

Metoprolol Tartrate and Hydrochlorothiazide Tablets

DEFINITION
Metoprolol Tartrate and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ and hydrochlorothiazide $(C_7H_8ClN_3O_4S_2)$.

IDENTIFICATION

- A.** The retention times of the metoprolol and hydrochlorothiazide peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.
- B.** The UV spectra of the metoprolol and hydrochlorothiazide peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

- PROCEDURE**
Solution A: 4.1 g/L of [monobasic sodium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 3.0.
Solution B: [Acetonitrile](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	85	15
4.0	85	15
10.0	10	90
10.1	85	15
13	85	15

Diluent: [Acetonitrile](#) and *Solution A* (15:85)
Standard solution: 0.1 mg/mL of [USP Metoprolol Tartrate RS](#) and 0.05 mg/mL of [USP Hydrochlorothiazide RS](#) in *Diluent*
Sample solution: Nominally 0.1 mg/mL of metoprolol tartrate and 0.05 mg/mL of hydrochlorothiazide in *Diluent* prepared as follows. Transfer a portion of the powder from NLT 20 finely powdered Tablets to a suitable volumetric flask and dissolve in a suitable amount of *Diluent*. Sonication may be necessary for complete dissolution. Dilute with *Diluent* to volume.

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

Mode: LC
Detector: UV 223 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.
Column: 4.6-mm × 10-cm; 3.5-μm packing [L1](#)
Autosampler temperature: 4°
Flow rate: 1 mL/min
Injection volume: 10 μL

System suitability
Sample: *Standard solution*

[NOTE—The relative retention times for hydrochlorothiazide and metoprolol are 0.56 and 1.0, respectively.]

Suitability requirements**Tailing factor:** NMT 2.0 for metoprolol and hydrochlorothiazide**Relative standard deviation:** NMT 1.0% for metoprolol and hydrochlorothiazide**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ and hydrochlorothiazide $(C_7H_8ClN_3O_4S_2)$ 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 or hydrochlorothiazide from the *Sample solution*

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

C_S = concentration of [USP Metoprolol Tartrate RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of the corresponding analyte in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of metoprolol tartrate $[(C_{15}H_{25}NO_3)_2 \cdot C_4H_6O_6]$ and hydrochlorothiazide $(C_7H_8ClN_3O_4S_2)$

PERFORMANCE TESTS• **[DISSOLUTION \(711\)](#)****Medium:** [Simulated gastric fluid TS](#) (without enzyme); 900 mL**Apparatus 1:** 100 rpm**Time:** 30 min**Determination of dissolved metoprolol tartrate****Standard solution:** 0.05 mg/mL of [USP Metoprolol Tartrate RS](#) in *Medium*

Sample solution: Remove 125 mL of the solution under test, allow to cool to room temperature, and filter, discarding the first 25 mL of the filtrate. [NOTE—Retain 30 mL of the remaining filtrate of the solution under test for the *Determination of dissolved hydrochlorothiazide*.] If necessary, prepare 0.05 mg/mL of metoprolol tartrate from the filtrate in fresh *Medium*.

Instrumental conditions**Mode:** UV**Analytical wavelength:** 276 nm**Cell:** 2 cm**Blank:** *Medium***Analysis****Samples:** *Standard solution*, *Sample solution*, and *Blank*

Transfer to separate separators 50.0 mL each of the *Standard solution*, *Sample solution*, and *Blank*. Add 10 mL of 2.5 N [sodium hydroxide](#) to each separator, and extract each with three 15-mL portions of [chloroform](#), filtering the [chloroform](#) extracts through pledgets of [chloroform](#)-prerinsed glass wool into individual 50-mL volumetric flasks. Dilute the contents of each flask with [chloroform](#) to volume, and mix. Determine the absorbances of the solutions obtained.

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

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (100/L)$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Determination of dissolved hydrochlorothiazide**Standard solution:** 0.03 mg/mL of [USP Hydrochlorothiazide RS](#) in *Medium*