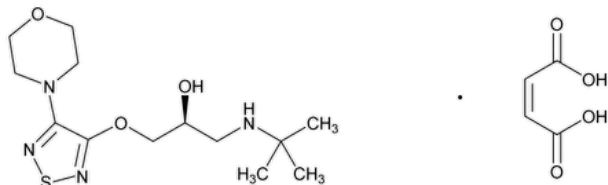


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Timolol Maleate



$C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$ 432.49
2-Propanol, 1-[(1,1-dimethylethyl)amino]-3- [[4-(4-morpholinyl)-1,2,5-thiadiazol-3-yl]oxy]-, (S)-, (Z)-2-butenedioate (1:1) (salt);
(-)-1-(tert-Butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-yl)oxy]-2-propanol maleate (1:1) (salt) CAS RN®: 26921-17-5; UNII: P8Y54F701R.

DEFINITION
Timolol Maleate contains NLT 98.0% and NMT 102.0% of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$), calculated on the dried basis.

IDENTIFICATION
Change to read:
• **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy*: 197M or 197A ▲ (CN 1-May-2020)
• **B.** The retention time of the timolol peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the *Enantiomeric Purity* test.

ASSAY
• **PROCEDURE**
Solution A: Dilute 0.5 mL of [trifluoroacetic acid](#) with [water](#) to 1 L.
Solution B: Dilute 0.5 mL of [trifluoroacetic acid](#) with [acetonitrile](#) to 1 L.
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	84	16
2.4	84	16
8	20	80
8.1	84	16
11	84	16

Diluent: [Methanol](#) and [water](#) (60:40)
System suitability solution: 100 µg/mL of [USP Timolol Maleate RS](#) and 10 µg/mL of [USP Timolol Related Compound D RS](#) in *Diluent*
Standard solution: 100 µg/mL of [USP Timolol Maleate RS](#) in *Diluent*
Sample solution: 100 µg/mL of Timolol Maleate in *Diluent*
Chromatographic system
(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 295 nm

Column: 2.1-mm × 10-cm; 2.6-μm packing [L1](#)

Autosampler temperature: 4°

Flow rate: 0.4 mL/min

Injection volume: 2.5 μL

System suitability

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

Suitability requirements

Resolution: NLT 2 between timolol and timolol related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$) in the portion of Timolol Maleate taken:

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

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

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

C_S = concentration of [USP Timolol Maleate RS](#) in the *Standard solution* (μg/mL)

C_U = concentration of Timolol Maleate in the *Sample solution* (μg/mL)

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

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, and Chromatographic system: Proceed as directed in the Assay.

▲ **Sensitivity solution:** 0.5 μg/mL of [USP Timolol Maleate RS](#) in *Diluent* ▲ (USP 1-Dec-2019)

System suitability solution: 100 μg/mL each of [USP Timolol Maleate RS](#), [USP Timolol Related Compound B RS](#), [USP Timolol Related Compound C RS](#), [USP Timolol Related Compound D RS](#), [USP Timolol Related Compound E RS](#), and [USP Timolol Related Compound F RS](#) in *Diluent*. [NOTE—Prepare fresh and analyze immediately as [USP Timolol Related Compound E RS](#) degrades rapidly.]

Standard solution: 1 μg/mL of [USP Timolol Maleate RS](#) and 4 μg/mL each of [USP Timolol Related Compound B RS](#), [USP Timolol Related Compound C RS](#), [USP Timolol Related Compound D RS](#), [USP Timolol Related Compound E RS](#), and [USP Timolol Related Compound F RS](#) in *Diluent*. Sonicate if needed for 0.5 min.

Sample solution: 1 mg/mL of Timolol Maleate in *Diluent*

System suitability

Samples: ▲ *Sensitivity solution*, ▲ (USP 1-Dec-2019) *System suitability solution*, and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between timolol and timolol related compound D, *System suitability solution*

Relative standard deviation: NMT 4.0% for timolol, *Standard solution*

▲ **Signal-to-noise ratio:** NLT 10 for timolol, *Sensitivity solution* ▲ (USP 1-Dec-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

▲ Calculate the percentage of timolol maleate ester (free base of timolol related compound E) in the portion of Timolol Maleate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of timolol maleate ester from the *Sample solution*

r_S = peak response of timolol maleate ester from the *Standard solution*