Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2017
Document Type: USP Monographs
DocId: GUID-3BF56B2D-1A34-47AB-8DA1-2DC57960238D_1_en-US
DOI: https://doi.org/10.31003/USPNF_M53550_01_01
DOI Ref: 334ia

Metoprolol Tartrate Tablets

DEFINITION
Metoprolol Tartrate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of metoprolol tartrate [$(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6$].

IDENTIFICATION

• **A.**

Standard solution: 0.1 mg/mL of USP Metoprolol Tartrate RS in water

Sample solution: Transfer an amount equivalent to 50 mg of metoprolol tartrate from a quantity of finely powdered Tablets to a 500-mL volumetric flask, dilute with water to volume, and mix. Pass a portion of the solution through a filter of 1-µm or finer pore size.

Acceptance criteria: The UV spectrum of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the *Standard solution*.

• **B.** The retention time of the metoprolol peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: 961 mg of sodium 1-pentanesulfonate and 82 mg of anhydrous sodium acetate in a mixture of 550 mL of methanol and 470 mL of water. Add 0.57 mL of glacial acetic acid.

Diluent: Methanol and 0.1 N hydrochloric acid (1:1)

System suitability stock solution: 0.72 mg/mL of USP Oxprenolol Hydrochloride RS in *Diluent*

Standard stock solution: 1 mg/mL of USP Metoprolol Tartrate RS in *Diluent*

System suitability solution: *System suitability stock solution* and *Standard stock solution* (1:1)

Standard solution: 0.5 mg/mL of USP Metoprolol Tartrate RS from the *Standard stock solution* in *Mobile phase*

Sample stock solution: Nominally 1 mg/mL of metoprolol tartrate from Tablets prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20), equivalent to about 50 mg of metoprolol tartrate, to a 50-mL volumetric flask, add 30 mL of *Diluent*, shake by mechanical means for 30 min, sonicate for 15 min, and heat on a steam bath for 10 min. Allow the solution to cool to room temperature, dilute with *Diluent* to volume, and centrifuge a portion of the solution. Use the supernatant.

Sample solution: Nominally 0.5 mg/mL of metoprolol tartrate prepared from the *Sample stock solution* in *Mobile phase*. Pass a portion of the solution through a filter of 0.5-µm or finer pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 30 µL

System suitability

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

[Note—The relative retention times for metoprolol and oxprenolol are 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between metoprolol and oxprenolol, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metoprolol tartrate [$(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6$] in the portion of Tablets taken:

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

r_U = peak response of metoprolol from the *Sample solution*

r_S = peak response of metoprolol from the *Standard solution*

C_S = concentration of USP Metoprolol Tartrate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of metoprolol tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Simulated gastric fluid TS (without enzyme); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: USP Metoprolol Tartrate RS with a known concentration in *Medium*

Sample solution: Sample per the chapter. Dilute with *Medium* as needed.

Instrumental conditions

Mode: UV

Analytical wavelength: 275 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 75% (*Q*) of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Solution A: 3.9 g of ammonium acetate in 810 mL of water. Add 2.0 mL of triethylamine, 10.0 mL of glacial acetic acid, and 3.0 mL of phosphoric acid. [Note—Adjust the pH of the solution to 3.7 if needed.]

Solution B: Acetonitrile and *Solution A* (70:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
15.0	80	20
30.0	40	60
40.0	40	60
40.1	90	10
45.0	90	10

Diluent: Acetonitrile and *Solution A* (17:83)

System suitability solution: 0.01 mg/mL each of tyrosol and USP Metoprolol Related Compound C RS in *Diluent*

Standard solution: 0.01 mg/mL of USP Metoprolol Tartrate RS in *Diluent*

Sensitivity solution: 0.7 µg/mL of USP Metoprolol Tartrate RS from the *Standard solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of metoprolol tartrate from Tablets prepared as follows. Transfer 100 mg of metoprolol tartrate from a quantity of finely powdered Tablets (NLT 20) to a 100-mL volumetric flask, and add 50 mL of *Diluent*. Sonication and stirring may be necessary for complete dissolution. Dilute with *Diluent* to volume. Centrifuge a portion of the solution. Use the supernatant.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between tyrosol and metoprolol related compound C, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*

r_S = peak response of metoprolol from the *Standard solution*

C_S = concentration of USP Metoprolol Tartrate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of metoprolol tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard peaks below 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tyrosol[a]	0.41	—
Metoprolol related compound C[b]	0.43	—
Metoprolol related compound A[b,c]	0.83	—
Metoprolol	1.00	—
Metoprolol related compound D[b,d]	1.57	—
Metoprolol related compound D[b,d]	1.58	—
Metoprolol related compound B[b,e]	1.68	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	1.0

[a] 2-(4-Hydroxyphenyl)ethanol. For resolution measurement only.

[b] Specified impurities controlled in the drug substance.

[c] (±)-1-(Ethylamino)-3-[4-(2-methoxyethyl)phenoxy]-propan-2-ol.

[d] (±)-*N*,*N*-Bis-[2-hydroxy-3-[4-(2-methoxyethyl)phenoxy]propyl](1-methylethyl)amine hydrochloride. It has two diastereomers.

[e] (±)-1-Chloro-2-hydroxy-3-[4-(2-methoxyethyl)phenoxy]-propane.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Metoprolol Related Compound C RS

4-[2-Hydroxy-3-(isopropylamino)propoxy]benzaldehyde hydrochloride.

$C_{13}H_{19}NO_3 \cdot HCl$ 273.76

USP Metoprolol Tartrate RS

USP Oxprenolol Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
METOPROLOL TARTRATE TABLETS	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:
Pharmacopeial Forum: Volume No. PF 42(3)

Current DocID: GUID-3BF56B2D-1A34-47AB-8DA1-2DC57960238D_1_en-US

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