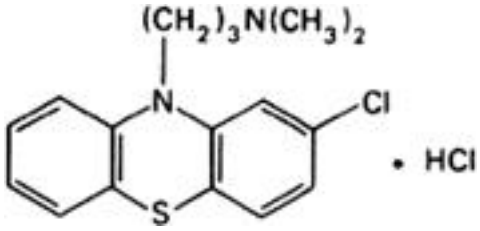
Chlorpromazine hydrochloride (Chlorpromazini hydrochloridum)

2018-01

Molecular formula. $C_{17}H_{19}ClN_2S$, HCl

Relative molecular mass. 355.3

Graphic formula.



Chemical name. 2-Chloro-10-[3-(dimethylamino)propyl]phenothiazine monohydrochloride; 2-chloro-*N,N*-dimethyl-10*H*-phenothiazine-10-propanamine monohydrochloride; CAS Reg. No. 69-09-0.

Description. A white or slightly creamy white, crystalline powder; odour, slight.

Solubility. Soluble in 0.4 part of water; freely soluble in ethanol (~750 g/l) TS; practically insoluble in ether R.

Category. Neuroleptic.

Storage. Chlorpromazine hydrochloride should be kept in a tightly closed container, protected from light.

Additional information. Chlorpromazine hydrochloride has a very bitter taste. It darkens on prolonged exposure to light. Even in the absence of light, Chlorpromazine hydrochloride is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperature.

Requirements

Definition. Chlorpromazine hydrochloride contains not less than 98.0% and not more than 101.0% of $C_{17}H_{19}ClN_2S$,HCl, 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 chlorpromazine hydrochloride RS or with the *reference spectrum* of chlorpromazine hydrochloride.

B. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography, using kieselguhr R1 as the coating substance and a mixture of 10 volumes of 2-phenoxyethanol R, 5 volumes of macrogol 400R, and 85 volumes of acetone R to impregnate the plate. After the solvent has reached the top of the plate, remove the plate from the chromatographic chamber, and use it immediately. As the mobile phase use a mixture of 2 volumes of diethylamine R and 100 volumes of light petroleum R1 saturated with 2-phenoxyethanol R. Apply separately to the plate 2 µl of each of 2 solutions in chloroform R containing (A) 2.0 mg of the test substance per mL and (B) 2.0 mg of chlorpromazine hydrochloride RS per mL. After removing the plate from the chromatographic chamber, allow it to dry in air, and examine the chromatogram in ultraviolet light (365 nm), observing the fluorescence produced after about 2 minutes. Spray the plate with sulfuric acid/ethanol TS and examine the chromatogram in daylight. The principal spot obtained with solution A corresponds in position, appearance, and intensity with that obtained with solution B.

C. A 0.1 g/mL solution yields reaction B described under 2.1 General identification tests as characteristic of chlorides.

D. Melting temperature, about 196°C.

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.

pH value. pH of a freshly prepared 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 80 volumes of cyclohexane R, 10 volumes of acetone R, and 10 volumes of

diethylamine R as the mobile phase. Apply separately to the plate 10 µl of each of 2 freshly prepared solutions in a mixture of 95 volumes of methanol R and 5 volumes of diethylamine R containing (A) 20 mg of the test substance per mL and (B) 0.50 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). Ignore any spot on the baseline. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay. Dissolve 0.250 g in a mixture of 5.0 mL of hydrochloric acid (0.01 mol/L) VS and 50 mL of dehydrated ethanol R. Carry out a potentiometric titration using sodium hydroxide (0.1 mol/L) VS, as described under *2.6 Non-aqueous titration*, Method A. Read the volume added between the two points of inflexion.

1 mL of sodium hydroxide (0.1 mol/L) VS is equivalent to 35.53 mg of $C_{17}H_{19}ClN_2S,HCl$.

Additional requirements for Chlorpromazine hydrochloride 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 6.9 IU of endotoxin RS per mg.