

2 mL of this solution, add 10 mL of methanol and water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 5  $\mu$ L each of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions, and determine the peak areas,  $A_T$  and  $A_S$ , of ethyl acetate of these solutions. Calculate the amount of ethyl acetate by the following equation: not more than 2.0%.

Amount (%) of ethyl acetate

$$= \frac{\text{amount (mg) of ethyl acetate}}{\text{amount (mg) of the sample}} \times \frac{A_T}{A_S} \times \frac{1}{5}$$

**Operating conditions—**

**Detector:** A hydrogen flame-ionization detector.

**Column:** A column 3 mm in inside diameter and 1 m in length, packed with porous styrene-divinylbenzene copolymer for gas chromatography (0.0085  $\mu$ m in average pore size and 300–400 m<sup>2</sup>/g in specific surface area) (150 to 180  $\mu$ m in particle diameter).

**Column temperature:** A constant temperature of about 155°C.

**Carrier gas:** Nitrogen

**Flow rate:** Adjust the flow rate so that the retention time of ethyl acetate is about 6 minutes.

**System suitability—**

**System performance:** When the procedure is run with 5  $\mu$ L of the standard solution under the above operating conditions, the number of theoretical steps and the symmetry coefficient of the peak of ethyl acetate are not less than 500 steps and not more than 1.5, respectively.

**System repeatability:** When the test is repeated 6 times with 5  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of ethyl acetate is not more than 5%.

**Water** 4.0–6.0% (0.5 g, volumetric titration, direct titration).

**Residue on ignition** Not more than 0.20% (1 g).

**Assay** Perform the procedure rapidly. Weigh accurately an amount of Sultamicillin Tosilate and Sultamicillin Tosilate Reference Standard, equivalent to about 0.05 g (potency), dissolve each in the mobile phase to make exactly 50 mL. Pipet 5 mL each of these solutions, add exactly 5 mL of the internal standard solution, add the mobile phase to make 25 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10  $\mu$ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios,  $Q_T$  and  $Q_S$ , of the peak area of sultamicillin to that of the internal standard of each solution.

$$\begin{aligned} &\text{Amount } [\mu\text{g (potency)}] \text{ of sultamicillin (C}_{25}\text{H}_{30}\text{N}_4\text{O}_9\text{S}_2) \\ &= \text{amount [mg (potency)] of Sultamicillin Tosilate} \\ &\quad \text{Reference Standard} \\ &\quad \times \frac{Q_T}{Q_S} \times 1000 \end{aligned}$$

**Internal standard solution—**A solution of isopropyl-4-aminobenzoate in the mobile phase (1 in 2500).

**Operating conditions—**

**Detector:** An ultraviolet absorption photometer (wavelength: 215 nm).

**Column:** A stainless steel column 3.9 mm in inside di-

ameter and 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10  $\mu$ m in particle diameter).

**Column temperature:** A constant temperature of about 35°C.

**Mobile phase:** Dissolve 3.12 g of sodium dihydrogenphosphate in about 750 mL of water, adjust to pH 3.0 with diluted phosphoric acid (1 in 10), and add water to make 1000 mL. To 400 mL of acetonitrile for liquid chromatography add this solution to make 1000 mL.

**Flow rate:** Adjust the flow rate so that the retention time of sultamicillin is about 4 minutes.

**System suitability—**

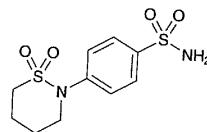
**System performance:** When the procedure is run with 10  $\mu$ L of the standard solution under the above operating conditions, *p*-toluenesulfonic acid, sultamicillin and the internal standard are eluted in this order with the resolution between these peaks being not less than 2.0.

**System repeatability:** When the test is repeated 6 times with 10  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the peak area of sultamicillin is not more than 2.0%.

**Containers and storage** Containers—Tight containers.

## Sultiamine

スルチアム



C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: 290.36

4-(Tetrahydro-2H-1,2-thiazin-2-yl)benzenesulfonamide S,S-dioxide [61-56-3]

Sultiamine, when dried, contains not less than 98.5% of C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>.

**Description** Sultiamine occurs as white crystals or crystalline powder. It is odorless, and has a slightly bitter taste.

It is very soluble in *N,N*-dimethylformamide, freely soluble in *n*-butylamine, slightly soluble in methanol and in ethanol (95), very slightly soluble in water, and practically insoluble in diethyl ether.

It dissolves in sodium hydroxide TS.

**Identification (1)** Dissolve 0.02 g of Sultiamine in 5 mL of water and 1 mL of *n*-butylamine, add 2 to 3 drops of copper (II) sulfate TS, and shake well. To this solution add 5 mL of chloroform, shake, and allow to stand: a green color develops in the chloroform layer.

**(2)** Mix 0.1 g of Sultiamine with 0.5 g of sodium carbonate decahydrate, and melt carefully: the gas evolved changes moistened red litmus paper to blue. After cooling, crush the fused substance with a glass rod, stir with 10 mL of water, and filter. To 4 mL of the filtrate add 2 drops of hydrogen peroxide (30), 5 mL of diluted hydrochloric acid (1 in 5) and 2 to 3 drops of barium chloride TS: a white precipitate is formed.

(3) Determine the absorption spectrum of a solution of Sultiame in methanol (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

**Melting point** 185 – 188°C

**Purity (1) Chloride**—Dissolve 1.0 g of Sultiame in 20 mL of sodium hydroxide TS by warming, cool, and add 2 mL of acetic acid (100) and water to make 100 mL. After shaking, filter, and discard the first 10 mL of the filtrate. To the subsequent 40 mL add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.25 mL of 0.01 mol/L hydrochloric acid VS add 8 mL of sodium hydroxide TS, 0.8 mL of acetic acid (100), 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.022%).

(2) **Sulfate**—Dissolve 1.0 g of Sultiame in 20 mL of sodium hydroxide TS by warming, cool, and add 8 mL of dilute hydrochloric acid and water to make 100 mL. After shaking, filter, and discard the first 10 mL of the filtrate. To the subsequent 40 mL add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.40 mL of 0.005 mol/L sulfuric acid VS add 8 mL of sodium hydroxide TS, 4.2 mL of dilute hydrochloric acid and water to make 50 mL (not more than 0.048%).

(3) **Heavy metals**—Proceed with 2.0 g of Sultiame according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) **Arsenic**—Prepare the test solution with 1.0 g of Sultiame according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) **Related substances**—Dissolve 0.10 g of Sultiame in methanol to make exactly 20 mL, and use this solution as the sample solution. Separately, dissolve 0.010 g of sulfanilamide in methanol to make exactly 100 mL. Pipet 10 mL of this solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20  $\mu$ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform, methanol and ammonia solution (28) (30:8:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 3 hours).

**Residue on ignition** Not more than 0.10% (1 g).

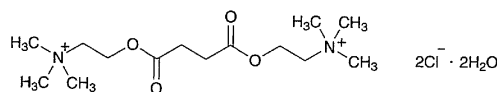
**Assay** Weigh accurately about 0.8 g of Sultiame, previously dried, dissolve in 70 mL of *N,N*-dimethylformamide, and titrate with 0.2 mol/L tetramethylammonium hydroxide VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.2 mol/L tetramethylammonium hydroxide VS  
= 58.07 mg of  $C_{10}H_{14}N_2O_4S_2$

**Containers and storage** Containers—Well-closed containers.

## Suxamethonium Chloride

塩化スキサメトニウム



$C_{14}H_{30}Cl_2N_2O_4 \cdot 2H_2O$ : 397.34

2,2'-Succinyldioxybis(*N*-ethyl-*N,N,N*-trimethylammonium) dichloride dihydrate [6101-15-1]

Suxamethonium Chloride contains not less than 98.0% of  $C_{14}H_{30}Cl_2N_2O_4$  (mol. wt.: 361.31), calculated on the anhydrous basis.

**Description** Suxamethonium Chloride occurs as a white, crystalline powder.

It is freely soluble in water, in methanol and in acetic acid (100), slightly soluble in ethanol (95), very slightly soluble in acetic anhydride, and practically insoluble in diethyl ether.

**Identification (1)** Determine the infrared absorption spectrum of Suxamethonium Chloride as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(2) A solution of Suxamethonium Chloride (1 in 20) responds to the Qualitative Tests for chloride.

**pH** The pH of a solution of Suxamethonium Chloride (1 in 100) is between 4.0 and 5.0.

**Melting point** 159 – 164°C (hydrate form).

**Purity (1) Clarity and color of solution**—Dissolve 1.0 g of Suxamethonium Chloride in 10 mL of water: the solution is clear and colorless.

(2) **Related substances**—Dissolve 0.25 g of Suxamethonium Chloride in 5 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 1  $\mu$ L each of the sample solution and the standard solution on a plate of cellulose for thin-layer chromatography. Develop the plate with a mixture of a solution of ammonium acetate (1 in 100), acetone, *n*-butanol and formic acid (20:20:20:1) to a distance of about 10 cm, and dry the plate at 105°C for 15 minutes. Spray evenly platinum chloride-potassium iodide TS on the plate, and allow to stand for 15 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Water** 8.0 – 10.0% (0.4 g, direct titration).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.4 g of Suxamethonium Chloride, dissolve in 80 mL of a mixture of acetic anhydride