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Bisoprolol Fumarate Tablets

DEFINITION

Bisoprolol Fumarate Tablets contain NLT 90.0% and NMT 105.0% of the labeled amount of bisoprolol fumarate $[(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4]$.

IDENTIFICATION

• [THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST \(201\)](#)

Sample solution: Equivalent to 40 mg of bisoprolol fumarate, from powdered Tablets (NLT 5), in a 50-mL flask. Add about 20 mL of a mixture of dichloromethane and methanol (7:3), shake for 30 min, centrifuge, and use the clear solution.

Application volume: 20 μ L

Developing solvent system: Dichloromethane, methanol, and ammonia TS, stronger (70:10:0.8)

Analysis

Sample: *Sample solution*

Proceed as directed in the chapter, except to develop the chromatogram until the solvent front has moved about two-thirds of the length of the plate and to dry the plate in a current of cold air.

ASSAY

• PROCEDURE

Diluent: Acetonitrile and water (7:13)

Mobile phase: A 1-L portion of *Diluent*. Add 5 mL of heptafluorobutyric acid, 5 mL of diethylamine, and 2.5 mL of formic acid.

System suitability solution: 0.5 mg/mL of propranolol hydrochloride and 1 mg/mL of bisoprolol fumarate in *Diluent*

Standard solution: 1 mg/mL of [USP Bisoprolol Fumarate RS](#) in *Diluent*

Sample solution: Transfer an equivalent of 25 mg of bisoprolol fumarate, from powdered Tablets (NLT 20), to a 25-mL volumetric flask. Add 10 mL of *Diluent*, and sonicate for 10 min. Cool, dilute with *Diluent* to volume, and mix. Centrifuge for 20 min, and use the clear supernatant.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 273 nm

Column: 4.6-mm $\times$ 12.5-cm; packing L7

Flow rate: 1 mL/min

Injection size: 10 μ L

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 7.0 between bisoprolol and propranolol, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$ in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Bisoprolol Fumarate RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of bisoprolol fumarate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–105.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1**Medium:** Water; 900 mL**Apparatus 2:** 75 rpm**Time:** 20 minDetermine the amount of $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$ dissolved by using the following method.**Diluent:** Methanol, triethylamine, phosphoric acid, and water (160:5:2.5:35)**Mobile phase:** Methanol, triethylamine, and water (34:1:50). Adjust with phosphoric acid to a pH of 4.0 ± 0.1 .**Standard stock solution:** [USP Bisoprolol Fumarate RS](#) in water to obtain a solution having a known concentration of about twice the concentration of bisoprolol fumarate in the *Sample solution***Standard solution:** *Standard stock solution* and *Diluent* (1:1)**Sample solution:** Sample per [Dissolution <711>](#). Withdraw a portion of the solution under test, filter, and dilute with an equal volume of *Diluent*.**Chromatographic system**(See [Chromatography <621>](#), [System Suitability](#).)**Mode:** LC**Detector:** UV 227 nm**Column:** 4.6-mm $\times$ 33-mm; packing L7**Flow rate:** 1 mL/min**Injection size:** 50 μ L**System suitability****Sample:** *Standard solution***Suitability requirements****Relative standard deviation:** NMT 2.0%**Analysis****Samples:** *Standard solution* and *Sample solution***Tolerances:** NLT 80% (Q) of the labeled amount of $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$ is dissolved.**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.**Medium:** 0.5 M sodium chloride; 900 mL**Apparatus 2:** 75 rpm**Time:** 20 min**Analysis:** Proceed as directed for *Test 1* with the following modifications.**Diluent:** Prepare a mixture of methanol, 0.1 N hydrochloric acid, triethylamine, and phosphoric acid (160:35:5:2.5). The dimensions of the column are 4.6 mm $\times$ 25 cm.**Tolerances:** NLT 80% (Q) of the labeled amount of $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$ is dissolved.

- **UNIFORMITY OF DOSAGE UNITS <905>**: Meet the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS <11>**.

[USP Bisoprolol Fumarate RS](#)2-Propanol, 1-[4-[[2-(1-methylethoxy)ethoxy]methyl]phenoxy]-3-[(1-methylethyl)amino]-, ($\pm$)-, (*E*)-2-butenedioate (2:1) (salt). $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$

766.96

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
BISOPROLOL FUMARATE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)**Most Recently Appeared In:**

Pharmacopeial Forum: Volume No. PF 44(5)

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