(4) Related substances—Dissolve 0.20 g of Tiaramide Hydrochloride in 10 mL of diluted ethanol (99.5) (7 in 10), and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add diluted ethanol (99.5) (7 in 10) to make exactly 100 mL. Pipet 2 mL of this solution, add diluted ethanol (99.5) (7 in 10) to make exactly 10 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. After air-drying, immediately develop the plate with a mixture of 1-butanol, water and acetic acid (100) (4:2:1) to a distance of about 10 cm, air-dry the plate, and then dry at 100°C for 30 minutes. After cooling, examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot and the spot of the starting point from the sample solution are not more intense than the spot from the standard solution. Allow the plate to stand in iodine vapor for 30 minutes: the spots other than the principal spot and the spot of the starting point 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 0.5 g of Tiaramide Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3) by warming, cool, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from red through purple to blue-purple (indicator: 3 drops of neutral red TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 39.231 mg of $C_{15}H_{18}ClN_3O_3S.HCl$

Containers and storage Containers—Well-closed containers.

Ticarcillin Sodium

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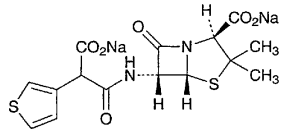

$C_{15}H_{14}N_2Na_2O_6S_2$: 428.39
Disodium (2*S*,5*R*,6*R*)-6-(2-carboxylato-2-thiophen-2-ylacetylamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate [*4697-14-7*]

Ticarcillin Sodium contains not less than 800 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ticarcillin Sodium is expressed as mass (potency) of ticarcillin ($C_{15}H_{16}N_2O_6S_2$: 384.43).

Description Ticarcillin Sodium occurs as a white to pale yellowish white powder. It has a characteristic oder.

It is very soluble in water, freely soluble in methanol, and sparingly soluble in ethanol (95).

It is hygroscopic.

Identification (1) Determine the infrared absorption spectrum of Ticarcillin Sodium, previously dried in a desiccator (in vacuum, phosphorus (V) oxide, 60°C) for 2 hours, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Ticarcillin Sodium Reference Standard, previously dried in a desiccator (in vacuum, phosphorus (V) oxide at 60°C) for 2 hours: both spectra exhibit similar intensities of absorption at the same wave numbers.

(2) Ticarcillin Sodium responds to the Quantitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{20}$: +170 - +190° (0.50 g calculated on the anhydrous bases, water, 50 mL, 100 mm).

pH Dissolve 1.0 g of Ticarcillin Sodium in 10 mL of water: the pH of this solution is between 5.0 and 7.5.

Purity (1) Heavy metals—Proceed with 2.0 g of Ticarcillin Sodium 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).

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

(3) 3-Thienylethylpenicillin sodium—When perform the test under the following condition, the value from the sample solution is not more than the value from the standard solution.

(i) Standard solution—Weigh accurately a suitable amount of 3-thienylethylpenicillin sodium, dissolve in phosphate buffer solution, pH 6.0, and add phosphate buffer solution, pH 6.0 to make a solution so that each mL contains 5.0 μg.

(ii) Sample solution—Weigh accurately a suitable amount of Ticarcillin Sodium, dissolve in phosphate buffer solution, pH 6.0, and add phosphate buffer solution, pH 6.0 to make a solution so that each mL contains 100 μg.

(iii) Test organism—*Bacillus subtilis* ATCC 6633

(iv) Culture medium—Use the medium i in 1) Medium for test organism [5] under (1) Agar media for seed and base layer of the Cylinder-plate method under the Microbial Assay for Antibiotics. Adjust the pH of the medium so that it will be 6.4 to 6.5 after sterilization.

(v) Developing solvent—Phosphate buffer solution, pH 6.0.

(vi) Preparation of thin-layer plate—Apply silica gel for thin-layer chromatography on a uniform thick glass plate 200 mm × 200 mm in size to make a uniform thick layer of 0.2 to 0.3 mm. Dry the plate, then dry further by heating at 105°C for 30 minutes. After cooling, develop the plate with a mixture of diethyl ether and silicone oil (19:1) for about 3 hours, and air-dry the plate.

(vii) Procedure—Designate a line about 20 mm distant from the bottom of the thin-layer plate as the starting line, spot three of 10 μL each of the sample solution and the standard solution at points on this line, separated alternately about 30 mm and 10 mm distant from the both sides, and air-dry within 15 minutes. Develop the plate at a room temperature with about 10 mm depth of the developing solvent in a vessel saturated with a vapor of the solvent to a distance of about 100 mm, and air-dry the plate. Place the plate

horizontally, put a sterilized flame (200 mm × 200 mm, 5 mm in flame width, 5 to 20 mm in depth) on the plate, pour 150 mL of agar medium for seed into the flame, and incubate the medium after harden the agar at 37°C for 16 to 20 hours. Measure the diameter at the developing direction of each zone of inhibition near *Rf* of 0.1 to the nearest 0.1 mm accuracy, and calculate the averages of the diameter obtained by the sample solution and the standard solution.

(4) Iodine adsorption substances—When the test is run according to the following conditions, the amount of iodine adsorption substances is not more than 8.0%. Weigh accurately about 0.20 g of Ticarcillin Sodium, dissolve in water to make exactly 100 mL, and use this solution as the sample solution. Pipet 0.5 mL of 1 mol/L hydrochloric acid TS and 10 mL of 0.01 mol/L iodine VS in a glass-stoppered conical flask, add exactly 10 mL of the sample solution, mix, and titrate immediately with 0.02 mol/L sodium thiosulfate VS (indicator: 1 mL of starch TS). Designate the consumed amount of 0.02 mol/L sodium thiosulfate VS for the test as *A* mL. Perform a blank determination in the same manner and designate the consumed amount for the blank as *B* mL.

$$\text{Amount (\%) of the iodine absorption substances} = \frac{(B - A) \times 446.4 \times 0.02 \times f}{\text{amount (g) of the sample} \times 10.4}$$

f: Factor of 0.02 mol/L sodium thiosulfate VS

Water Not more than 6.0% (0.4 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Ticarcillin Sodium and Ticarcillin Sodium Reference Standard, equivalent to about 0.075 g (potency), dissolve each in a suitable amount of water, add exactly 10 mL of the internal standard solution and water to make 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 10 μL 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 ticarcillin to that of the internal standard of each solution. Both the sample solution and the standard solution are keep at not exceeding 5°C and use within 24 hours.

$$\text{Amount [μg (potency)] of ticarcillin } (C_{15}H_{16}N_2O_6S_2) = \text{amount [mg (potency)] of Ticarcillin Sodium Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—Dissolve 0.63 g of *o*-toluic acid in 100 mL of a solution of sodium hydrogen carbonate (21 in 5000), and add water to make 250 mL.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 230 nm).

Column: A stainless steel column 4 mm in inside diameter and 15 cm in length, packed with trimethylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 30°C.

Mobile phase: Dissolve 3.9 g of sodium dihydrogenphosphate dihydrate and 1.61 g of tetra *n*-butylammonium bromide in 750 mL of water, adjust to pH 3.0 with phosphoric acid, and add water to make 1000 mL. To this solution add 225 mL of acetonitlile and 2.5 mL of aceteic acid (100).

Flow rate: Adjust the flow rate so that the retention time of *o*-toluic acid is about 10 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the internal standard and ticarcillin are eluted in this order with the resolution between these peaks being not less than 3.7.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ticarcillin to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Storage—In a cold place.

Ticlopidine Hydrochloride

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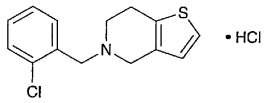

$C_{14}H_{14}ClNS.HCl$: 300.25

5-(2-Chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine monohydrochloride [*53885-35-1*]

Ticlopidine Hydrochloride contains not less than 99.0% of $C_{14}H_{14}ClNS.HCl$, calculated on the anhydrous basis.

Description Ticlopidine Hydrochloride occurs as a white to pale yellowish white crystalline powder.

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

Identification **(1)** Determine the infrared absorption spectrum of Ticlopidine Hydrochloride 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 Ticlopidine Hydrochloride (1 in 20) responds to the Qualitative Tests (2) for chloride.

Purity **(1)** Heavy metals—Proceed with 2.0 g of Ticlopidine Hydrochloride according to Method 3, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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

(3) Related substances—Dissolve 0.5 g of Ticlopidine Hydrochloride in 20 mL of a solution of hydrochloric acid in methanol (1 in 20,000), and use this solution as the sam-