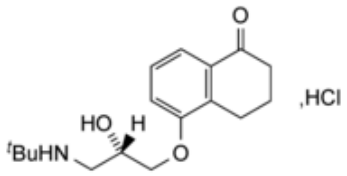
Edition: BP 2025 (Ph. Eur. 11.6 update)

Levobunolol Hydrochloride

General Notices



$C_{17}H_{25}NO_3$,HCl 327.9 *27912-14-7*

Action and use

Beta-adrenoceptor antagonist.

Preparation

Levobunolol Eye Drops

DEFINITION

Levobunolol Hydrochloride is (*S*)-5-(3-*tert*-butylamino-2-hydroxypropoxy)-1,2,3,4-tetrahydronaphthalen-1-one hydrochloride. It contains not less than 98.5% and not more than 101.0% of $C_{17}H_{25}NO_3$,HCl, calculated with reference to the dried substance.

CHARACTERISTICS

A white or pinkish white, crystalline powder.

Freely soluble in *water*; sparingly soluble in *ethanol (96%)*.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of levobunolol hydrochloride *(RS 200)*.
B. Yields the reactions characteristic of *chlorides*, Appendix VI.

TESTS

Acidity

pH of a 5% w/v solution, 4.5 to 6.5, Appendix V L.

Specific optical rotation

In a 3% w/v solution in *methanol*, –19.0 to –20.0, calculated with reference to the dried substance, Appendix V F.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using solutions in the mobile phase containing (1) 0.10% w/v of the substance being examined, (2) 0.00050% w/v of the substance being examined, (3) 0.0050% w/v of each of *levobunolol hydrochloride BPCRS* and *atenolol*.

The chromatographic procedure described under Assay may be used.

For solution (1) allow the chromatography to proceed for 3 times the retention time of the principal peak. The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the two principal peaks is at least 8.

In the chromatogram obtained with solution (1) the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%) and the sum of the areas of any *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Loss on drying

When dried over *phosphorus pentoxide* at 110° at a pressure not exceeding 2 kPa for 4 hours, loses not more than 0.5% of its weight. Use 1 g.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using solutions in the mobile phase containing (1) 0.01% w/v of the substance being examined, (2) 0.01% w/v of *levobunolol hydrochloride BPCRS* and (3) 0.0050% w/v of each of *levobunolol hydrochloride BPCRS* and *atenolol*.

The chromatographic procedure may be carried out using (a) a stainless steel column (25 cm × 3.9 mm) packed with *end-capped octylsilyl silica gel for chromatography* (10 µm) (Lichrosorb RP 8 is suitable), (b) a solution prepared by mixing 53 volumes of 0.005M *sodium heptanesulfonate* in *methanol* with 47 volumes of 0.005M *sodium heptanesulfonate* in *water* containing 1 mL of 0.5M *sulfuric acid* as the mobile phase with a flow rate of 1 mL per minute and (c) a detection wavelength of 223 nm.

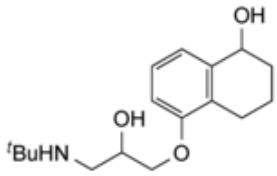
The test is not valid unless in the chromatogram obtained with solution (3) the *resolution factor* between the two principal peaks is at least 8.

Calculate the content of $C_{17}H_{25}NO_3$,HCl from the declared content of $C_{17}H_{25}NO_3$,HCl in *levobunolol hydrochloride BPCRS*.

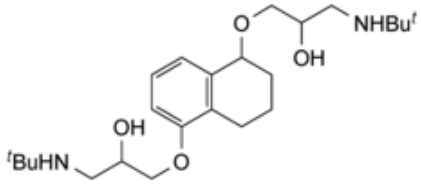
STORAGE

Levobunolol Hydrochloride should be protected from light.

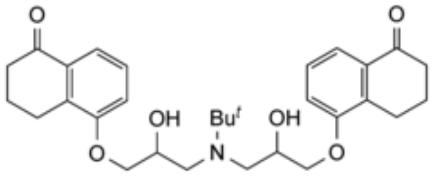
IMPURITIES



A. 5-(3-*tert*-butylamino-2-hydroxypropoxy)-1,2,3,4-tetrahydro-1-naphthol



B. 1,1′-(1,2,3,4-tetrahydro-1,5-naphthalenedioxy)bis(3-*tert*-butylamino)-2-propanol



C. *meso*-5,5′-[(3,3′-*tert*-butylamino)bis(2-hydroxypropoxy)]bis-3,4-dihydronaphthalen-1(2 *H*)-one