Streptomycin sulfate (Streptomycini sulfas)

Streptomycin sulfate (non-injectable)

Streptomycin sulfate, sterile

**Molecular formula.** \((\text{C}_{21}\text{H}_{39}\text{N}_7\text{O}_{12})_2\cdot3\text{H}_2\text{SO}_4\)

**Relative molecular mass.** 1457

**Graphic formula.**

Chemical name. O-2-Deoxy-2-(methylamino)-α-L-glucopyranosyl-(1→2)-O-5-deoxy-3-C-formyl-α-L-lyxofuranosyl-(1→4)-N,N'-bis(aminomethyl)-D-streptamine sulfate (2:3) (salt); CAS Reg. No. 3810-74-0.

Description. A white or almost white powder; odourless or with a slight odour.

Solubility. Very soluble in water; practically insoluble in ethanol (~750 g/l) TS and ether R.

Category. Antibiotic.

Storage. Streptomycin sulfate should be kept in a well-closed container and protected from moisture.

Labelling. The designation sterile Streptomycin sulfate indicates that the substance complies with the additional requirements for sterile Streptomycin sulfate and may be used for parenteral administration or for other sterile applications.

Additional information. Streptomycin sulfate is hygroscopic, but it is stable in air and on exposure to light.

Requirements

Definition. Streptomycin sulfate contains not less than 90.0% of \((\text{C}_{21}\text{H}_{39}\text{N}_7\text{O}_{12})_2\cdot3\text{H}_2\text{SO}_4\) and not less than 720 International Units per mg, both calculated with reference to the dried substance.

Manufacture. The method of manufacture is validated to demonstrate that the product, if tested, would comply with the following test.
Histamine-like substances. Carry out the test as described under 3.6 Test for histamine-like substances (vasodepressor substances) using, per kg of body weight, a solution containing 3 mg of streptomycin base in 1 mL of saline TS.

Identity tests

A. Dissolve 20 mg in 5 mL of water and boil for a few minutes with 10 drops of sodium hydroxide (1 mol/l) VS; add 3 drops of hydrochloric acid (~250 g/l) TS and 1 mL of ferric chloride (25 g/l) TS; an intense violet colour is produced.

B. Dissolve 0.1 g in 2 mL of water, add 1 mL of 1-naphthol TS1 and 2 mL of a mixture of equal volumes of sodium hypochlorite (~40 g/l) TS and water; a red colour is produced.

C. A 20 mg/mL solution yields reaction A described under 2.1 General identification tests as characteristic of sulfates.

Clarity and colour of solution. A solution of 1.0 g in 10 mL of water is clear and not more intensely coloured than standard colour solution Yw4 when compared as described in 1.11.1 Colour of liquids.

Loss on drying. Dry at 60°C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury) for 3 hours; it loses not more than 70 mg/g.

pH value. pH of a 0.25 g/mL solution in carbon-dioxide-free water R, 4.5-7.0.

Methanol. Transfer 0.2 g, accurately weighed, to a flask, dissolve in 5 mL of water and add 0.05 mL of sulfuric acid (0.05 mol/l) VS; connect the flask to a distillation apparatus, distil and collect about 2.5 mL of distillate in a 10-mL test-tube. Transfer the distillate to a conical flask, rinsing the test-tube twice with water, using 1 mL each time, and add 25 mL of potassium dichromate (0.0167 mol/l) VS. Cautiously add 10 mL of sulfuric acid (~1760 g/l) TS and heat the resulting solution for 30 minutes on a water-bath; cool and dilute to about 500 mL with water. Add 12.5 mL of potassium iodide (80 g/l) TS, allow to stand for 5 minutes, and then titrate with sodium thiosulfate (0.1 mol/l) VS, using starch TS as indicator, added towards the end of the titration, the end-point being reached when the dark blue colour turns pale green. Repeat the operation without the substance being tested; the difference between the volumes used for the two titrations represents the amount of sodium thiosulfate (0.1 mol/l) VS, equivalent to the methanol present. Each mL of sodium thiosulfate (0.1 mol/l) VS is equivalent to 0.534 mg of CH₄O; the methanol content is not more than 40 mg/g, calculated as CH₄O.

Assay

For streptomycin sulfate. Dissolve about 0.10 g, accurately weighed, in sufficient water to produce 100 mL. To 5 mL add 5 mL of sodium hydroxide (0.2 mol/l) VS and heat in a water-bath for exactly 10 minutes. Cool in ice for exactly 5 minutes, add 3 mL of ferric ammonium sulfate TS2 and sufficient water to produce 25 mL, and mix. Exactly 20 minutes after the addition of the ferric ammonium sulfate TS2 measure the absorbance of a 1-cm layer at the maximum at about 525 nm, against a solvent cell containing a solution prepared in the same manner but omitting the substance being examined. Calculate the content of (C₂₁H₃₉N₇O₁₂)₂•3H₂SO₄ in the substance, using the absorptivity value of 1.18 (%A₁cm = 11.8).

For potency. Carry out the assay as described under 3.1 Microbiological assay of antibiotics, using either (a) Bacillus subtilis (NCTC 8236, or ATCC 11774) as the test organism, culture medium Cm1 with a final pH of 7.9-8.0, sterile phosphate buffer pH 8.0, TS1 or TS2, an appropriate concentration of streptomycin (usually between 5 and 20 IU), and an incubation temperature of 36-39°C, or (b) Bacillus subtilis (ATCC 6633) as the test organism, culture medium Cm1 with a final pH of 8.0-8.1, sterile phosphate buffer pH 8.0, TS1 or TS2, an appropriate concentration of streptomycin (usually between 3 and 15 IU), and an incubation temperature of 35-37°C. The precision of the assay is such that the fiducial limits of error of the estimated potency (P = 0.95) are not less than 95% and not more than 105% of the estimated potency. The upper fiducial limit of error of the estimated potency (P = 0.95) is not less than 720 IU per mg, calculated with reference to the dried substance.

Additional Requirements for Streptomycin Sulfate for sterile use

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 0.25 IU of endotoxin RS per mg of streptomycin.

Sterility. Complies with 3.2 Test for sterility.