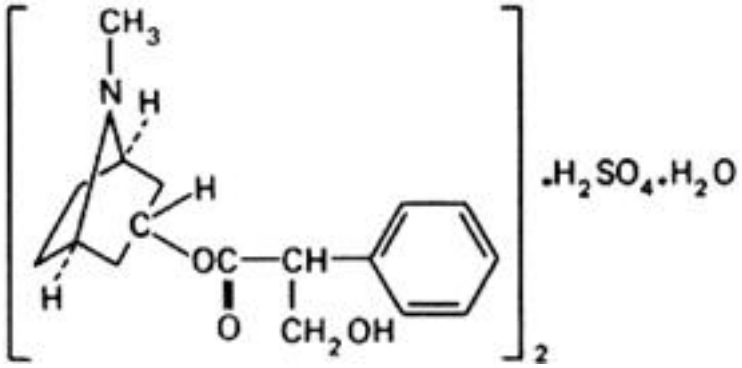
Atropine sulfate (Atropini sulfas)

Molecular formula. $(C_{17}H_{23}NO_3)_2,H_2SO_4,H_2O$

Relative molecular mass. 694.8

Graphic formula.



Chemical name. 1*αH*,5*αH*-Tropan-3*α*-ol (±)-tropate (ester) sulfate (2:1) (salt) monohydrate; (±)-*endo*-8-methyl-8-azabicyclo[3.2.1]oct-3-yl *α*-(hydroxymethyl)benzeneacetate sulfate (2:1) (salt) monohydrate; CAS Reg. No. 5908-99-6.

Description. Colourless crystal or a white, crystalline powder; odourless.

Solubility. Soluble in less than 1 part of water; freely soluble in ethanol (~750 g/l) TS; practically insoluble in ether R and benzene R.

Category. Cholinergic blocking agent (parasympatholytic).

Storage. Atropine sulfate should be kept in a tightly closed container, protected from light.

Additional information. Atropine sulfate is very poisonous; it effloresces in dry air; it is slowly affected by light.

Requirements

Definition. Atropine sulfate contains not less than 98.5% and not more than 101.0% of $(C_{17}H_{23}NO_3)_2,H_2SO_4$, calculated with reference to the dried substance.

Identity tests

• Either test A alone or all 3 tests B, C, and D 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 atropine sulfate RS or with the *reference spectrum* of atropine sulfate.

B. Mix 1 mg with 5 drops of fuming nitric acid R and evaporate to dryness on a water-bath. To the cooled residue add 2 mL of acetone R and 3-4 drops of potassium hydroxide/methanol TS; a deep violet colour is produced.

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

D. Dissolve 0.6 g in 30 mL of carbon-dioxide-free water R and add 2 mL of sodium hydroxide (~80 g/l) TS. Filter, wash the precipitate with water and dry at 100°C. Melting temperature, about 116°C (atropine base).

Optical rotation. Use a solution containing the equivalent of 0.10 g/mL of the dried substance, in a 200-mm tube; optical rotation = - 0.50 to + 0.10° (distinction from hyoscyamine).

Sulfated ash. Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 120°C; it loses not less than 25 mg/g and not more than 40 mg/g.

Acidity. Dissolve 1.0 g in 20 mL of carbon-dioxide-free water R and titrate with sodium hydroxide (0.02 mol/l) VS, using methyl red/ethanol TS as indicator; not more than 0.3 mL is required to obtain the midpoint of the indicator (orange).

Readily oxidizable substances. To 10 mL of a 10 mg/mL solution add 0.1 mL of potassium permanganate (0.02 mol/l) VS; the colour is not completely discharged at the end of 3 minutes.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 6 volumes of ethylmethylketone R, 3 volumes of methanol R and 1 volume of

ammonia (~100 g/l) TS as the mobile phase. Apply to the plate 10 µl of a solution in methanol R containing 12.5 mg/mL of the test substance. After removing the plate from the chromatographic chamber, allow it to dry in air, spray with potassium iodobismuthate TS2 and examine the chromatogram in daylight. No spot is obtained, other than the principal spot.

Assay. Dissolve about 0.6 g, accurately weighed, in 30 mL of glacial acetic acid R1, and titrate with perchloric acid (0.1 mol/l) VS as described under 2.6 Non-aqueous titration, Method A. Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 67.68 mg of $(C_{17}H_{23}NO_3)_2,H_2SO_4$.

Additional requirements for Atropine sulfate for parenteral use

Complies with the monograph for "Parenteral preparations".

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 55.6 IU of endotoxin RS per mg.

Additional requirement for Atropine sulfate for sterile use

Complies with 3.2 Test for sterility.