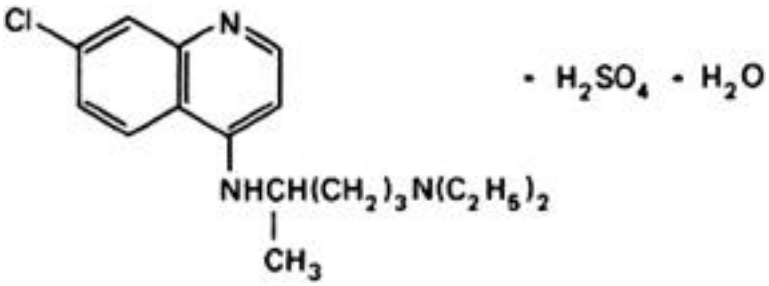
Chloroquine sulfate (Chloroquini sulfas)

Molecular formula. $C_{18}H_{26}ClN_3,H_2SO_4,H_2O$

Relative molecular mass. 436.0

Graphic formula.



Chemical name. 7-Chloro-4-[[4-(diethylamino)-1-methylbutyl]amino]quinoline sulfate (1:1) monohydrate; N^4-(7-chloro-4-quinolinyl)-N^1,N^1-diethyl-1,4-pentanediamine sulfate (1:1) monohydrate; CAS Reg. No. 6823-83-2.

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

Solubility. Soluble in 3 parts of water; practically insoluble in ethanol (~750 g/l) TS; sparingly soluble in ether R.

Category. Antimalarial.

Storage. Chloroquine sulfate should be kept in a well-closed container protected from light.

Additional information. Chloroquine sulfate has a bitter taste.

Requirements

Definition. Chloroquine sulfate contains not less than 98.0% and not more than 101.0% of $C_{18}H_{26}ClN_3,H_2SO_4$, calculated with reference to the dried substance.

Identity tests

A. The absorption spectrum (1.6) of a 10 µg/mL solution in hydrochloric acid (0.01 mol/l) VS, when observed between 240 nm and 360 nm, exhibits 3 maxima at about 257 nm, 329 nm, and 343 nm. The absorbances at those wavelengths are about 0.39, 0.44, and 0.46, respectively (preferably use 2-cm cells for the measurements and calculate the absorbances of 1-cm layers). The ratio of the absorbance of a 1-cm layer at 257 nm to that at 343 nm is between 0.83 and 0.98 and the ratio of the absorbance at 329 nm to that at 343 nm is between 0.94 and 1.03.

B. A 0.05 g/mL solution yields reaction A described under 2.1 General identification tests as characteristic of sulfates.

C. To a solution of 0.05 g in 20 mL of water R add 5 mL of trinitrophenol (7 g/l) TS. Filter, wash the precipitate with water R until the filtrate is colourless and dry the precipitate over silica gel, desiccant, R. Melting temperature, about 207°C (picrate).

Sulfated ash (*2.3*). Not more than 1.0 mg/g.

Loss on drying. Dry to constant weight at 105°C under reduced pressure (not exceeding 0.6 kPa or about 5 mm of mercury); it loses not less than 30 mg/g and not more than 50 mg/g.

pH value (*1.13*). pH of a 0.10 g/mL solution, 4.0-5.0.

Related substances. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R2 as the coating substance and a mixture of 5 volumes of chloroform R, 4 volumes of cyclohexane R, and 1 volume of diethylamine R as the mobile phase. Apply separately to the plate 5 µl of each of 3 solutions containing (A) 40 mg of the test substance per mL, (B) 0.40 mg of the test substance per mL and (C) 0.20 mg of the test substance per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (254 nm).

Any spot in the chromatogram obtained with solution A, other than the principal spot, is not more intense than that in the chromatogram obtained with solution B (1.0%) and not more than one such spot is more intense than that in the chromatogram obtained with solution C (0.5%).

Assay. Dissolve about 0.4 g, accurately weighed, in 20 mL of glacial acetic acid R1 with the aid of heat (preferably under a reflux

condenser), cool, and add 20ml of dioxan R. 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 41.8mg of $C_{18}H_{26}ClN_3,H_2SO_4$.

Additional requirement for Chloroquine sulfate for parenteral use

Complies with the monograph for "Parenteral preparations".