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

Timolol Tablets

General Notices

Action and use

Beta-adrenoceptor antagonist.

DEFINITION

Timolol Tablets contain Timolol Maleate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of timolol maleate, $C_{13}H_{24}N_4O_3S,C_4H_4O_4$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the powdered tablets containing 30 mg of Timolol Maleate with 2 mL of 0.1M *hydrochloric acid* until a smooth paste is formed, add 5 mL of *methanol* and continue shaking for about 20 minutes. Add sufficient *methanol* to produce 50 mL, centrifuge until a clear solution is produced and use the supernatant liquid.
(2) Dissolve, with shaking, 60 mg of *timolol maleate BPCRS* in 4 mL of 0.1M *hydrochloric acid* and add sufficient *methanol* to produce 100 mL.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}* (Analtech Uniplates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1 volume of 18M *ammonia*, 19 volumes of *methanol* and 80 volumes of *chloroform*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

Disregard any spot remaining on the line of application (maleic acid).

B. To a quantity of the powdered tablets containing 70 mg of Timolol Maleate add 20 mL of *carbonate buffer pH 9.7* and extract with two 40-mL quantities of *dichloromethane*. Filter the aqueous layer and evaporate to about 1 mL. Add 1 mL of *bromine solution*, heat in a water bath for 10 minutes, boil, cool and add 0.1 mL of the solution to a solution of 10 mg of *resorcinol* in 3 mL of *sulfuric acid*. A bluish black colour is produced on heating in a water bath for 15 minutes.

TESTS

Related substances

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

(1) Shake a quantity of the powdered tablets containing 0.1 g of Timolol Maleate with 10 mL of the mobile phase for 10 minutes and filter.
(2) Dilute 1 volume of solution (1) to 250 volumes.
(3) Dilute 1 volume of solution (1) to 500 volumes.
(4) 0.30% w/v of *maleic acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 295 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 4 times the retention time of the principal peak.

MOBILE PHASE

42.5 volumes of 0.02M *sodium octanesulfonate* and 57.5 volumes of *methanol*, adjusted to pH 3.0 using *glacial acetic acid*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak*, other than the peak corresponding to maleic acid, is not greater than the area of the peak obtained with solution (2) (0.4%);

not more than two such peaks have an area greater than that of the peak obtained with solution (3) (0.2%).

ASSAY

Weigh and powder 20 tablets. To a quantity of the powder containing 15 mg of Timolol Maleate add 25 mL of 0.05M *sulfuric acid*, shake for 20 minutes and centrifuge until clear. Add 5 mL of the resulting supernatant liquid to 15 mL of *carbonate buffer pH 9.7* and extract with three 20-mL quantities and one 10-mL quantity of *toluene*. Wash each extract successively with the same 10-mL volume of *carbonate buffer pH 9.7*, combine the toluene extracts and extract with four 20-mL quantities of 0.05M *sulfuric acid*. Combine the acid extracts, dilute to 100 mL, filter and measure the *absorbance* at the maximum at 295 nm, Appendix II B, using in the reference cell a solution prepared by treating a mixture of 5 mL of *water* and 15 mL of *carbonate buffer pH 9.7* in the same manner. Calculate the content of $C_{13}H_{24}N_4O_3S,C_4H_4O_4$ taking 204 as the value of A(1%, 1 cm) at the maximum at 295 nm.