VALUES: <p style="text-align: center;">Intrinsic solubility^a of sulfamethylthiadiazole in a solution 0.025 M in Na_2HPO_4 and 0.05 M in citric acid, of pH 4, at 37°C is $(33.2 \pm 0.8 \times 10^{-4} \text{ mol liter}^{-1})$, compiler)</p> <p>^aUnder "intrinsic solubility" a minimum on the solubility - pH curve is meant which corresponds to the limiting concentration of the undissociated form of sulfamethylthiadiazole.</p>	
AUXILIARY INFORMATION	
METHOD/APPARATUS/PROCEDURE: The soln was equilibrated for 48 h in a thermostat under occasional stirring. Samples were withdrawn through a 1- μ membrane filter, dild with 0.155M NaOH soln to ensure total dissoen of sulfamethylthiadiazole, and the sulfonamide was assayed by UV spectrophotometry.	SOURCE AND PURITY OF MATERIALS: Nothing specified. ESTIMATED ERROR: Soly: std error of 8 measurements was $\pm 0.8 \times 10^{-4} \text{ mol liter}^{-1}$ (authors). pH: accuracy ± 0.5 pH unit (authors). Temp: $\pm 0.1^\circ C$ (authors). REFERENCES:

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethylthiadiazole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Calcium chloride; $CaCl_2$; [10043-52-4] (3) Magnesium chloride; $MgCl_2$; [7786-30-3] (4) Phosphoric acid, monoammonium salt; $NH_4H_2PO_4$; [7722-76-1] (5) Potassium chloride; KCl ; [7447-40-7] (6) Sodium chloride; $NaCl$; [7647-14-5] (7) Urea; CH_4N_2O ; [57-13-6] (8) Water; H_2O ; [7732-18-5]	ORIGINAL MEASUREMENTS: Bandelin, F. J.; Malesh, W. <i>J. Am. Pharm. Assoc. Sci. Ed.</i> <u>1959</u> , 48, 177-81.																							
VARIABLES: pH at 37°C	PREPARED BY: R. Piekos																							
EXPERIMENTAL VALUES: Solubility of sulfamethylthiadiazole in a solution containing $CaCl_2$ 0.143, $MgCl_2$ 0.121, $NH_4H_2PO_4$ 0.300, KCl 1.660, $NaCl$ 2.950 and urea 20 g/dm ³ (synthetic urea, Mosher Vehicle) at 37°C. <table border="1" data-bbox="307 701 842 1024" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">Equilibrium pH</th> <th colspan="2">Solubility</th> </tr> <tr> <th>mg/100 ml</th> <th>10² mol/dm³ a</th> </tr> </thead> <tbody> <tr> <td>4.5</td> <td>120</td> <td>0.444</td> </tr> <tr> <td>5.0</td> <td>150</td> <td>0.555</td> </tr> <tr> <td>5.5</td> <td>260</td> <td>0.962</td> </tr> <tr> <td>6.0</td> <td>620</td> <td>2.293</td> </tr> <tr> <td>6.5</td> <td>1980</td> <td>7.324</td> </tr> <tr> <td>6.9</td> <td>8400</td> <td>31.074</td> </tr> </tbody> </table> <p style="text-align: center;">^aCalculated by compiler</p>		Equilibrium pH	Solubility		mg/100 ml	10 ² mol/dm ³ a	4.5	120	0.444	5.0	150	0.555	5.5	260	0.962	6.0	620	2.293	6.5	1980	7.324	6.9	8400	31.074
Equilibrium pH	Solubility																							
	mg/100 ml	10 ² mol/dm ³ a																						
4.5	120	0.444																						
5.0	150	0.555																						
5.5	260	0.962																						
6.0	620	2.293																						
6.5	1980	7.324																						
6.9	8400	31.074																						
AUXILIARY INFORMATION																								
METHOD/APPARATUS/PROCEDURE: Excess sulfamethylthiadiazole was added to aliquots of synthetic urine solns and 1% H_3PO_4 or 1% $NaOH$ solns were used to adjust the pH to the required value. The solns were agitated for 24 h with addn of acid or base to keep them at the desired pH level until equilibrium was attained. Then the solns were filtered and in aliquots the sulfonamide was assayed spectrophotometrically by the method described by Biamonte and Schneller (1).	SOURCE AND PURITY OF MATERIALS: Nothing specified																							
	ESTIMATED ERROR: Soly: average values of 2 detns were given. Temp: not specified. pH : not specified.																							
	REFERENCES: 1. Biamonte, A. R.; Schneller, G. E. <i>J. Am. Pharm. Assoc. Sci. Ed.</i> <u>1952</u> , 41, 341.																							

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); [144-82-1] (2) Sulfuric acid monododecyl ester, sodium salt (Na lauryl sulfate); C ₁₂ H ₂₅ NaO ₄ S; [151-21-3] (3) Water; H ₂ O; [7732-18-5]	ORIGINAL MEASUREMENTS: Watari, N.; Kaneniwa, N. <i>Chem. Pharm. Bull.</i> <u>1976</u> , <i>24</i> (11), 2577-84.																																				
VARIABLES: Concentration of Na lauryl sulfate	PREPARED BY: R. Piekos																																				
EXPERIMENTAL VALUES: <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2" style="text-align: center;">Concentration of Na lauryl sulfate</th> <th colspan="2" style="text-align: center;">Total solubility of sulfamethizole at 37°C</th> </tr> <tr> <th style="text-align: center;">% w/v</th> <th style="text-align: center;">mg/ml solution</th> <th style="text-align: center;">10³ mol dm⁻³ a</th> </tr> </thead> <tbody> <tr><td style="text-align: center;">0.01</td><td style="text-align: center;">0.864</td><td style="text-align: center;">3.196</td></tr> <tr><td style="text-align: center;">0.05</td><td style="text-align: center;">0.877</td><td style="text-align: center;">3.504</td></tr> <tr><td style="text-align: center;">0.10</td><td style="text-align: center;">0.899</td><td style="text-align: center;">3.325</td></tr> <tr><td style="text-align: center;">0.25</td><td style="text-align: center;">1.00</td><td style="text-align: center;">3.70</td></tr> <tr><td style="text-align: center;">0.50</td><td style="text-align: center;">1.36</td><td style="text-align: center;">5.03</td></tr> <tr><td style="text-align: center;">1.00</td><td style="text-align: center;">1.86</td><td style="text-align: center;">6.88</td></tr> <tr><td style="text-align: center;">2.00</td><td style="text-align: center;">2.64</td><td style="text-align: center;">9.77</td></tr> <tr><td style="text-align: center;">3.00</td><td style="text-align: center;">3.42</td><td style="text-align: center;">12.65</td></tr> <tr><td style="text-align: center;">4.00</td><td style="text-align: center;">4.05</td><td style="text-align: center;">14.98</td></tr> <tr><td style="text-align: center;">6.00</td><td style="text-align: center;">5.45</td><td style="text-align: center;">20.16</td></tr> </tbody> </table> <p style="text-align: center;">^aCalculated by compiler</p>		Concentration of Na lauryl sulfate	Total solubility of sulfamethizole at 37°C		% w/v	mg/ml solution	10 ³ mol dm ⁻³ a	0.01	0.864	3.196	0.05	0.877	3.504	0.10	0.899	3.325	0.25	1.00	3.70	0.50	1.36	5.03	1.00	1.86	6.88	2.00	2.64	9.77	3.00	3.42	12.65	4.00	4.05	14.98	6.00	5.45	20.16
Concentration of Na lauryl sulfate	Total solubility of sulfamethizole at 37°C																																				
	% w/v	mg/ml solution	10 ³ mol dm ⁻³ a																																		
0.01	0.864	3.196																																			
0.05	0.877	3.504																																			
0.10	0.899	3.325																																			
0.25	1.00	3.70																																			
0.50	1.36	5.03																																			
1.00	1.86	6.88																																			
2.00	2.64	9.77																																			
3.00	3.42	12.65																																			
4.00	4.05	14.98																																			
6.00	5.45	20.16																																			
AUXILIARY INFORMATION																																					
METHOD/APPARATUS/PROCEDURE: An excess of sulfamethizole 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 sulfamethizole 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. <i>Chem. Pharm. Bull.</i> <u>1974</u> , <i>22</i> , 1699.																																				

COMPONENTS: (1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-(sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) Ethanol; C_2H_6O ; [64-17-5]	ORIGINAL MEASUREMENTS: Sekikawa, H.; Nakano, M.; Arita, T. <i>Chem. Pharm. Bull.</i> <u>1978</u> , <i>26</i> (1), 118-26.												
VARIABLES: Temperature	PREPARED BY: R. Piekos												
EXPERIMENTAL VALUES: <table style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th style="text-align: center;">$t/^\circ C$</th> <th style="text-align: center;">Solubility^a 10² mol dm⁻³ solution</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">10</td> <td style="text-align: center;">2.44</td> </tr> <tr> <td style="text-align: center;">20</td> <td style="text-align: center;">3.24</td> </tr> <tr> <td style="text-align: center;">30</td> <td style="text-align: center;">4.28</td> </tr> <tr> <td style="text-align: center;">40</td> <td style="text-align: center;">5.84</td> </tr> <tr> <td style="text-align: center;">50</td> <td style="text-align: center;">7.90</td> </tr> </tbody> </table> <p style="text-align: center;"> ^a Original data are presented graphically. The numerical values are given by the authors. </p>		$t/^\circ C$	Solubility ^a 10 ² mol dm ⁻³ solution	10	2.44	20	3.24	30	4.28	40	5.84	50	7.90
$t/^\circ C$	Solubility ^a 10 ² mol dm ⁻³ solution												
10	2.44												
20	3.24												
30	4.28												
40	5.84												
50	7.90												
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 sulfamethizole was assayed spectrophotometrically at 284 nm using a Hitachi Type 200-20 spectrophotometer.	SOURCE AND PURITY OF MATERIALS: Sulfamethizole (Eisai Co.) was of the Japanese Pharmacopeia IX grade. 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-(5-methyl-1,3,4-thiadiazol-2-yl)- (sulfamethizole); $C_9H_{10}N_4O_2S_2$; [144-82-1] (2) 2-Pyrrolidinone-, 1-ethenyl-, polymers (poly-vinyl pyrrolidone)); $(C_6H_9NO)_x$; [9003-39-8] K-15 (3) Ethanol; C_2H_6O ; [64-17-5]	ORIGINAL MEASUREMENTS: Sekikawa, H.; Nakano, M.; Arita, T. <i>Chem. Pharm. Bull.</i> <u>1978</u> , <i>26</i> (1), 118-26.												
VARIABLES: Temperature	PREPARED BY: R. Piekos												
EXPERIMENTAL VALUES: <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th style="text-align: center;">$t/^\circ C$</th> <th style="text-align: center;">$M \times 10^2$ sulfamethizole solubilized by 1M vinyl pyrrolidone equivalent</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">10.0</td> <td style="text-align: center;">5.51</td> </tr> <tr> <td style="text-align: center;">20.0</td> <td style="text-align: center;">6.58</td> </tr> <tr> <td style="text-align: center;">30.0</td> <td style="text-align: center;">7.85</td> </tr> <tr> <td style="text-align: center;">40.0</td> <td style="text-align: center;">9.75</td> </tr> <tr> <td style="text-align: center;">50.0</td> <td style="text-align: center;">12.1</td> </tr> </tbody> </table>		$t/^\circ C$	$M \times 10^2$ sulfamethizole solubilized by 1M vinyl pyrrolidone equivalent	10.0	5.51	20.0	6.58	30.0	7.85	40.0	9.75	50.0	12.1
$t/^\circ C$	$M \times 10^2$ sulfamethizole solubilized by 1M vinyl pyrrolidone equivalent												
10.0	5.51												
20.0	6.58												
30.0	7.85												
40.0	9.75												
50.0	12.1												
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 sulfamethizole was assayed spectrophotometrically at 284 nm using a Hitachi Type 200-20 spectrophotometer. No significant absorbance was found for poly-vinyl pyrrolidone.	SOURCE AND PURITY OF MATERIALS: Poly(vinyl pyrrolidone) K-15 was from Daiichi Pure Chemicals Co., Tokyo. Sulfamethizole (Esai Co.) was of the Japanese Pharmacopeia IX grade. Abs EtOH was obtained by drying and distn of EtOH following the conventional procedures.												
	ESTIMATED ERROR: Nothing specified.												
	REFERENCES:												