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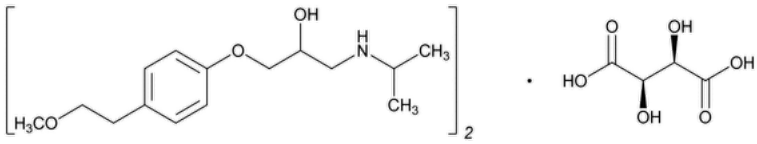
Metoprolol Tartrate

Change to read:



$(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6$ 684.81

2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]-, (±)-, [*R*-(*R**,*R**)]-2,3-dihydroxy butanedioate (2:1) (salt);

▲(±)-1-(Isopropylamino)-3-[*p*-(2-methoxyethyl)phenoxy]-2-propanol (+)-tartrate (2:1) (salt);

1-(Isopropylamino)-3-[4-(2-methoxyethyl)phenoxy]propan-2-ol L-tartrate▲ (ERR 1-Dec-2018) CAS RN®: 56392-17-7; UNII: W5S57Y3A5L.

DEFINITION

Metoprolol Tartrate contains NLT 98.0% and NMT 102.0% of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$, calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)

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

ASSAY

• **Procedure**

[Note—Use all solutions within 48 h.]

Buffer: 1.3 g/L of sodium dodecyl sulfate in 0.1% (w/v) phosphoric acid

Mobile phase: Acetonitrile and *Buffer* (400:600)

Standard solution: 1 mg/mL of USP Metoprolol Tartrate RS in *Mobile phase*

Sample solution: 1 mg/mL of Metoprolol Tartrate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 223 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ in the portion of sample 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 = concentration of Metoprolol Tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

[Note—Use all solutions within 48 hrs.]

Buffer, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 5 µg/mL each of USP Metoprolol Tartrate RS, USP Metoprolol Related Compound A RS, USP Metoprolol Related Compound B RS, and USP Metoprolol Related Compound C RS in *Mobile phase*

Standard solution: 1 µg/mL each of USP Metoprolol Tartrate RS, USP Metoprolol Related Compound A RS, USP Metoprolol Related Compound B RS, USP Metoprolol Related Compound C RS, and USP Metoprolol Related Compound D RS in *Mobile phase*

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between metoprolol related compound A and metoprolol related compound B; NLT 2.5 between metoprolol related compound B and metoprolol related compound C, *System suitability solution*

Relative standard deviation: NMT 5.0% for the metoprolol peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of sample taken:

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

r_U = peak response of each individual impurity in the *Sample solution*

r_S = peak response of the corresponding metoprolol related compound or metoprolol (for calculating any individual unspecified impurity) in the *Standard solution*

C_S = concentration of the corresponding USP Metoprolol Related Compound RS or USP Metoprolol Tartrate RS (for calculating any individual unspecified impurity) in the *Standard solution* (mg/mL)

C_U = concentration of Metoprolol Tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Metoprolol related compound C[a]	0.65	0.10
Metoprolol related compound B[b]	0.72	0.10
Metoprolol related compound A[c]	0.83	0.10
Metoprolol	1.00	—
Metoprolol related compound D[d,e]	4.78/5.00	0.10
Any individual unspecified impurity	—	0.10
Total impurities[f]	—	0.50

[a] (±)-4-[2-Hydroxy-3-(1-isopropyl)aminopropoxy]benzaldehyde).

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

[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.

[e] The sum of the peak responses of the two diastereomers is used to calculate the amount of metoprolol related compound D.

[f] Disregard any peak due to tartaric acid at about RRT 0.17.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩

  Sample solution: 20 mg/mL in water

  Acceptance criteria: +6.5° to +10.5° (t = 20°)

- **pH** ⟨791⟩

  Sample solution: 100 mg/mL of Metoprolol Tartrate in water

  Acceptance criteria: 6.0–7.0

- **Loss on Drying** ⟨731⟩

  Sample solution: Dry a sample in a vacuum at 60° for 4 h.

  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Metoprolol Tartrate RS

USP Metoprolol Related Compound A RS

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

$C_{14}H_{23}NO_3$ 253.34

USP Metoprolol Related Compound B RS

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

$C_{12}H_{17}ClO_3$ 244.71

USP Metoprolol Related Compound C RS

(±)-4-[2-Hydroxy-3-(1-isopropyl)aminopropoxy]benzaldehyde.

$C_{13}H_{19}NO_3$ 237.29

USP Metoprolol Related Compound D RS

(±)-*N,N*-bis-[2-Hydroxy-3-[4-(2-methoxyethyl)phenoxy]propyl](1-methylethyl)amine hydrochloride.

$C_{27}H_{41}NO_6$ 512.08

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

Topic/Question	Contact	Expert Committee
METOPROLOL TARTRATE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 39(1)

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