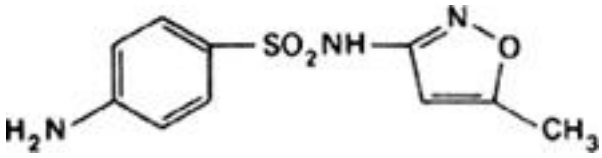
Sulfamethoxazole (Sulfamethoxazolum)

Molecular formula. $C_{10}H_{11}N_3O_3S$

Relative molecular mass. 253.3

Graphic formula.



Chemical name. *N*′-(5-Methyl-3-isoxazolyl)sulfanilamide: 4-amino-*N*-(5-methyl-3-isoxazolyl)benzenesulfonamide; CAS Reg. No. 723-46-6.

Description. A white or yellowish white, crystalline powder; odourless.

Solubility. Very slightly soluble in water; soluble in 50 parts of ethanol (~750 g/l) TS and in 3 parts of acetone R.

Category. Antibacterial.

Storage. Sulfamethoxazole should be kept in a well-closed container, protected from light.

Requirements

Definition. Sulfamethoxazole contains not less than 99.0% and not more than 101.0% of $C_{10}H_{11}N_3O_3S$, calculated with reference to the dried substance.

Identity tests

• Either tests A and C or tests B and C may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from sulfamethoxazole RS or with the *reference spectrum* of sulfamethoxazole.

B. Dissolve 5 mg in 0.5 mL of sodium hydroxide (~80 g/l) TS and add 5 mL of water. Add 0.1 g of phenol R, heat to boiling, cool, and add 1 mL of sodium hypochlorite (~40 g/l) TS; a golden yellow colour is immediately produced and is persistent.

C. About 0.1 g yields the reaction described for the identification of primary aromatic amines under 2.1 General identification tests, producing a red-orange precipitate.

Melting range. 168-172°C.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals. Procedure 3; determine the heavy metals content according to Method A; not more than 20 µg/g.

Solution in alkali. Dissolve 0.40 g in a mixture of 8.0 mL of water and 2.0 mL of sodium hydroxide (1 mol/l) VS; the solution is clear.

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C; it loses not more than 5.0 mg/g.

Acidity. Heat 1.0 g with 50 mL of carbon-dioxide-free water R at about 70°C for 5 minutes, cool quickly to 20°C, and filter; titrate 25 mL of the filtrate, phenolphthalein/ethanol TS being used as indicator; not more than 0.35 mL of sodium hydroxide (0.1 mol/l) VS is required to obtain the midpoint of the indicator.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R3 as the coating substance and a mixture of 20 volumes of chloroform R, 2 volumes of methanol R, and 1 volume of dimethylformamide R as the mobile phase. Apply separately to the plate 10 µl of each of 2 solutions in a mixture of 9 volumes of ethanol (~750 g/l) TS and 1 volume of ammonia (~260 g/l) TS containing (A) 2.5 mg of the test substance per mL and (B) 12.5 µg of sulfanilamide RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air until the solvents have evaporated. Spray the dried plate with sulfuric acid/ethanol TS, heat at 105°C for 30 minutes, and immediately expose to nitrous fumes in a closed chamber for 15 minutes (the nitrous fumes may be generated by adding sulfuric acid (~700 g/l) TS drop by drop to a solution containing 10 g of sodium nitrite R and 3 g of potassium iodide R in 100 mL). Place the plate in a current of warm air for 15 minutes and spray with *N*-(1-naphthyl)ethylenediamine hydrochloride/ethanol TS. If necessary, allow to dry before repeating the spraying and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal

spot, is not more intense than that obtained with solution B.

Assay. Carry out the assay as described under 2.7 Nitrite titration, using about 0.5 g, accurately weighed, dissolved in a mixture of 40 mL of water and 20 mL of glacial acetic acid R; add 15 mL of hydrochloric acid (~70 g/l) TS and titrate with sodium nitrite (0.1 mol/l) VS. Each mL of sodium nitrite (0.1 mol/l) VS is equivalent to 25.33 mg of $C_{10}H_{11}N_3O_3S$.

Additional requirement for Sulfamethoxazole for parenteral use

Complies with the monograph for "Parenteral preparations".