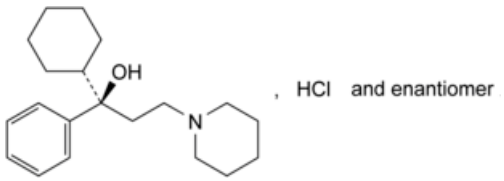
Edition: BP 2025 (Ph. Eur. 11.6 update)

Trihexyphenidyl Hydrochloride

General Notices

(Ph. Eur. monograph 1626)



$C_{20}H_{32}ClNO$ 337.9 *52-49-3*

Action and use

Anticholinergic.

Preparation

Trihexyphenidyl Tablets

Ph Eur

DEFINITION

(1*RS*)-1-Cyclohexyl-1-phenyl-3-(piperidin-1-yl)propan-1-ol hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Slightly soluble in water, sparingly soluble in ethanol (96 per cent) and in methylene chloride.

mp

About 250 °C, with decomposition.

IDENTIFICATION

First identification *A, D*.

Second identification *B, C, D*.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *trihexyphenidyl hydrochloride CRS*.

B. Thin-layer chromatography (2.2.27).

Test solution Dissolve 25 mg of the substance to be examined in a mixture of 20 volumes of *methanol R* and 80 volumes of *methylene chloride R* and dilute to 10 mL with the same mixture of solvents.

Reference solution Dissolve 25 mg of *trihexyphenidyl hydrochloride CRS* in a mixture of 20 volumes of *methanol R* and 80 volumes of *methylene chloride R* and dilute to 10 mL with the same mixture of solvents.

Plate *TLC silica gel G plate R*.

Mobile phase *diethylamine R*, *hexane R* (5:95 *V/V*).

Application 5 µL.

Development Over 2/3 of the plate.

Drying In air.

Detection Spray with a 0.1 g/L solution of *chloroplatinic acid R* in *hydrochloric acid R* containing 0.4 per cent *V/V* of *hydriodic acid R*.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. Dissolve 0.5 g in 5 mL of warm *methanol R* and make just alkaline to *red litmus paper R* with *sodium hydroxide solution R*. A precipitate is formed which, after recrystallisation from *methanol R*, melts (2.2.14) at about 113°C to 115 °C.
D. It gives reaction (a) of chlorides (2.3.1).

TESTS

pH (2.2.3)

5.2 to 6.2.

Dissolve 0.5 g with heating in 25 mL of *carbon dioxide-free water R*. Cool to room temperature and dilute to 50 mL with *carbon dioxide-free water R*.

Optical rotation (2.2.7)

-0.10° to + 0.10°.

Dissolve 1.25 g in a mixture of 20 volumes of *methanol R* and 80 volumes of *methylene chloride R* and dilute to 25.0 mL with the same mixture of solvents.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 20.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 200.0 mL with the mobile phase. Dilute 10.0 mL to 50.0 mL with the mobile phase.

Reference solution (b) Dissolve 10.0 mg of *trihexyphenidyl impurity A CRS* in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (c) Dilute 1.0 mL of reference solution (b) to 100.0 mL with the mobile phase.

Reference solution (d) To 1 mL of reference solution (b), add 1 mL of the test solution and dilute to 100 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Mix 200 mL of *water R* with 0.2 mL of *triethylamine R*. Adjust to pH 4.0 with *phosphoric acid R* and add 800 mL of *acetonitrile R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 210 nm.

Injection 20 µL.

Run time 3 times the retention time of trihexyphenidyl.

System suitability Reference solution (d):

— *resolution*: minimum 4.0 between the peaks due to trihexyphenidyl and to impurity A.

Limits:

— *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: not more than 0.5 per cent;

— *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.02 per cent).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

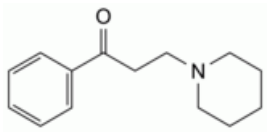
Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 50 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mLof *0.1 M sodium hydroxide* is equivalent to 33.79 mg of $C_{20}H_{32}ClNO$.

IMPURITIES



A. 1-phenyl-3-(piperidin-1-yl)propan-1-one.

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