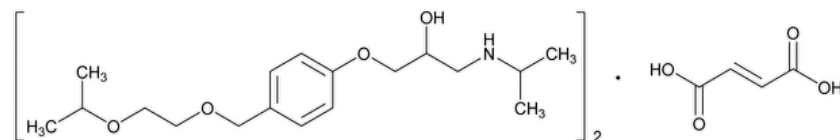


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Bisoprolol Fumarate

Change to read:



$(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$ 766.96

2-Propanol, 1-[4-[[2-(1-methylethoxy)ethoxy]methyl]phenoxy]-3-[(1-methylethyl)amino]-, (±)-, (E)-2-butenedioate (2:1) (salt).

(±)-1-[[α-(2-Isopropoxyethoxy)-p-tolyl]oxy]-3-(▲isopropylamino▲ (ERR 1-May-2023))-2-propanol fumarate (2:1) (salt) CAS RN®: 104344-23-2;
 UNII: UR59KN573L.

» Bisoprolol Fumarate contains not less than 97.5 percent and not more than 102.0 percent of $(C_{18}H_{31}NO_4)_2 \cdot C_4H_4O_4$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at controlled room temperature.

USP REFERENCE STANDARDS (11).—

[USP Bisoprolol Fumarate RS](#)

Identification—

A: [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#).

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

SPECIFIC ROTATION (781): between -2° and $+2^\circ$.

Test solution: 10 mg per mL, in methanol.

WATER DETERMINATION, Method I (921): not more than 0.5%.

RESIDUE ON IGNITION (281): not more than 0.1%.

Chromatographic purity—

Diluent, Mobile phase, System suitability solution, and Chromatographic system—Proceed as directed in the *Assay*.

Standard solution—Prepare as directed for *Standard preparation* in the *Assay*.

Test solution—Prepare as directed for *Assay preparation* in the *Assay*.

Procedure—Inject a volume (about 10 μ L) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak areas. Calculate the percentage of total impurities in the portion of Bisoprolol Fumarate taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the sum of areas for all the peaks, excluding the fumaric acid and bisoprolol peaks; and r_s is the sum of the areas of all the peaks in the chromatogram: not more than 0.5% of total impurities is found.

Content of fumaric acid—Transfer about 500 mg of Bisoprolol Fumarate, accurately weighed, to a beaker, and dissolve in 70 mL of dehydrated alcohol. Add 8.0 mL of 0.1 N tetrabutylammonium hydroxide VS, and stir for 2 minutes. Titrate with 0.1 N tetrabutylammonium hydroxide VS, determining the endpoint potentiometrically, using a glass-calomel electrode system. Perform a blank determination, and make any necessary correction (see [Titrimetry \(541\)](#)). Each mL of 0.1 N tetrabutylammonium hydroxide is equivalent to 5.804 mg of fumaric acid: not less than 14.8% and not more than 15.4% of fumaric acid is found, calculated on the anhydrous basis.

Assay—

Diluent—Prepare a mixture of water and acetonitrile (65:35).

Mobile phase—To a 1-L portion of *Diluent* add 5 mL of heptafluorobutyric acid, 5 mL of diethylamine, and 2.5 mL of formic acid. Mix, filter, and degas. Make adjustments if necessary (see *System Suitability* under [Chromatography \(621\)](#)).

System suitability solution—Prepare a solution in *Diluent* containing about 0.5 mg of propranolol hydrochloride and 1 mg of Bisoprolol Fumarate per mL.

Standard preparation—Quantitatively dissolve an accurately weighed quantity of [USP Bisoprolol Fumarate RS](#) in *Diluent* to obtain a solution having a known concentration of about 1 mg per mL.

Assay preparation—Transfer about 50 mg of Bisoprolol Fumarate, accurately weighed, to a 50-mL volumetric flask. Dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see [CHROMATOGRAPHY \(621\)](#))—The liquid chromatograph is equipped with a 273-nm detector and a 4.6-mm × 12.5-cm column that contains packing L7. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution*, and record the peak areas as directed for *Procedure*: the resolution, *R*, between bisoprolol and propranolol is not less than 7.0. Chromatograph the *Standard preparation*, and record the peak areas as directed for *Procedure*: the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of (C₁₈H₃₁NO₄)₂ · C₄H₄O₄ in the portion of Bisoprolol Fumarate taken by the formula:

$$50C(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of [USP Bisoprolol Fumarate RS](#) in the *Standard preparation*; and *r_U* and *r_S* are the peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

Topic/Question	Contact	Expert Committee
BISOPROLOL FUMARATE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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