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| COMPONENTS: (1) Acetamide, N-[4-[[[(4-methyl)-2-thiazolylamino]sulfonyl]phenyl]-(acetyl sulfamethylthiazole); $C_{12}H_{13}N_3O_3S_2$; [71119-13-6] (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: <p>For this compound, the acetyl derivative of the previously evaluated sulfonamide, two values were available (1,2) in water at 310K. Roblin et al. (1) give a value of 1.8×10^{-4} mol dm⁻³, and Durel and Allinne (2) 2×10^{-4} mol dm⁻³. Both groups used quite adequate equilibrium times, though Durel and Allinne (2) do not specify the analytical technique. The similarity of the two values is considered to be evidence of accuracy and an average value of 1.9×10^{-4} mol dm⁻³ is the recommended value in water at 310K. It is interesting to note that the acetyl-derivative possesses a solubility of about one fifth (20%) of the parent compound, sulfamethylthiazole. This is usually the case, decreasing solubility for acetyl-derivative compounds.</p> REFERENCES: (1) Roblin, R.O., Jr.; Williams, J.H.; Winnek, P.S.; English, J.P. <i>J. Am. Chem. Soc.</i> <u>1940</u> , <i>62</i> , 2002-5. (2) Durel, M.P.; Allinne, M. <i>Bull. Soc. Med. Hop. Paris III</i> <u>1941</u> , 251-9. | |

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| VARIABLES: One temperature: 37°C | PREPARED BY: R. Piekos |
| EXPERIMENTAL VALUES: Solubility of acetyl sulfamethylthiazole in water at 37°C is 5.5 mg/100 cm^3 solution (1.8×10^{-4} mol dm^{-3} , compiler). | |
| AUXILIARY INFORMATION | |
| METHOD/APPARATUS/PROCEDURE: Excess acetyl sulfamethylthiazole in water was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h in a thermostat at 37°C. A sample of the satd soln was withdrawn through a glass filter, dild, and analyzed by the Marshall method (1) using a General Electric spectrophotometer for comparing the colors developed with those of the standards. | SOURCE AND PURITY OF MATERIALS: Acetyl sulfamethylthiazole was prep'd by treating 2 moles of 2-amino-4-methylthiazole with 1 mole of acetylsulfanilyl chloride in an AcOEt or dioxane soln. Purity of the water was not specified. ESTIMATED ERROR: Nothing specified REFERENCES: 1. Bratton, A. C.; Marshall, E. K., Jr. <i>J. Pharmacol.</i> <u>1939</u> , <i>66</i> , 4. |

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| VARIABLES: One temperature: $37^\circ C$ | PREPARED BY: R. Piekos |
| EXPERIMENTAL VALUES: <p>Solubility of acetyl sulfamethylthiazole in water at $37^\circ C$ is 0.07 g/liter (2×10^{-4} mol dm^{-3}, compiler).</p> | |
| AUXILIARY INFORMATION | |
| METHOD/AppARATUS/PROCEDURE: A mixt of acetyl sulfamethylthiazole and water was agitated for 24 hours at $37^\circ C$. | SOURCE AND PURITY OF MATERIALS: Source and purity of acetyl sulfamethylthiazole was not specified. Distilled water was used. |
| | ESTIMATED ERROR: Nothing specified. |
| | REFERENCES: |

| COMPONENTS: (1) Acetamide, N-[4-[[4-methyl-2-thiazolyl-amino)sulfonyl]phenyl]- (acetyl sulfamethylthiazole); $C_{12}H_{13}N_3O_3S_2$; [71119-13-6] (2) Water; H_2O ; [7732-18-5] | ORIGINAL MEASUREMENTS: Sapozhnikova, N. V.; Postovskii, I. Ya. <i>Zh. Prikl. Khim.</i> <u>1944</u> , <u>17</u> , 427-34. | | | | | | | | | | | | | | | | | |
|--|--|--|------------|--|---------|--|----|--------|-------|----|-----------------------------|--------------|----|--------|-------|----|---------------------|-------|
| VARIABLES: Temperature | PREPARED BY: R. Piekos | | | | | | | | | | | | | | | | | |
| EXPERIMENTAL VALUES: <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2" style="text-align: center;">t°/C</th> <th colspan="2" style="text-align: center;">Solubility</th> </tr> <tr> <th style="text-align: center;">Weight%</th> <th style="text-align: center;">$10^3 \text{ mol kg}^{-1} \text{ water}^a$</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">20</td> <td style="text-align: center;">0.0022</td> <td style="text-align: center;">0.071</td> </tr> <tr> <td style="text-align: center;">50</td> <td style="text-align: center;">0.0080; 0.0100^b</td> <td style="text-align: center;">0.260; 0.320</td> </tr> <tr> <td style="text-align: center;">75</td> <td style="text-align: center;">0.0350</td> <td style="text-align: center;">1.100</td> </tr> <tr> <td style="text-align: center;">99</td> <td style="text-align: center;">0.0860^b</td> <td style="text-align: center;">2.800</td> </tr> </tbody> </table> <p style="margin-left: 40px;"> ^a Calculated by compiler ^b Calculated from the heat of dissolution (10,548 cal mol⁻¹). </p> | | t°/C | Solubility | | Weight% | $10^3 \text{ mol kg}^{-1} \text{ water}^a$ | 20 | 0.0022 | 0.071 | 50 | 0.0080; 0.0100 ^b | 0.260; 0.320 | 75 | 0.0350 | 1.100 | 99 | 0.0860 ^b | 2.800 |
| t°/C | Solubility | | | | | | | | | | | | | | | | | |
| | Weight% | $10^3 \text{ mol kg}^{-1} \text{ water}^a$ | | | | | | | | | | | | | | | | |
| 20 | 0.0022 | 0.071 | | | | | | | | | | | | | | | | |
| 50 | 0.0080; 0.0100 ^b | 0.260; 0.320 | | | | | | | | | | | | | | | | |
| 75 | 0.0350 | 1.100 | | | | | | | | | | | | | | | | |
| 99 | 0.0860 ^b | 2.800 | | | | | | | | | | | | | | | | |
| AUXILIARY INFORMATION | | | | | | | | | | | | | | | | | | |
| METHOD/APPARATUS/PROCEDURE: Acetyl sulfamethylthiazole 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 sulfamethylthiazole was used. Its mp conformed to that reported in the literature. Purity of the water was not specified. ESTIMATED ERROR: Soly: quite reliable results were obtained over the temp range 20-75°C. At higher temps the accuracy was poor due to evapn of water during sampling (authors). Temp: $\pm 0.05^{\circ} C$ (authors). REFERENCES: | | | | | | | | | | | | | | | | | |

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| COMPONENTS: (1) Acetamide, N-[4-[[[(4-methyl-2-thiazolyl)-amino]sulfonyl]phenyl]- (acetyl sulfamethylthiazole); $C_{12}H_{13}N_3O_3S_2$; [71119-13-6] (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> , 183, 90-116. |
| VARIABLES: One temperature: ca 20°C; one pH: 8.74 | PREPARED BY: R. Piekos |
| EXPERIMENTAL VALUES: Solubility of acetyl sulfamethylthiazole in a 0.705 M (10%) Na_2HPO_4 solution of pH 8.74 at room temperature (about 20°C) is 0.052 g% (1.67×10^{-3} mol dm ⁻³ solution, compiler). | |
| AUXILIARY INFORMATION | |
| METHOD/APPARATUS/PROCEDURE: Acetyl sulfamethylthiazole (0.5 g) was dissolved in 10 cm ³ of the 0.705 M (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 sulfamethylthiazole) by the Marshall method modified by Kimmig (1) using an Autenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode. | SOURCE AND PURITY OF MATERIALS: Acetyl sulfamethylthiazole (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfamethylthiazole. The source and purity of the remaining materials was not specified. ESTIMATED ERROR: Soly: precision ±5% (author) Temp: not specified pH : ±0.05 pH unit (author) |
| | REFERENCES: 1. Kimmig, J. <i>Arch. Dermatol.</i> <u>1938</u> , 176, 722; <i>Erg. Hyg.</i> <u>1941</u> , 24, 398. |

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| COMPONENTS: (1) Acetamide, N-[4-[[[(4-methyl-2-thiazolyl)-amino]sulfonyl]phenyl]- (acetyl sulfamethylthiazole); $C_{12}H_{13}N_3O_3S_2$; [71119-13-6] (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> , 183, 90-116. |
| VARIABLES: One temperature: ca 20°C; one pH: 4.37 | PREPARED BY: R. Piekos |
| EXPERIMENTAL VALUES: Solubility of acetyl sulfamethylthiazole in a 0.735 M (10%) KH_2PO_4 solution of pH 4.37 at room temperature (about 20°C) is 0.0039 g% (1.25×10^{-4} mol dm ⁻³ , compiler). | |
| AUXILIARY INFORMATION | |
| METHOD/APPARATUS/PROCEDURE: Acetyl sulfamethylthiazole (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. 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 sulfamethylthiazole) by the Marshall method modified by Kimmig (1) using an Autenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode. | SOURCE AND PURITY OF MATERIALS: Acetyl sulfamethylthiazole (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfamethylthiazole. The source and purity of the remaining materials was not specified. |
| | ESTIMATED ERROR: Soly: precision ±5% (author) Temp: not specified pH : ±0.05 pH unit (author) |
| | REFERENCES: 1. Kimmig, J. <i>Arch. Dermatol.</i> <u>1938</u> , 176, 722, <i>Erg. Hyg.</i> <u>1941</u> , 24, 398. |

| COMPOSITIONS: | | | | ORIGINAL MEASUREMENTS: | | | |
|---|------------|--------------------|-------|---|-------------------------------|--------|-------------------------------|
| (1) Acetamide, N-[4-[(4-methyl-2-thiazolyl)-amino]sulfonyl]phenyl]- (acetyl sulfamethylthiazole); $C_{12}H_{13}N_3O_3S_2$; [71119-13-6] | | | | Krüger-Thiemer, E. <i>Arch. Dermatol. Syphilis</i> <u>1942</u> , 183, 90-116. | | | |
| (2) Phosphoric acid, disodium salt; Na_2HPO_4 ; [7558-94-4] | | | | | | | |
| (3) Phosphoric acid, monopotassium salt; KH_2PO_4 ; [7778-77-0] | | | | PREPARED BY: R. Piekos | | | |
| (4) Water; H_2O ; [7732-18-5] | | | | | | | |
| VARIABLES: | | | | | | | |
| Temperature; pH | | | | | | | |
| EXPERIMENTAL VALUES: | | | | | | | |
| Composition of 1/15 M phosphate buffer solutions | | | | Solubility | | | |
| Na_2HPO_4 | KH_2PO_4 | %content | pH | Room temp (ca 20°C) | | 37°C | |
| | | | | g% | 10^4 mol dm^{-3} solution | g% | 10^4 mol dm^{-3} solution |
| 1.0 | 99.0 | 0.91 | 4.944 | 0.0069 | 2.215 | - | - |
| 10.0 | 90.0 | 0.91 | 5.906 | 0.0070 | 2.248 | 0.0092 | 2.954 |
| 61.0 | 38.9 | 0.93 | 7.005 | 0.0078 | 2.505 | 0.0188 | 6.037 |
| 9.5 | 0.5 | 0.733 ^b | 7.510 | 0.0097 | 3.115 | - | - |
| 94.7 | 5.3 | 0.95 | 8.018 | 0.0199 | 6.391 | - | - |
| ^a Calculated by compiler ^b Molar content; 10% buffer solution | | | | | | | |
| AUXILIARY INFORMATION | | | | | | | |
| METHOD/APPARATUS/PROCEDURE: | | | | SOURCE AND PURITY OF MATERIALS: | | | |
| Acetyl sulfamethylthiazole (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 sulfamethylthiazole) by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode. | | | | Acetyl sulfamethylthiazole (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfamethylthiazole. 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. <i>Arch. Dermatol.</i> <u>1938</u> , 176, 722; <i>Erg. Hyg.</i> <u>1941</u> , 24, 398. | | | |