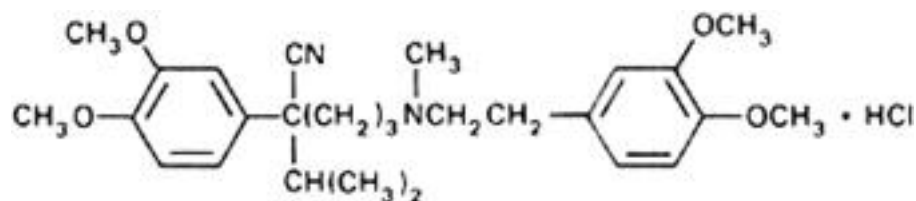


Verapamil hydrochloride (Verapamili hydrochloridum)

2018-01

Molecular formula. $C_{27}H_{38}N_2O_4 \cdot HCl$ **Relative molecular mass.** 491.1**Graphic formula.**

Chemical name. 5-[(3,4-Dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxy-phenyl)-2-isopropylvaleronitrile hydrochloride; α -[3-[[2-(3,4-dimethoxyphenyl)-ethyl]methylamino]propyl]-3,4-dimethoxy- α -(1-methylethyl)benzeneacetonitrile monohydrochloride; CAS Reg. No. 152-11-4.

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

Solubility. Soluble in 20 parts of water; sparingly soluble in ethanol (~750 g/l) TS.

Category. Antianginal drug.

Storage. Verapamil hydrochloride should be kept in a well-closed container, protected from light.

Requirements

Definition. Verapamil hydrochloride contains not less than 99.0% and not more than 101.0% of $C_{27}H_{38}N_2O_4 \cdot HCl$, calculated with reference to the dried substance.

Identity tests

• Either tests A and D or tests B, C, D and E 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 verapamil hydrochloride RS or with the *reference spectrum* of verapamil hydrochloride.

B. The absorption spectrum of a 20 $\mu\text{g/mL}$ solution in hydrochloric acid (0.01 mol/l) VS, when observed between 220 nm and 350 nm, exhibits maxima at about 229 nm and 278 nm; the absorbances of a 1-cm layer at these maxima are about 0.63 and 0.24, respectively.

C. Dissolve 20 mg in 2.5 mL of water, add 0.5 mL of sulfuric acid (~570 g/l) TS and 0.2 mL of potassium permanganate (10 g/l) TS; a violet precipitate is produced, which quickly dissolves to produce a very pale yellow solution.

D. A 20 mg/mL solution yields reaction A described under [2.1 General identification tests](#) as characteristic of chlorides.

E. Melting temperature, about 143 °C.

Clarity and colour of solution. A solution of 0.50 g in 10 mL of carbon-dioxide-free water R is clear and colourless.

Readily carbonizable substances. Dissolve 0.10 g in 5 mL of sulfuric acid (~1760 g/L) TS. After 5 minutes the solution is clear and not more intensely coloured than standard colour solution Yw2 when compared as described under [1.11.1 Colour of liquids](#).

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 0.05 g/mL solution in carbon-dioxide-free water R, 4.5-6.5.

Related substances

A. Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using silica gel R5 as the coating substance (a precoated plate from a commercial source is suitable) and a mixture of 85 volumes of cyclohexane R and 15 volumes of diethylamine R as the mobile phase. Apply separately to the plate 10 μl of each of 3 solutions in chloroform R containing (A) 50 mg of the test substance per mL, (B) 25 μg of the test substance per mL, and (C) 50 μg of the test substance

per mL. After removing the plate from the chromatographic chamber, allow it to dry at room temperature for 10 minutes and develop the plate a second time. Remove the plate, heat it at 110 °C for 1 hour, allow it to cool, and spray it with a solution prepared by dissolving 5 g of ferric chloride R and 2 g of iodine R in 50 mL of tartaric acid (200 g/l) TS, applying a total of 15-20 mL of the reagent. Examine the plate immediately in daylight disregarding any spot on the line of application. Up to 3 secondary spots may be more intense than the spot obtained with solution B but they must be less intense than the spot obtained with solution C. Any other secondary spots in the chromatogram obtained with solution A must be less intense than the spot obtained with solution B.

B. Carry out test A once more using a mixture of 70 volumes of toluene R, 20 volumes of methanol R, 5 volumes of acetone R, and 5 volumes of glacial acetic acid R as the mobile phase. The result is the same as that with test A.

Assay. Dissolve 0.400 g in 50 mL of dehydrated ethanol R and add 5.0 mL of hydrochloric acid (0.01 mol/L) VS. Carry out a potentiometric titration using sodium hydroxide (0.1 mol/L) VS, as described under [2.6 Non-aqueous titration](#). Measure the volume added between the two points of inflexion.

1 mL of sodium hydroxide (0.1 mol/L) VS is equivalent to 49.11 mg of $C_{27}H_{38}N_2O_4 \cdot HCl$.

Additional requirements for Verapamil 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 16.7 IU of endotoxin RS per mg.