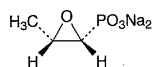


Fosfomycin Sodium

ホスホマイシンナトリウム



$C_3H_5Na_2O_4P$: 182.02

Disodium (2*R*,3*S*)-3-methyloxiran-2-ylphosphonate
[26016-99-9]

Fosfomycin Sodium contains not less than 725 μ g (potency) per mg, calculated on the anhydrous basis. The potency of Fosfomycin Sodium is expressed as mass (potency) of fosfomycin ($C_3H_7O_4P$: 138.06).

Description Fosfomycin Sodium occurs as a white crystalline powder.

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

Identification (1) Determine the infrared absorption spectrum of Fosfomycin 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.

(2) Determine the spectrum of a solution of Fosfomycin Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 300), using sodium 3-trimethylsilylpropanesulfonate for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (1H): it exhibits sharp single signals, at around δ 1.48 ppm, δ 2.84 ppm and δ 3.27 ppm, respectively, and exhibit no signal at around δ 1.32 ppm.

(3) A solution of Fosfomycin Sodium (1 in 500) responds to the Quantitative Test (1) for sodium salt.

Optical rotation $[\alpha]_D^{20}$: $-3.5 - -5.5^\circ$ (0.50 g calculated on the anhydrous bases, water, 10 mL, 100 mm).

pH Dissolve 0.70 g of Fosfomycin Sodium in 10 mL of water: the pH of the solution is between 8.5 and 10.5.

Phosphorus Content Weigh accurately about 0.1 g of Fosfomycin Sodium, add 40 mL of a solution of sodium periodate (107 in 10,000) and 2 mL of perchloric acid, and heat in a water bath for 1 hour. After cooling, add water to make exactly 200 mL. Pipet 10 mL of this solution, and add 1 mL of potassium iodide TS. To this solution add sodium thiosulfate TS until the solution is colorless, add water to make exactly 100 mL, and use this solution as the sample stock solution. Separately, weigh accurately about 0.07 g of potassium dihydrogenphosphate, proceed with this solution in the same manner as directed for the preparation of the sample stock solution, and use the solution so obtained as the standard stock solution. Proceed and prepare a solution in the same manner for the preparation of the sample stock solution without using Fosfomycin Sodium, and use the solution so obtained as the blank stock solution. Pipet 5 mL each of the sample stock solution, the standard stock solution, and the blank stock solution, add 2.5 mL of ammonium molybdate-sulfuric acid TS and 1 mL of 1-amino-2-

naphthol-4-sulfonic acid TS, mix, and add water to make 25 mL, and use these solutions as the sample solution, the standard solution, and the blank solution, respectively. After allowing these solutions to stand for 30 minutes at $20 \pm 1^\circ C$, perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry, using water as a blank, and determine the absorbances at 740 nm, A_T , A_S and A_B , of the sample solution, the standard solution and the blank solution: the content of phosphorus is 16.2–17.9%.

Amount (mg) of phosphorus (P)

$$= \text{amount (mg) of potassium dihydrogenphosphate} \\ \times \frac{A_T - A_B}{A_S - A_B} \times 0.22760$$

Purity (1) Clarity and color of solution—A solution of Fosfomycin Sodium (1 in 10) is clear and colorless to pale yellow.

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

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

Water Not more than 3.0% (0.2 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—*Proteus* sp. (MB838)

(2) Culture medium—Mix 5.0 g of peptone, 3.0 g of meat extract, 2.0 g of yeast extract, and 15 g of agar in 1000 mL of water, sterilize, and use as the agar media for base layer and seed layer with the pH of between 6.5 and 6.6 after sterilization.

(3) Seeded agar layer—Incubate the test organism on the slant of the agar medium for transferring test organisms at $37^\circ C$ for 40–48 hours. Subcultures at least three times. Inoculate the grown organisms onto the surface of 300 mL of the agar medium for transferring test organisms in a Roux bottle, incubate at $37^\circ C$ for 40–48 hours, and suspend the grown organisms in about 30 mL of water. To the suspension add water, and use this as the stock suspension of test organism. The amount of the water to be added is adjust so that the percent transmission at 560 nm of the suspension diluted ten times with water is 17%. Keep the stock suspension at $10^\circ C$ or below and use within 7 days. Add 1.0–2.0 mL of the stock suspension of test organism to 100 mL of the agar medium for seed layer previously kept at $48^\circ C$, mix thoroughly, and use this as the seeded agar layer.

(4) Standard solution—Weigh accurately an amount of Fosfomycin Phenethylammonium Reference Standard equivalent to about 0.02 g (potency), dissolve in 0.05 mol/L Tris 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 $5^\circ C$ or below and use within 7 days. Take exactly a suitable amount of the standard stock solution before use, add 0.05 mol/L Tris buffer solution, pH 7.0 to make solutions so that each mL contains 10 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration standard solution and the low concentra-

tion standard solution, respectively.

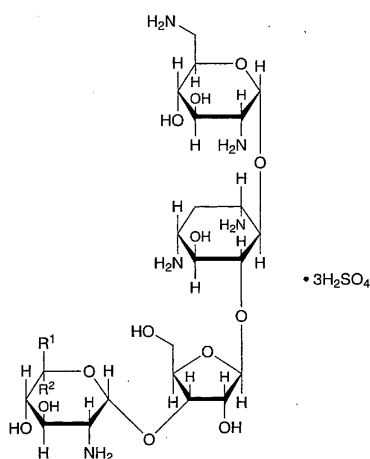
(5) Sample solution—Weigh accurately an amount of Fosfomycin Sodium equivalent to about 0.02 g (potency), and dissolve in 0.05 mol/L Tris buffer solution, pH 7.0 to make exactly 50 mL. To exactly a suitable amount of this solution add 0.05 mol/L Tris buffer solution, pH 7.0 to make solutions so that each mL contains 10 μ g (potency) and 5 μ g (potency), and use these solutions as the high concentration sample solution and the low concentration sample solution, respectively.

Containers and storage Containers—Hermetic containers.

Fradiomycin Sulfate

Neomycin Sulfate

硫酸フラジオマイシン



Fradiomycin B: R¹=H R²=CH₂NH₂

Fradiomycin C: R¹=CH₂NH₂ R²=H

C₂₃H₄₆N₆O₁₃·3H₂SO₄: 908.88

Fradiomycin Sulfate B

O-2,6-Diamino-2,6-dideoxy- α -D-glucopyranosyl-(1 \rightarrow 4)-*O*-[*O*-2,6-diamino-2,6-dideoxy- α -D-glucopyranosyl-(1 \rightarrow 3)- β -D-ribofuranosyl-(1 \rightarrow 5)]-2-deoxy-D-streptamine trisulfate [119-04-0]

Fradiomycin Sulfate C

O-2,6-Diamino-2,6-dideoxy- α -D-glucopyranosyl-(1 \rightarrow 4)-*O*-[*O*-2,6-diamino-2,6-dideoxy- β -L-idopyranosyl-(1 \rightarrow 3)- β -D-ribofuranosyl-(1 \rightarrow 5)]-2-deoxy-D-streptamine trisulfate [66-86-4] [1405-10-3, Neomycin Sulfate]

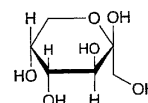
Fradiomycin Sulfate conforms to the requirements of Fradiomycin Sulfate in the Requirements for Antibiotic Products of Japan.

Description Fradiomycin Sulfate occurs as a white to light yellow powder.

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

Fructose

果糖



C₆H₁₂O₆: 180.16

β -D-Fructopyranose [57-48-7]

Fructose, when dried, contains not less than 98.0% of C₆H₁₂O₆.

Description Fructose occurs as colorless to white crystals or crystalline powder. It is odorless and has a sweet taste.

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

It is hygroscopic.

Identification (1) Add 2 to 3 drops of a solution of Fructose (1 in 20) to 5 mL of boiling Fehling's TS: a red precipitate is produced.

(2) Determine the infrared absorption spectrum of Fructose as directed in the paste 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.

pH Dissolve 4.0 g of Fructose in 20 mL of water: the pH of the solution is between 4.0 and 6.5.

Purity (1) Clarity and color of solution—Dissolve 25.0 g of Fructose in 50 mL of water: the solution is clear and has no more color than the following control solution.

Control solution: To a mixture of 1.0 mL of Cobaltous Chloride Stock CS, 3.0 mL of Ferric Chloride Stock CS and 2.0 mL of Cupric Sulfate Stock CS, and add water to make 10.0 mL. To 3.0 mL of the solution add water to make 50 mL.

(2) Acid—Dissolve 5.0 g of Fructose in 50 mL of freshly boiled and cooled water, and add 3 drops of phenolphthalein TS and 0.60 mL of 0.01 mol/L sodium hydroxide VS: a red color develops.

(3) Chloride—Perform the test with 2.0 g of Fructose. Prepare the control solution with 1.0 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.018%).

(4) Sulfate—Perform the test with 2.0 g of Fructose. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS (not more than 0.024%).

(5) Sulfite—Dissolve 0.5 g of Fructose in 5 mL of water, and add 0.25 mL of 0.02 mol/L iodine: the color of the solution is yellow.

(6) Heavy metals—Proceed with 5.0 g of Fructose according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 4 ppm).

(7) Calcium—Dissolve 0.5 g of Fructose in 5 mL of water, add 2 to 3 drops of ammonia TS and 1 mL of ammonium oxalate TS, and allow to stand for 1 minute: the solution is clear.

(8) Arsenic—Dissolve 1.5 g of Fructose in 5 mL of water, heat with 5 mL of dilute sulfuric acid and 1 mL of