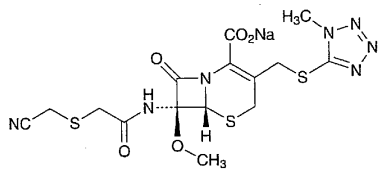
Cefmetazole Sodium

セフメタゾールナトリウム



$C_{15}H_{16}N_7NaO_5S_3$: 493.52
Monosodium (6*R*,7*R*)-7-(2-cyanomethylsulfanylacetylamino)-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylsulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate
[*56796-20-4*]

Cefmetazole Sodium contains not less than 860 μg (potency) per mg, calculated on the anhydrous basis. The potency of Cefmetazole Sodium is expressed as mass (potency) of cefmetazole ($C_{15}H_{16}N_7O_5S_3$: 438.47).

Description Cefmetazole Sodium occurs as a white to light yellowish white, powder or mass.

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

Identification **(1)** Determine the absorption spectrum of a solution of Cefmetazole Sodium (1 in 40,000) 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 Cefmetazole 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 Cefmetazole Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy (^{1}H), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits single signals, A, B and C, at around δ 3.6 ppm, at around δ 4.1 ppm and at around δ 5.2 ppm, respectively. The ratio of integrated intensity of each signal, A:B:C, is about 3:3:1.

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

Optical rotation $[\alpha]_D^{20}$: +73 – +85° (0.25 g, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Cefmetazole Sodium in 10 mL of water: the pH of the solution is between 4.2 and 6.2.

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

(2) Heavy metals—Proceed with 1.0 g of Cefmetazole 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).

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

(4) Related substances—Dissolve 0.10 g of Cefmetazole Sodium in 2 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 25 mL, and use this solution as the standard solution (1). Separately, dissolve 0.10 g of 1-methyl-1*H*-tetrazole-5-thiol in water to make exactly 100 mL, and use this solution as the standard solution (2). Immediately perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 1 μL each of the sample solution, the standard solution (1) and the standard solution (2) on a plate of silica gel for thin-layer chromatography. Develop with a mixture of 1-buthanol, water and acetic acid (100) (4:1:1) to a distance of about 12 cm, and air-dry the plate. Allow the plate to stand in iodine vapor: the spot obtained from the sample solution corresponding to the spot from the standard solution (2) is not more intense than the spot from the standard solution (2), and the spots other than this spot and other than the principal spot are not more intense than the spot from the standard solution (1).

Water Not more than 1.0% (1 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Cefmetazole Sodium and Cefmetazole Reference Standard, equivalent to about 0.05 g (potency), and dissolve each in the mobile phase to make exactly 25 mL. Pipet 1 mL each of these solutions, add exactly 10 mL of the internal standard solution, 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 cefmetazole to that of the internal standard of each solution.

$$\text{Amount [}\mu\text{g (potency)] of } C_{15}H_{17}N_7O_5S_3 = \text{amount [mg (potency)] of Cefmetazole Reference Standard} \times \frac{Q_T}{Q_S} \times 1000$$

Internal standard solution—A solution of methyl parahydroxybenzoate in the mobile phase (1 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 214 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 25°C.

Mobile phase: Dissolve 5.75 g of ammonium dihydrogenphosphate in 700 mL of water, add 280 mL of methanol, 20 mL of tetrahydrofuran and 3.2 mL of 40% tetrabutylammonium hydroxide TS, and adjust to pH 4.5 with phosphoric acid.

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

System suitability—

System performance: When the procedure is run with 10

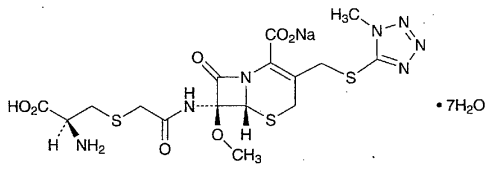
μL of the standard solution under the above operating conditions, cefmetazole and the internal standard are eluted in this order with the resolution between these peaks being not less than 10.

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.

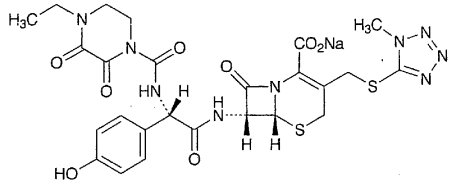
(4) Sample solution—Weigh accurately an amount of Cefminox Sodium equivalent to about 0.04 g (potency), dissolve in 0.05 mol/L phosphate buffer solution, pH 7.0 to make exactly 50 mL. Take exactly a suitable amount of this solution, add 0.05 mol/L phosphate buffer solution, pH 7.0 to make solutions so 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*]