C_{17}H_{20}Cl_{2}N_{2}S \quad M_{r} \text{ 355.3}

**DEFINITION**
Chlorpromazine hydrochloride contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 3-(2-chloro-10H-phenothiazin-10-yl)-N,N-dimethylpropan-1-amine hydrochloride, calculated with reference to the dried substance.

**CHARACTERS**
A white or almost white, crystalline powder, very soluble in water, freely soluble in alcohol. It decomposes on exposure to air and light.

It melts at about 196 °C.

**IDENTIFICATION**
First identification: B, C, D.
Second identification: A, C, D.

A. Prepare the solutions protected from bright light and measure the absorbances immediately. Dissolve 50.0 mg in 0.1 M hydrochloric acid and dilute to 500.0 ml with the same acid. Dilute 5.0 ml of the solution to 100.0 ml with 0.1 M hydrochloric acid. Examined between 230 nm and 340 nm (2.2.25), the solution shows two absorption maxima, at 254 nm and 306 nm respectively. The specific absorbance at the maximum at 254 nm is 890 to 960.

B. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the spectrum obtained with chlorpromazine hydrochloride CRS. Examine the substances as 60 g/l solutions in methylene chloride R using a 0.1 mm cell.

C. It complies with the identification test for phenothiazines by thin-layer chromatography (2.3.3).

D. It gives reaction (b) of chlorides (2.3.1).

**TESTS**

**pH** (2.2.3). Dissolve 1.0 g in carbon dioxide-free water R and dilute to 10 ml with the same solvent. The pH of the freshly prepared solution is 3.5 to 4.5.

**Related substances.** Carry out the test protected from bright light.

Examine by thin-layer chromatography (2.2.27), using silica gel GF_{254} R as the coating substance.

**Test solution.** Dissolve 0.2 g of the substance to be examined in a mixture of 5 volumes of diethyamine R and 95 volumes of methanol R and dilute to 10 ml with the same mixture of solvents. Prepare immediately before use.

---

CHLORPROMAZINE HYDROCHLORIDE

Chlorpromazini hydrochloridum

C_{17}H_{20}Cl_{2}N_{2}S \quad M_{r} \text{ 355.3}

**DEFINITION**
Chlorpromazine hydrochloride contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 3-(2-chloro-10H-phenothiazin-10-yl)-N,N-dimethylpropan-1-amine hydrochloride, calculated with reference to the dried substance.

**CHARACTERS**
A white or almost white, crystalline powder, very soluble in water, freely soluble in alcohol. It decomposes on exposure to air and light.

It melts at about 196 °C.

**IDENTIFICATION**
First identification: B, C, D.
Second identification: A, C, D.

A. Prepare the solutions protected from bright light and measure the absorbances immediately. Dissolve 50.0 mg in 0.1 M hydrochloric acid and dilute to 500.0 ml with the same acid. Dilute 5.0 ml of the solution to 100.0 ml with 0.1 M hydrochloric acid. Examined between 230 nm and 340 nm (2.2.25), the solution shows two absorption maxima, at 254 nm and 306 nm respectively. The specific absorbance at the maximum at 254 nm is 890 to 960.

B. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the spectrum obtained with chlorpromazine hydrochloride CRS. Examine the substances as 60 g/l solutions in methylene chloride R using a 0.1 mm cell.

C. It complies with the identification test for phenothiazines by thin-layer chromatography (2.3.3).

D. It gives reaction (b) of chlorides (2.3.1).

**TESTS**

**pH** (2.2.3). Dissolve 1.0 g in carbon dioxide-free water R and dilute to 10 ml with the same solvent. The pH of the freshly prepared solution is 3.5 to 4.5.

**Related substances.** Carry out the test protected from bright light.

Examine by thin-layer chromatography (2.2.27), using silica gel GF_{254} R as the coating substance.

**Test solution.** Dissolve 0.2 g of the substance to be examined in a mixture of 5 volumes of diethyamine R and 95 volumes of methanol R and dilute to 10 ml with the same mixture of solvents. Prepare immediately before use.

---

CHLORPROPAMIDE

Chlorpropamidum

C_{10}H_{13}ClN_{2}O_{3}S \quad M_{r} \text{ 276.7}

**DEFINITION**
Chlorpropamide contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 1-[(4-chlorophenyl)sulphonyl]-3-propylurea, calculated with reference to the dried substance.

**CHARACTERS**
A white, crystalline powder, practically insoluble in water, freely soluble in acetone and in methylene chloride, soluble in alcohol. It dissolves in dilute solutions of alkali hydroxides. It shows polymorphism.

**IDENTIFICATION**
First identification: C, D.
Second identification: A, B, D.

A. Melting point (2.2.14): 126 °C to 130 °C.

B. Dissolve 0.1 g in methanol R and dilute to 50.0 ml with the same solvent. Dilute 5.0 ml of the solution to 100.0 ml with 0.01 M hydrochloric acid. Dilute 10.0 ml of the solution to 100.0 ml with 0.01 M hydrochloric acid.
acid. Examined between 220 nm and 350 nm (2.2.25), the solution shows an absorption maximum at 232 nm. The specific absorption at the maximum is 570 to 630.

C. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the spectrum obtained with chlorpropamide CRS. Examine the substances prepared as discs. If the spectra obtained show differences, dissolve the substance to be examined and the reference substance in methylene chloride, evaporate to dryness and record the new spectra using the residues.

D. Heat 0.1 g with 2 g of anhydrous sodium carbonate R until a dull red colour appears for 10 min. Allow to cool, extract the residue with about 5 ml of water R, dilute to 10 ml with water R and filter. The solution gives the reaction (a) of chloride (2.3.1).

TESTS

Related substances. Examine by thin-layer chromatography (2.2.27), using a suitable silica gel as the coating substance. Test solution. Dissolve 0.50 g of the substance to be examined in acetone R and dilute to 10 ml with the same solvent.

Reference solution (a). Dissolve 15 mg of 4-chlorobenzenesulphonamide R (chlorpropamide impurity A) in acetone R and dilute to 100 ml with the same solvent.

Reference solution (b). Dissolve 15 mg of chlorpropamide impurity B CRS in acetone R and dilute to 100 ml with the same solvent.

Reference solution (c). Dilute 0.3 ml of the test solution to 100 ml with acetone R.

Reference solution (d). Dilute 5 ml of reference solution (c) to 15 ml with acetone R.

Reference solution (e). Dissolve 0.10 g of the substance to be examined, 5 mg of 4-chlorobenzenesulphonamide R and 5 mg of chlorpropamide impurity B CRS in acetone R and dilute to 10 ml with the same solvent.

Apply to the plate 5 µl of each solution. Develop over a path of 15 cm using a mixture of 11.5 volumes of concentrated ammonia R, 30 volumes of cyclohexane R, 50 volumes of methanol R and 100 volumes of methylene chloride R. Allow the plate to dry in a current of cold air, heat at 110 °C for 10 min. At the bottom of a chromatographic tank, place an evaporating dish containing a mixture of 1 volume of hydrochloric acid R, 1 volume of water R and 2 volumes of a 50 g/l solution of potassium permanganate R, close the tank and allow to stand for 15 min. Place the dried hot plate in the tank and close the tank. Leave the plate in contact with the chloride vapour for 2 min. Draw the plate and place it in a current of cold air until the excess of chlorine is removed and an area of coating below the points of application does not give a blue colour with a drop of potassium iodide and starch solution R. Spray with potassium iodide and starch solution R. In the chromatogram obtained with the test solution: any spot corresponding to impurity A is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.3 per cent); any spot corresponding to impurity B is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.3 per cent); any spot, apart from the principal spot and any spot corresponding to impurity A and B, is not more intense than the spot in the chromatogram obtained with reference solution (c) (0.3 per cent); not more than two such spots are more intense than the spot in the chromatogram obtained with reference solution (d) (0.1 per cent). The test is not valid unless the chromatogram obtained with reference solution (e) shows three clearly separated spots with approximate Rf values of 0.4, 0.6 and 0.9 corresponding to chlorpropamide, impurity A and impurity B respectively.

Heavy metals (2.4.8). Dissolve 2.0 g in a mixture of 15 volumes of water R and 85 volumes of acetone R and dilute to 20 ml with the same mixture of solvents. 12 ml of solution complies with limit test B for heavy metals (20 ppm). Prepare the standard using lead standard solution (2 ppm Pb) prepared by diluting lead standard solution (100 ppm Pb) R with a mixture of 15 volumes of water R and 85 volumes of acetone R. Loss on drying (2.2.32). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 100 °C to 105 °C.

Sulphated ash (2.4.14). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 50 ml of alcohol R previously neutralised using phenolphthalein solution R1 as indicator and add 25 ml of water R. Titrate with 0.1 M sodium hydroxide until a pink colour is obtained. 1 ml of 0.1 M sodium hydroxide is equivalent to 27.67 mg of C₃₀H₂₈ClN₂O₅S.

STORAGE

Store protected from light.

IMPURITIES

A. R = H: 4-chlorobenzenesulphonamide,
B. 1,3-dipropylurea,
C. R = CO-NH₂ : [(4-chlorophenyl)sulphonyl]urea.

01/2005:0815

CHLORPROTHIXENE HYDROCHLORIDE

Chlorprothixeni hydrochloridum

C₁₀H₁₄Cl₂NS \( M, 352.3 \)

DEFINITION


Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.