Bisoprolol Tablets

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

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Bisoprolol Tablets

Bisoprolol Fumarate Tablets

Bisoprolol Tablets contain not less than 90.0 per cent and not more than 105.0 per cent of the stated amount of bisoprolol fumarate, $(C_{18}H_{31}NO_4)_2$, $C_4H_4O_4$.

Usual strengths.1.25 mg; 2.5mg; 3.75 mg; 5 mg; 7.5 mg; 10 mg.

Identification

A. Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel GF 254.*

Solvent mixture. 70 volumes of *dichloromethane* and 30 volumes of *methanol*.

Mobile phase. A mixture of 70 volumes of *dichloromethane,* 10 volumes of *methanol* and 0.8 volume of *ammonia solution.*

Test solution. Disperse a quantity of the powdered tablets containing 40 mg of Bisoprolol Fumarate in the solvent mixture, with the aid of mechanical shaker for about 30 minutes and dilute to 50.0 ml with the solvent mixture, centrifuge and use the clear supernatant.

Reference solution. A 0.08 per cent w/v solution of *bisoprolol fumarate IPRS* in the solvent mixture.

Apply to the plate 20 µl of each solution. After development, dry the plate in current of cool air and examine under ultraviolet light at 254 nm. The principal spot in the chromatogram obtained with the test solution corresponds to the chromatogram obtained with the reference solution.

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 900 ml of *water*,
Speed and time. 75 rpm and 20 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14)

Solvent mixture. 16 volumes of *methanol,* 3.5 volumes of *water,* 0.5 volume of *triethylamine* and 0.25 volume of *orthophosphoric acid*.

Test solution. Dilute the filtrate with an equal volume of the solvent mixture and use.

Reference solution. Dissolve a suitable quantity of *bisoprolol fumarate IPRS* in *water* to obtain a solution having a known concentration of about twice the concentration of bisoprolol fumarate in the test solution. Dilute a suitable volume of the solution with equal volume of the solvent mixture to obtain a solution having similar concentration to that of the test solution.

Chromatographic system
- a stainless steel column 3.3cm x 4.6 mm, packed with octylsilane bonded to porous silica (3µm) (Such as ACE Excel 3 C8) ,
- mobile phase: a mixture of 34 volumes of *methanol,* 50 volumes of *water* and 1 volume of *triethylamine,* adjusted to pH 4.0 with *orthophosphoric acid*,
- flow rate: 1 ml per minute,

- spectrophotometer set at 227 nm,
- injection volume: 50 µl.

Inject the reference solution. The test is not valid unless relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $(C_{18}H_{31}NO_4)_2$, $C_4H_4O_4$ in the medium.

Q. Not less than 80 per cent of the stated amount of $(C_{18}H_{31}NO_4)_2$, $C_4H_4O_4$.

Uniformity of content. Complies with the test stated under Tablets.

Determine by liquid chromatography (2.4.14), as described under Assay with the following modifications.

Test solution. Disperse 1 intact tablet in the solvent mixture with the aid of ultrasound for 10 minutes and dilute to 25.0 ml with the solvent mixture. Dilute, if necessary, with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *bisoprolol fumarate IPRS* in the solvent mixture.

Inject the reference solution and the test solution.

Calculate the content of $(C_{18}H_{31}NO_4)_2$, $C_4H_4O_4$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

*Solvent mixture.*35 volumes of *acetonitrile* and 65 volumes of *water*.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 25 mg of Bisoprolol Fumarate in the solvent mixture, with the aid of ultrasound for 10 minutes and dilute to 25.0 ml with the solvent mixture. Centrifuge for 20 minutes and use the clear supernatant.

Reference solution (a). A 0.1 per cent w/v solution of *bisoprolol fumarate IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.05 per cent w/v of *propranolol hydrochloride IPRS* and 0.1 per cent w/v of *bisoprolol fumarate IPRS* in the solvent mixture.

Chromatographic system

- a stainless steel column 12.5 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5 µm) (Such as ACE Excel 3 C8),
- mobile phase: a mixture of 100 volumes of the solvent mixture, 0.5 volume of *heptafluorobutyric acid*, 0.5 volume of *diethylamine* and 0.25 volume of *formic acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 273 nm,
- injection volume: 10 µl.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to bisoprolol and propranolol is not less than 7.0 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $(C_{18}H_{31}NO_4)_2$, $C_4H_4O_4$ in the tablets.

Storage. Store protected from light and moisture, at temperature not exceeding 30º.