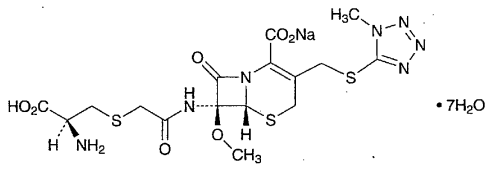
μL of the standard solution under the above operating conditions, cefmetazole and the internal standard are eluted in this order with the resolution between these peaks being not less than 10.

System repeatability: When the test is repeated 5 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 cefmetazole to that of the internal standard is not more than 2.0%.

Containers and storage Containers—Hermetic containers.

Cefminox Sodium

セフミノクスナトリウム



$C_{16}H_{20}N_7NaO_7S_3.7H_2O$: 667.66
Monosodium (6*R*,7*S*)-7-{2-[(2*S*)-2-amino-2-carboxyethylsulfanyl]acetylamino}-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate heptahydrate [*75498-96-3*]

Cefminox Sodium contains not less than 865 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefminox Sodium is expressed as mass (potency) of cefminox sodium ($C_{16}H_{20}N_7NaO_7S_3$).

Description Cefminox Sodium occurs as a white to light yellow crystalline powder.

It is freely soluble in methanol, sparingly soluble in ethanol (99.5), and practically insoluble in water.

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

(2) Determine the infrared absorption spectrum of Cefminox 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 Cefminox Sodium Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefminox Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 30) as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a multiple signal, A, at around δ 3.2 ppm, a single signal, B, at around δ 3.5 ppm, a single signal, C, at around δ 4.0 ppm, and a single signal, D, at around δ 5.1 ppm. The ratio of integrated intensity of each signal, A:B:C:D, is about 2:3:3:1.

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

Optical rotation $[\alpha]_D^{20}$: +62 – +72° (0.050 g, water, 10 mL, 100 mm).

pH Dissolve 0.70 g of Cefminox Sodium in 10 mL of water: the pH of the solution is between 4.5 and 6.0.

Water Not less than 18.0% and not more than 20.0% (0.1 g, volumetric titration, direct titration).

Assay Perform the test according to the Cylinder-plate method as directed under the Microbial Assay for Antibiotics according to the following conditions.

(1) Test organism—*Escherichia coli* NIHJ

(2) Culture medium—Use the medium iii in 3) Medium for other organisms under (1) Agar media for seed and base layer. Adjust the pH of the medium so that it will be 6.5 to 6.6 after sterilization.

(3) Standard solution—Weigh accurately an amount of Cefminox Sodium Reference Standard, equivalent to about 0.04 g (potency), dissolve in 0.05 mol/L phosphate buffer solution, pH 7.0 to make exactly 50 mL, and use this solution as the standard stock solution. Keep the standard stock solution at 5°C or below and use within 7 days. Take exactly a suitable amount of the standard stock solution before use, add 0.05 mol/L phosphate buffer solution, pH 7.0 to make solutions so that each mL contains 40 μg (potency) and 20 μg (potency), and use these solutions as the high concentration standard solution and the low concentration standard solution, respectively.

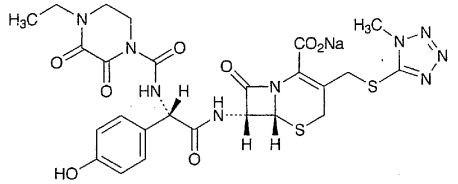
(4) Sample solution—Weigh accurately an amount of Cefminox Sodium equivalent to about 0.04 g (potency), dissolve in 0.05 mol/L phosphate buffer solution, pH 7.0 to make exactly 50 mL. Take exactly a suitable amount of this solution, add 0.05 mol/L phosphate buffer solution, pH 7.0 to make solutions so that each mL contains 40 μg (potency) and 20 μg (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

(5) Procedure—Incubate between 32°C and 35°C.

Containers and storage Containers—Hermetic containers.

Cefoperazone Sodium

セフォペラゾンナトリウム



$C_{25}H_{26}N_9NaO_8S_2$: 667.65
Monosodium (6*R*,7*R*)-7-{(2*R*)-2-[(4-ethyl-2,3-dioxopiperazine-1-carbonyl)amino]-2-(4-hydroxyphenyl)acetylamino}-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [*62893-20-3*]

Cefoperazone Sodium contains not less than 871 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefoperazone Sodium is expressed as mass (potency) of cefoperazone ($C_{25}H_{27}N_9O_8S_2$: 645.67).

Description Cefoperazone Sodium occurs as a white to yellowish white crystalline powder.

It is very soluble in water, soluble in methanol, and slightly soluble in ethanol (99.5).

Identification **(1)** Determine the absorption spectrum of a solution of Cefoperazone 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 spectrum of a solution of Cefoperazone Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 4) as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a triplet signal A at around δ 1.2 ppm, and double signals, B and C, at around δ 6.8 ppm and at around δ 7.3 ppm. The ratio of integrated intensity of these signals, A:B:C, is about 3:2:2.

(3) Cefoperazone Sodium responds to the Qualitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{20}$: -15 – $-25°$ (1 g, water, 100 mL, 100 mm).

pH Dissolve 1.0 g of Cefoperazone Sodium in 4 mL of water: the pH of the solution is between 4.5 and 6.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Cefoperazone Sodium in 10 mL of water: the solution is clear and pale yellow.

(2) Heavy metals—Proceed with 1.0 g of Cefoperazone Sodium according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

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

(4) Related substances—Dissolve 0.1 g of Cefoperazone Sodium in 100 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with 25 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the areas of each peak by the automatic integration method. Calculate the percentages of each peak area from the sample solution to 50 times of the peak area of cefoperazone from the standard solution: the related substance I with the retention time of about 8 minutes is not more than 5.0%, the related substance II with that of about 17 minutes is not more than 1.5%, and the total of all related substances is not more than 7.0%. Use the peak areas of the related substances I and II after multiplying by their sensitivity coefficients, 0.90 and 0.75, respectively.

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 cefoperazone after the solvent peak.

System suitability—

Test for required detection: Pipet 1 mL of the standard solution, and add the mobile phase to make exactly 20 mL. Confirm that the peak area of cefoperazone obtained from 25 μL of this solution is equivalent to 3.5 to 6.5% of that of cefoperazone obtained from 25 μL of the standard solution.

System performance: When the procedure is run with 25 μL of the standard solution under the above operating conditions, the number of theoretical steps and the symmetry coefficient of the peak of cefoperazone are not less than 5000 steps and not more than 1.5, respectively.

System repeatability: When the test is repeated 6 times with 25 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefoperazone is not more than 2.0%.

Water Not more than 1.0% (3.0 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefoperazone Sodium equivalent to about 0.1 g (potency), and dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately an amount of Cefoperazone Reference Standard equivalent to about 0.1 g (potency), dissolve in 5 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and add water to make exactly 100 mL. Pipet 5 mL of this solution, add exactly 5 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 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 ratios, Q_T and Q_S, of the peak area of cefoperazone to that of the internal standard.

$$\text{Amount [}\mu\text{g (potency)] of } C_{25}H_{27}N_9O_8S_2 = \text{amount [mg (potency)] of Cefoperazone Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of acetanilide in a mixture of water and acetonitrile (43:7) (3 in 8000).

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 35°C.

Mobile phase: To 57 mL of acetic acid (100) add 139 mL of triethylamine and water to make 1000 mL. To 20 mL of this solution add 835 mL of water, 140 mL of acetonitrile and 5 mL of dilute acetic acid.

Flow rate: Adjust the flow rate so that the retention time of cefoperazone 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 cefoperazone are eluted in

this order with the resolution between these peaks being not less than 5.

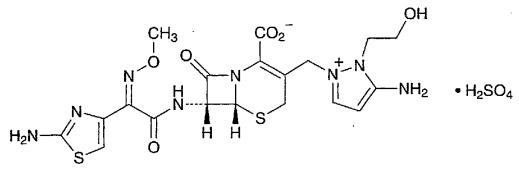
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefoperazone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Hermetic containers.

Storage—In a cold place.

Cefoselis Sulfate

硫酸セフォセリス



$C_{19}H_{22}N_8O_6S_2.H_2SO_4$: 620.64

(6*R*,7*R*)-3-{[3-Amino-2-(2-hydroxyethyl)-2*H*-pyrazol-1-ium-1-yl]methyl}-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylamino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate monosulfate

[*122841-12-7*]

Cefoselis Sulfate contains not less than 770 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefoselis Sulfate is expressed as mass (potency) of cefoselis ($C_{19}H_{22}N_8O_6S_2$: 522.56).

Description Cefoselis Sulfate occurs as a white to pale yellowish white crystalline powder.

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

It is hygroscopic.

Identification **(1)** Determine the absorption spectra of solutions of Cefoselis Sulfate and Cefoselis Sulfate Reference Standard (1 in 80,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectra of Cefoselis Sulfate and Cefoselis Sulfate Reference Standard as directed in the paste method under the Infrared Spectrophotometry, and compare the spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefoselis Sulfate in deuterated dimethyl sulfoxide for nuclear magnetic resonance spectroscopy (1 in 20), using tetramethylsilane for nuclear magnetic sesonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (^1H): it exhibits a triple signal A at around δ 3.6 ppm, single signals B and C, at around δ 3.8 ppm and at around δ 6.7 ppm, and a double signal D, at around δ 8.0 ppm. The ratio of integrated intensity of each signal, A:B:C:D, is about 2:3:1:1.

(4) A solution of Cefoselis Sulfate (1 in 100) responds to the Qualitative Test (1) for sulfate salt.

Optical rotation $[\alpha]_D^{25}$: −26 – −31° (0.4 g, dimethyl sulfoxide, 20 mL, 100 mm).

pH Dissolve 0.1 g of Cefoselis Sulfate in 10 mL of water: the pH of the solution is between 1.8 and 2.4.

Purity **(1)** Heavy metals—Proceed with 2.0 g of Cefoselis Sulfate according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution. Use a solution of magnesium nitrate hexahydrate in ethanol (95) (3 in 10) instead of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10) (not more than 10 ppm).

(2) Arsenic—Being specified separately.

(3) Related substances—Being specified separately.

(4) Monoethanolamine—Being specified separately.

(5) Residual solvents—Being specified separately.

Water Not more than 1.0% (0.5 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. Taking care the sampling to avoid moisture absorption).

Residue on ignition Being specified separately.

Foreign Insoluble Matter Test Being specified separately.

Bacterial endotoxins Less than 0.05 EU/mg (potency). Use tris buffer solution for bacterial endotoxins test instead of water for bacterial endotoxins test as the diluent of the standard solution and as the solution for endotoxin spike of gel-clot technique or turbidimetric technique.

Sterility Being specified separately.

Assay Weigh accurately an amount of Cefoselis Sulfate and Cefoselis Sulfate Reference Standard, equivalent to about 0.025 g (potency), dissolve in 0.1 mol/L phosphate buffer solution, pH 7.0 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 peak areas, A_T and A_S, of cefoselis of each solution.

$$\text{Amount [}\mu\text{g (potency)] of cefoselis } (C_{19}H_{22}N_8O_6S_2) = \text{amount [mg (potency)] of Cefoselis Sulfate Reference Standard} \times \frac{A_T}{A_S} \times 1000$$

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 25°C.

Mobile phase: A mixture of phosphate buffer solution, pH 6.5 and acetonitrile for liquid chromatography (10:1).

Flow rate: Adjust the flow rate so that the retention time of cefoselis is about 5 minutes.