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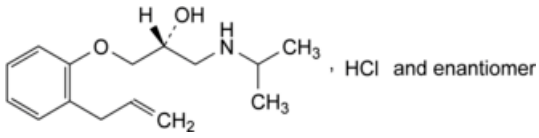
Edition: BP 2025 (Ph. Eur. 11.6 update)

Alprenolol Hydrochloride

General Notices

(Ph. Eur. monograph 0876)



$C_{15}H_{24}ClNO_2$ 285.8 *13707-88-5*

Action and use

Beta-adrenoceptor antagonist.

Ph Eur

DEFINITION

(2*RS*)-1-[(1-Methylethyl)amino]-3-[2-(prop-2-enyl)phenoxy]propan-2-ol hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder or colourless crystals.

Solubility

Very soluble in water, freely soluble in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Melting point (2.2.14): 108 °C to 112 °C.
B. Infrared absorption spectrophotometry (2.2.24).

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Comparison *alprenolol hydrochloride CRS*.

C. Examine the chromatograms obtained in the test for impurity D.

Detection Examine in daylight, after exposure to iodine vapour for 30 min.

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

D. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_9 (*2.2.2, Method II*).

Acidity or alkalinity

To 10 mL of solution S add 0.2 mL of *methyl red solution R* and 0.2 mL of *0.01 M hydrochloric acid*; the solution is red. Add 0.4 mL of *0.01 M sodium hydroxide*; the solution is yellow.

Impurity C

Maximum 0.1 per cent.

Dissolve 0.25 g in *ethanol (96 per cent) R* and dilute to 25 mL with the same solvent. The absorbance (*2.2.25*) measured at 297 nm is not greater than 0.20.

Impurity D

Thin-layer chromatography (*2.2.27*).

Test solution (a) Dissolve 0.50 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Test solution (b) Dilute 1 mL of test solution (a) to 50 mL with *methanol R*.

Reference solution (a) Dissolve 10 mg of *alprenolol hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution (b) Dissolve 10 mg of *alprenolol hydrochloride CRS* and 10 mg of *oxprenolol hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution (c) Dilute 5 mL of test solution (b) to 50 mL with *methanol R*.

Plate *TLC silica gel G plate R*.

Mobile phase Place 2 beakers each containing 30 mL of *ammonia R* at the bottom of the tank containing a mixture of 5 volumes of *methanol R* and 95 volumes of *ethyl acetate R*.

Application 5 µL.

Development Over a path of 15 cm in a tank saturated for at least 1 h.

Drying At 100 °C for 15 min.

Detection Expose to iodine vapour for up to 6 h.

System suitability Reference solution (b):

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— the chromatogram shows 2 clearly separated spots.

Limits Test solution (a):

— *impurity D*: any spot with an R_F value greater than that of the principal spot is not more intense than the principal spot in the chromatogram obtained with reference solution (c) (0.2 per cent).

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) Dissolve 4.0 mg of *alprenolol hydrochloride CRS* and 0.8 mg of *4-isopropylphenol R* in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (b) Dilute 4.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 4 mm;

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

Mobile phase Mix 0.656 g of *sodium octanesulfonate R* with 150 mL of *acetonitrile R* and dilute to 500 mL with phosphate buffer pH 2.8 prepared as follows: mix 1.78 g of *phosphoric acid R* and 15.6 g of *sodium dihydrogen phosphate R* and dilute to 2000 mL with *water R*.

Flow rate 1 mL/min.

Detection Spectrophotometer at 280 nm.

Equilibration With the mobile phase for about 1 h.

Injection 20 µL.

Run time Twice the retention time of alprenolol.

Retention time Alprenolol = about 11 min; 4-isopropylphenol = about 18 min.

System suitability Reference solution (a):

— *resolution*: minimum 5 between the peaks due to alprenolol and 4-isopropylphenol; if necessary, adjust the concentration of sodium octanesulfonate and/or acetonitrile in the mobile phase (increase the concentration of sodium octanesulfonate to increase the retention time of alprenolol and increase the concentration of acetonitrile to decrease the retention times of both compounds).

Limits:

— *unspecified impurities*: for each impurity, not more than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.4 per cent);

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.04 per cent).

Loss on drying (2.2.32)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo*.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

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ASSAY

Dissolve 0.400 g in 25 mL of a mixture of equal volumes of *anhydrous ethanol R* and *water R*. Add 10 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 mL of *0.1 M sodium hydroxide* is equivalent to 28.58 mg of $C_{15}H_{24}ClNO_2$.

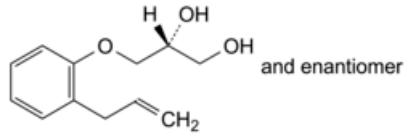
STORAGE

Protected from light.

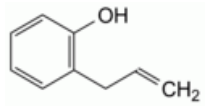
IMPURITIES

Specified impurities C, D.

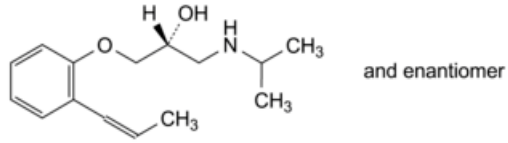
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B.



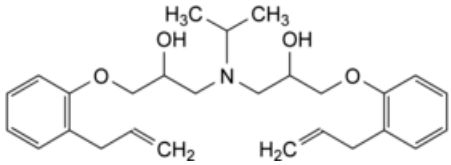
A. (2*RS*)-3-[2-(prop-2-enyl)phenoxy]propan-1,2-diol,



B. 2-(prop-2-enyl)phenol,



C. (2*RS*)-1-[(1-methylethyl)amino]-3-[2-(prop-1-enyl)phenoxy]propan-2-ol,



D. 1,1′-[(1-methylethyl)imino]bis[3-[2-(prop-2-enyl)phenoxy]propan-2-ol].

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