Identification (1) Determine the absorption spectrum of a solution of Cefapirin Sodium (3 in 200,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefapirin Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Cefapirin Sodium as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefapirin Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefapirin Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10), using sodium 3-(trimethylsilyl)propionate-d_4 for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H): it exhibits a single signal A at around δ 2.2 ppm, and multiple signals, B and C, at around δ 7.3 ppm and at around δ 8.3 ppm, respectively. The ratio of integrated intensity of these signals, A:B:C, is about 3:2:2.

(4) Cefapirin Sodium responds to the Qualitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{25}$: +157 - +175° (2 g calculated as the anhydrous basis, water, 100 mL, 100 mm).

pH Dissolve 1.0 g of Cefapirin Sodium in 10 mL of water: pH of the solution is between 6.5 and 8.5.

Purity (1) Heavy metals—Proceed with 1.0 g of Cefapirin Sodium according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Cefapirin Sodium according to Method 3, and perform the test using Apparatus B (not more than 2 ppm). Use a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 25).

(3) Related substances—Dissolve 0.1 g of Cefapirin Sodium in 5 mL of a mixture of acetone and water (3:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of acetone and water (3:1) 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 5 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop with a mixture of ethyl acetate, acetone, water and acetic acid (100) (5:2:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot and other than the spot at the original point from the sample solution are not more intense than the spot from the standard solution.

Water Not more than 2.0% (0.7 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefapirin Sodium and Cefapirin Sodium Reference Standard equivalent to about 0.1 g (potency), dissolve each in phosphate buffer solution, pH 6.0 to make exactly 100 mL. Pipet 5 mL of each solution, add exactly 5 mL of the internal standard solution and phosphate buffer solution, pH 6.0 to make 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 20 μL each of the sample solution and the standard solution 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 cefapirin to that of the internal standard.

Amount [μg (potency)] of cefapirin ($C_{17}H_{17}N_3O_6S_2$)
= amount [mg (potency)] of Cefapirin Sodium
Reference Standard $= \frac{Q_T}{Q_S} \times 1000$

Internal standard solution—A solution of vanillin (1 in 1000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of 0.05 mol/L sodium dihydrogenphosphate TS, pH 2.6 and acetonitrile (93:7).

Flow rate: Adjust the flow rate so that the retention time of cefapirin is about 7 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, cefapirin and the internal standard are eluted in this order with the resolution between these peaks being not less than 10.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefapirin to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Cefatrizine Propylene Glycolate

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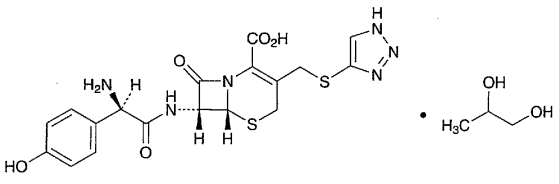

$C_{18}H_{18}N_6O_5S_2.C_3H_8O_2$: 538.60

(6*R*,7*R*)-7-[(2*R*)-2-Amino-2-(4-hydroxyphenyl)acetylamino]-8-oxo-3-[2(1*H*-1,2,3-triazol-4-yl)sulfanylmethyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monopropane-1,2-diolate (1/1) [*51627-14-6*, Cefatrizine]

Cefatrizine Propylene Glycolate contains not less than 785 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefatrizine Propylene

Glycolate is expressed as mass (potency) of cefatrizine ($C_{18}H_{18}N_6O_5S_2$: 462.50).

Description Cefatrizine Propylene Glycolate occurs as a white to yellowish white powder.

It is sparingly soluble in water, and practically insoluble in methanol and in ethanol (95).

Identification (1) Determine the absorption spectrum of a solution of Cefatrizine Propylene Glycolate (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefatrizine Propylene Glycolate Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Cefatrizine Propylene Glycolate as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Cefatrizine Propylene Glycolate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefatrizine Propylene Glycolate in a mixture of heavy water for nuclear magnetic resonance spectroscopy and deuterated hydrochloric acid for nuclear magnetic resonance spectroscopy (3:1) (1 in 10), using sodium 3-(trimethylsilyl) propionate-d_4 for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H): it exhibits a double signal A at around δ 1.2 ppm, a double signal B at around δ 7.0 ppm, a double signal C at around δ 7.5 ppm and a single signal D at around δ 8.3 ppm. The ratio of integrated intensity of these signals, A:B:C:D, is about 3:2:2:1.

Optical rotation $[\alpha]_D^{20}$: +52 – +58° (2.5 g calculated on the anhydrous bases, 1 mol/L hydrochloric acid TS, 50 mL, 100 mm).

Purity (1) Heavy metals—Proceed with 1.0 g of Cefatrizine Propylene Glycolate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Cefatrizine Propylene Glycolate according to Method 3, and perform the test using Apparatus B (not more than 2 ppm). Use a solution of magnesium nitrate in ethanol (1 in 25).

(3) Related substances—Dissolve 0.025 g of Cefatrizine Propylene Glycolate 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 20 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 for thin-layer chromatography. Develop with a mixture of 1-butanol, water and acetic acid (100) (3:1:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly ninhydrin-citric acid-acetic acid TS on the plate, and heat at 100°C for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Water Not more than 2.0% (0.5 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefatrizine Propylene Glycolate and Cefatrizine Propylene Glycolate Reference Standard equivalent to about 0.1 g (potency), dissolve each in water to make exactly 500 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas, A_T and A_S, of cefatrizine of these solutions

$$\text{Amount [}\mu\text{g (potency)] of cefatrizine } (C_{18}H_{18}N_6O_5S_2) = \text{amount [mg (potency)] of Cefatrizine Propylene Glycolate Reference Standard} \times \frac{A_T}{A_S} \times 1000$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 270 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: A mixture of a solution of potassium dihydrogenphosphate (17 in 12,500) and methanol (17:3).

Flow rate: Adjust the flow rate so that the retention time of cefatrizine is about 11 minutes.

System suitability—

System performance: Dissolve about 5 mg (potency) of Cefadroxil and about 0.01 g (potency) of Cefatrizine Propylene Glycolate in 50 mL of water. When the procedure is run with 10 μL of this solution under the above operating conditions, cefadroxil and cefatrizine are eluted in this order with the resolution between these peaks being not less than 4.

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 peak areas of cefatrizine is not more than 1.0%.

Containers and storage Containers—Tight containers.

Cefazolin Sodium

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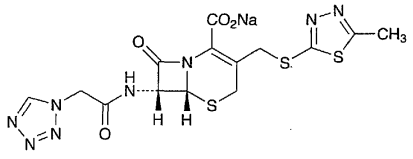

$C_{14}H_{13}N_8NaO_4S_3$: 476.49

Monosodium (6*R*,7*R*)-3-(5-methyl-1,3,4-thiadiazol-2-ylsulfanylmethyl)-8-oxo-7-[2-(1*H*-tetrazol-1-yl)acetylamino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate

[*27164-46-1*]

Cefazolin Sodium contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis.