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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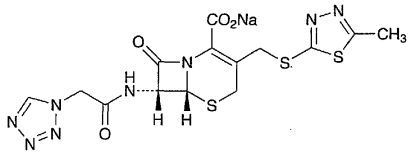

$C_{14}H_{13}N_8NaO_4S_3$: 476.49

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.

The potency of Cefazolin Sodium is expressed as mass (potency) of cefazolin ($C_{14}H_{14}N_8O_4S_3$: 454.51).

Description Cefazolin Sodium occurs as a white to light yellow-white, crystals or crystalline powder.

It is freely soluble in water and in formamide, slightly soluble in methanol, and practically insoluble in ethanol (95).

Identification **(1)** Determine the absorption spectrum of a solution of Cefazolin Sodium (1 in 50,000) 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 wavelength.

(2) Determine the infrared absorption spectrum of Cefazolin Sodium 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.

(3) Determine the spectrum of a solution of Cefazolin Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H): it exhibits single signals, A and B, at around δ 2.7 ppm and at around δ 9.3 ppm, respectively. The ratio of integrated intensity of these signals, A:B, is about 3:1.

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

Optical rotation $[\alpha]_D^{20}$: -19 – $-23°$ (2.5 g calculated as the anhydrous basis, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Cefazolin Sodium in 10 mL of water: pH of the solution is between 4.8 and 6.3.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Cefazolin Sodium in 10 mL of water: the solution is clear and colorless to pale yellow, and its absorbance at 400 nm determined as directed under the Ultraviolet-visible Spectrophotometry is not more than 0.35. The test should be performed within 10 minutes after preparing of the solution.

(2) Heavy metals—Proceed with 2.0 g of Cefazolin 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).

(3) Arsenic—Prepare the test solution with 2.0 g of Cefazolin Sodium according to Method 3, and perform the test using Apparatus B. When prepare the test solution, add 1.5 mL of hydrogen peroxide (30) after addition of 10 mL of a solution of magnesium nitrate in ethanol (95) (1 in 50), and then ignite (not more than 1 ppm).

(4) Related substances—Dissolve 0.10 g of Cefazolin Sodium in 20 mL of 0.1 mol/L phosphate buffer solution, pH 7.0 and use this solution as the sample solution. Prepare the sample solution before use. Perform the test with 5 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, and measure the areas of a peak appeared at the relative retention time of about 0.2 to the retention time of cefazolin and peaks other than cefazolin by the automatic integration method, and calculate the amounts of these peak areas by the area percentage method: the amount of each peak area is not more than 1.5%, and the total area of the peaks other than cefazolin is not more than 2.5%. The area of the peak appeared at the relative retention time of about 0.2 to the retention time of cefazolin obtained here is used after multiplying by its sensitivity coefficient, 1.43.

Operating conditions—

Detector, column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: About 3 times as long as the retention time of cefazolin after the solvent peak.

System suitability—

Test for required detection: Dissolve about 0.08 g of Cefazolin Reference Standard in 0.1 mol/L phosphate buffer solution, pH 7.0 to make 100 mL, and use this solution as the solution for system suitability test. Pipet 1 mL of the solution, and add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 20 mL. Confirm that the peak area of cefazolin obtained from 5 μL of this solution is equivalent to 3 to 7% of that of cefazolin obtained from 5 μL of the solution for system suitability test.

System performance: Proceed as directed in the system suitability in the Assay.

System repeatability: When the test is repeated 6 times with 5 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of cefazolin is not more than 1.0%.

Water Not less than 2.5% (1.0 g, volumetric titration, direct titration. Use a mixture of formamide for water determination and methanol for water determination (2:1) instead of methanol for water determination).

Assay Weigh accurately an amount of Cefazolin Sodium and Cefazolin Reference Standard, equivalent to about 0.1 g (potency), dissolve each in the internal standard solution to make exactly 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 5 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 cefazolin to that of the internal standard.

$$\text{Amount [}\mu\text{g (potency)] of cefazolin } (C_{14}H_{14}N_8O_4S_3) = \text{amount [mg (potency)] of Cefazolin Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of *p*-acetoanisidide in 0.1 mol/L phosphate buffer solution, pH 7.0 (11 in 20,000).

Operating conditions—

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

Column: A stainless steel column 4 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 2.27 g of disodium hydrogenphosphate 12-water and 0.47 g of citric acid monohydrate in water to make 935 mL, and add 65 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefazolin is about 8 minutes.

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, cefazolin and the internal standard 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 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefazolin to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Cefazolin Sodium Hydrate

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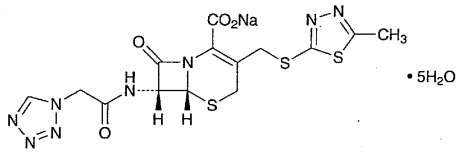

$C_{14}H_{13}N_8NaO_4S_3.5H_2O$: 566.57

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 pentahydrate [*115850-11-8*]

Cefazolin Sodium Hydrate contains not less than 890 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefazolin Sodium Hydrate is expressed as mass (potency) of cefazolin ($C_{14}H_{14}N_8O_4S_3$: 454.51).

Description Cefazolin Sodium Hydrate occurs as white to pale yellowish white crystals.

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

Identification (1) Determine the absorption spectrum of a solution of Cefazolin Sodium Hydrate (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 270 nm and 274 nm.

(2) Determine the infrared absorption spectrum of Cefazolin Sodium Hydrate as directed in the potassium bromide disk method under the Infrared Spectrophotometry: it exhibits absorption at the wave numbers of about 1761 cm^{-1}, 1667 cm^{-1}, 1599 cm^{-1}, 1540 cm^{-1} and 1389 cm^{-1}.

(3) Determine the spectrum of a solution of Cefazolin Sodium Hydrate in heavy water for nuclear magnetic resonance spectroscopy (1 in 10), using sodium 3-trimethylsilylpropionate-d_4 for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H): it exhibits single signals, A and B, at around δ 2.7 ppm and at around δ 9.3 ppm. The ratio of integrated intensity of each signal, A:B, is about 3:1.

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

Absorbance $E^{1\%}_{1\,cm}$ (272 nm): 272 - 292 (0.08 g calculated on the anhydrous basis, water, 5000 mL).

Optical rotation $[\alpha]^{20}_D$: −20 - −25° (2.5 g calculated on the anhydrous basis, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Cefazolin Sodium Hydrate in 10 mL of water: the pH of the solution is between 4.8 and 6.3.

Purity (1) Clarity and color of solution—Being specified separately.

(2) Heavy metals—Proceed with 2.0 g of Cefazolin Sodium Hydrate 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).

(3) Arsenic—Being specified separately.

(4) Related substances—Being specified separately.

(5) Residual solvents—Being specified separately.

Water Not less than 13.7% and not more than 16.0% (0.1 g, volumetric titration, direct titration. Use a mixture of formamide for water determination and methanol for water determination (2:1) instead of methanol for water determination).

Bacterial endotoxins Less than 0.10 EU/mg (potency).

Assay Weigh accurately an amount of Cefazolin Sodium Hydrate and Cefazolin Reference Standard, equivalent to about 0.1 g (potency), dissolve in the internal standard solution to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 5 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 cefazolin to that of the internal standard.

$$\text{Amount [}\mu\text{g (potency)] of cefazolin } (C_{14}H_{14}N_8O_4S_3) = \text{amount [mg (potency)] of Cefazolin Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of *p*-acetoanisidide in 0.1 mol/L phosphate buffer solution, pH 7.0 (11 in 20,000).

Operating conditions—

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

Column: A stainless steel column 4 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 2.27 g of disodium hydrogenphosphate 12-water and 0.47 g of citric acid monohydrate in water to make 935 mL. To this solution, add 65 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefazolin is about 8 minutes.

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, cefazolin and the internal standard are eluted in this order with the resolution between these peaks being not less