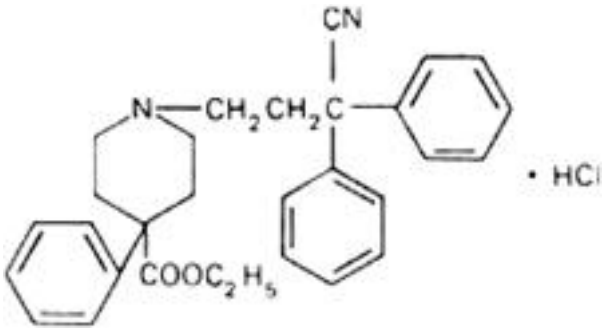
Diphenoxylate hydrochloride (Diphenoxylati hydrochloridum)

Molecular formula. $C_{30}H_{32}N_2O_2$,HCl

Relative molecular mass. 489.1

Graphic formula.



Chemical name. Ethyl 1-(3-cyano-3,3-diphenylpropyl)-4-phenylisonipecotate monohydrochloride; ethyl 1-(3-cyano-3,3-diphenylpropyl)-4-phenyl-4-piperidinecarboxylate monohydrochloride; CAS Reg. No. 3810-80-8.

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

Solubility. Sparingly soluble in water, acetone R and ethanol (~750 g/l) TS; practically insoluble in ether R.

Category. Antidiarrhoeal drug.

Storage. Diphenoxylate hydrochloride should be kept in a well-closed container.

Requirements

Definition. Diphenoxylate hydrochloride contains not less than 98.0% and not more than 101.0% of $C_{30}H_{32}N_2O_2$,HCl, calculated with reference to the dried substance.

Identity tests

• Either tests A and E 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 diphenoxylate hydrochloride RS or with the *reference spectrum* of diphenoxylate hydrochloride.

B. The absorption spectrum of a 0.50 mg/mL solution in a mixture of 1 volume of hydrochloric acid (1 mol/l) VS and 99 volumes of methanol R, when observed between 230 nm and 350 nm, exhibits maxima at about 252 nm, 258 nm, and 265 nm; the absorbances of a 1-cm layer at these wavelengths are about 0.55, 0.65 and 0.50, respectively.

C. Dissolve 25 mg in 5 mL of water and add 0.1 mL of potassio-mercuric iodide TS; a cream-coloured precipitate is produced.

D. Melting temperature, about 223 °C.

E. A 20 mg/mL solution yields reaction B 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 105°C; it loses not more than 5.0 mg/g.

Related substances. Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R1 as the coating substance and a mixture of 92 volumes of chloroform R, 3 volumes of methanol R, and 5 volumes of glacial acetic acid R as the mobile phase. Apply separately to the plate 10 µl of each of 2 solutions in chloroform R containing (A) 50 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, expose it to the vapour of iodine, and examine the chromatogram in daylight. Any spot obtained with solution A, other than the principal spot, is not more intense than that obtained with solution B.

Assay. Dissolve about 0.4 g, accurately weighed, in 40 mL of glacial acetic acid R1, add 10 mL of mercuric acetate/acetic acid TS and 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 48.91 mg of $C_{30}H_{32}N_2O_2$,HCl.