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

Levobunolol Eye Drops

General Notices

Action and use

Beta-adrenoceptor antagonist.

DEFINITION

Levobunolol Eye Drops are a sterile solution of Levobunolol Hydrochloride in Purified Water.

The eye drops comply with the requirements stated under Eye Preparations and with the following requirements.

Content of levobunolol hydrochloride, $C_{17}H_{25}NO_3$,HCl

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. The *light absorption*, Appendix II B, in the range 210 to 350 nm of a solution prepared by diluting the eye drops with *ethanol (96%)* to contain 0.001% w/v of Levobunolol Hydrochloride exhibits two maxima, at 223 nm and at 255 nm and a broad peak at 315 nm.
B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 5.5 to 7.5, Appendix V L.

Related substances

The nominal total amount of related substances determined by tests A and B below is not more than 2.5% of the stated content of Levobunolol Hydrochloride.

A. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.
(1) Dilute a suitable volume of the eye drops with the mobile phase to produce a solution containing 0.10% w/v of Levobunolol Hydrochloride.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) 0.0010% w/v of *disodium edetate* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Assay may be used.

LIMITS

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) (1%).

Determine the sum of the areas of any *secondary peaks*.

Disregard any peak corresponding to the principal peak in the chromatogram obtained with solution (3).

B. Carry out test A as described above but using a detection wavelength of 400 nm and injecting solution (1).

LIMITS

The area of any peak with a retention time corresponding to that of the principal peak in the chromatogram obtained with solution (2) in test A is not greater than one-fifth of the area of that peak (1%, assuming a response factor of 5).

Calculate the nominal percentage content of this impurity from the area of the peak in the chromatogram obtained with solution (1) taking one-fifth of the area of the peak in the chromatogram obtained with solution (2) in test A to be equivalent to 1%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a suitable volume of the eye drops with the mobile phase to produce a solution containing 0.005% w/v of Levobunolol Hydrochloride.
(2) 0.005% w/v of *levobunolol hydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (30 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (µBondapak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *glacial acetic acid*, 450 volumes of 0.005M *sodium heptanesulfonate* and 550 volumes of *methanol*.

DETERMINATION OF CONTENT

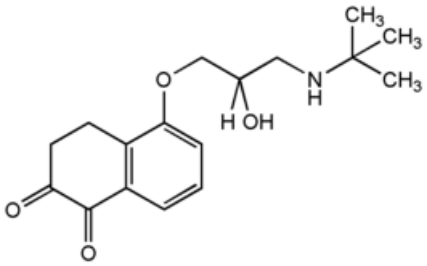
Calculate the content of $C_{17}H_{25}NO_3$,HCl in the eye drops from the declared content of $C_{17}H_{25}NO_3$,HCl in *levobunolol hydrochloride BPCRS*.

STORAGE

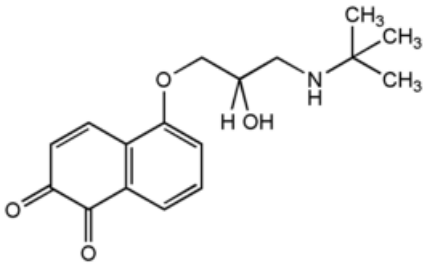
Levobunolol Eye Drops should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include:



A. 5-(3-*tert*-butylamino-2-hydroxypropoxy)-3,4-dihydro-1,2-naphthalene dione,



B. 5-(3-*tert*-butylamino-2-hydroxypropoxy)-1,2-naphthoquinone.