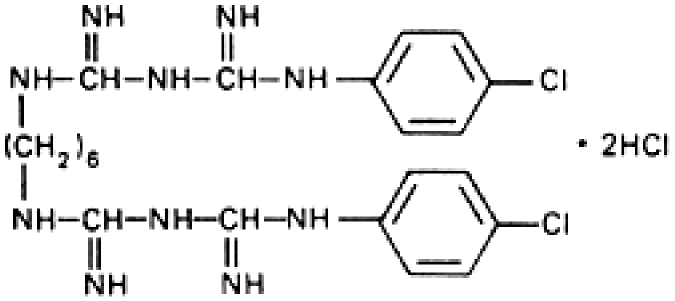
## Chlorhexidine dihydrochloride (Chlorhexidini dihydrochloridum)

2018-01

**Molecular formula.** $C_{22}H_{30}Cl_2N_{10}$,2HCl

**Relative molecular mass.** 578.4

**Graphic formula.**



**Chemical name.** 1,1'-Hexamethylenebis[5-(*p*-chlorophenyl)biguanide] dihydrochloride; *N,N″*-bis(4-chlorophenyl)-3,12-diimino-2,4,11,13-tetraazatetradecanediimidamide dihydrochloride; CAS Reg. No. 3697-42-5.

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

**Solubility.** Sparingly soluble in water; soluble in 450 parts of ethanol (~750 g/l) TS.

**Category.** Disinfectant.

**Storage.** Chlorhexidine dihydrochloride should be kept in a well-closed container, protected from light.

### Requirements

**Definition.** Chlorhexidine dihydrochloride contains not less than 98.0% and not more than 101.0% of $C_{22}H_{30}Cl_2N_{10}$,2HCl, calculated with reference to the dried substance.

### Identity tests

A. Dissolve 20 mg in 10 mL of methanol R by warming, and add a mixture of 2 mL of sodium hydroxide (~150 g/l) TS and 2 mL of bromine TS1; a deep red colour is produced.

B. Dissolve 0.1 g in 10 mL of water and add, with shaking, 0.15 mL of copper(II) chloride/ammonia TS; a purple precipitate is produced immediately. Continue to add 0.5 mL of copper(II) chloride/ammonia TS; the colour of the precipitate changes to blue.

C. Dissolve 0.1 g in 50 mL of nitric acid (~130 g/l) TS; the solution yields reaction A described under 2.1 General identification tests as characteristic of chlorides.

**Sulfated ash.** Not more than 1.0 mg/g.

**Loss on drying.** Dry to constant weight at 130°C; it loses not more than 20 mg/g.

**Chloraniline.** Dissolve 0.20 g in 30 mL of water. Add with mixing 5 mL of hydrochloric acid (1 mol/L) VS, 1 mL of sodium nitrite (35 g/L) TS, 2 mL of ammonium sulfamate (50 g/L) TS and shake. Then add 5 mL of freshly prepared *N*-(1-naphthyl)ethylenediamine hydrochloride(1 g/L)TS, 1 mL of ethanol (~750 g/L) TS, and sufficient water to produce 50 mL. Allow to stand for 30 minutes. Treat similarly 30 mL of a solution containing 0.10 mg of chloraniline R that has been slightly acidified with hydrochloric acid (~70 g/L) TS. The colour produced in the test solution is not more intense than that of the reference solution when compared as described in 1.11.1 Colour of liquids (0.5 mg/g).

**Related substances.** Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using silica gel R4 as the coating substance and preparing a slurry as follows: To 8 g of silica gel R4 add 16 mL of water containing 1 g of sodium formate R and coat the plates with a layer, 0.5 mm thick. Use a mixture of 50 volumes of chloroform R, 50 volumes of ethanol (~750 g/l) TS, and 7 volumes of formic acid (~1080 g/l) TS as the mobile phase. Prepare solution A by dissolving 1.1 g of the test substance in 35 mL of hydrochloric acid (~330 g/l) TS, add 100 mL of 2-propanol R, cool in ice, make alkaline with sodium hydroxide (~200 g/l) TS, cool in ice, add 200 mL of ice-cooled water, and extract with 100 mL of chloroform R. Dry the chloroform extract over anhydrous potassium carbonate R, filter, evaporate the chloroform almost to dryness under a stream of nitrogen R, add 50 mL of methanol R, evaporate to dryness under a stream of nitrogen R, and dry the residue at 65 °C for 30 minutes; dissolve 0.56 g of the dried residue in sufficient acetic acid (~90 g/l) TS to produce 100 mL. Apply to the plate in the form of a band, 4 cm wide, 20 µl of solution A. After removing the plate from the chromatographic chamber, allow it to dry in air and examine the chromatogram in ultraviolet light (254 nm). Score a rectangular area around each group of bands above and below the principal band, quantitatively transfer the enclosed areas of silica gel to a glass-stoppered test-tube, add 5 mL of methanol R, shake for 15 minutes, centrifuge, and measure the absorbance of the clear supernatant liquid in a 1-cm layer at the maximum at about 256 nm. For the blank solution treat in a similar manner equivalent-sized areas of silica gel removed from the coating adjacent to the areas previously removed. Prepare solution B in the following manner: Dissolve 0.11 g of the dried residue in sufficient acetic acid (~90 g/l) TS to produce 100 mL and dilute 200 µl of this solution to 50 mL with methanol R. The absorbance obtained from the eluted solution A is not greater than the absorbance obtained from solution B.

**Assay.** In order to avoid overheating in the reaction medium, mix thoroughly throughout the titration and stop the titration immediately after the end-point has been reached.

Dissolve 0.100 g in 5 mL of anhydrous formic acid R and add 70 mL of acetic anhydride R. Carry out a potentiometric titration using perchloric acid (0.1 mol/L) VS, as described under *2.6 Non-aqueous titration*, Method A.

1 mL of perchloric acid (0.1 mol/L) VS is equivalent to 14.46 mg of $C_{22}H_{30}Cl_2N_{10}$,2HCl.