Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Feb-2018
Document Type: USP Monographs
DocId: GUID-343578EA-85D7-477F-8DB3-1979D5D0F640_4_en-US
DOI: https://doi.org/10.31003/USPNF_M83685_04_01
DOI Ref: j15vp

Timolol Maleate Tablets

DEFINITION
Timolol Maleate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
• **B.** The UV (or UV-Vis) spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Solution A: Transfer 0.5 mL of trifluoroacetic acid to a 1-L volumetric flask and dilute with water to volume.

Solution B: Transfer 0.5 mL of trifluoroacetic acid to a 1-L volumetric flask and dilute with acetonitrile to volume.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	84	16
2.4	84	16
8	20	80
8.1	84	16
11	84	16

Buffer: Transfer 11.04 g of monobasic sodium phosphate to a 1-L volumetric flask and dilute with water to volume. Adjust with phosphoric acid to a pH of 2.8 ± 0.05.

Diluent: Methanol and *Buffer* (20:80)

System suitability solution: 0.1 mg/mL of USP Timolol Maleate RS and 10.0 µg/mL of USP Timolol Related Compound D RS in *Diluent* with sonication if necessary

Standard solution: 0.1 mg/mL of USP Timolol Maleate RS in *Diluent* with sonication if necessary

Sample solution: 0.1 mg/mL of timolol maleate from NLT 20 finely ground Tablets (ground with a mortar and pestle) in *Diluent* with sonication if necessary, and filtration with 0.2-µm syringe filters, discarding the first 2 mL

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

Mode: LC

Detector: UV 295 nm. For *Identification* test *B*, use a diode array detector in the range of 210–400 nm.

Column: 2.1-mm × 10-cm; 2.6-µm packing L1

Flow rate: 0.4 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 2.5 between timolol and timolol related compound D, *System suitability solution*

Tailing factor: NMT 2.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = nominal concentration of timolol maleate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 20 min

Standard solution: USP Timolol Maleate RS in *Medium*

Sample solution: Sample per the chapter. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Analysis: Determine the amount of timolol maleate in solution in filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the procedure in the *Assay*.

Tolerances: NLT 80% (*Q*) of the labeled amount of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

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

System suitability solution: 0.1 mg/mL of USP Timolol Maleate RS and 10 µg/mL of USP Timolol Related Compound D RS in *Diluent* with sonication if necessary

Standard solution: 2.0 µg/mL each of USP Timolol Maleate RS, USP Timolol Related Compound B RS, and USP Timolol Related Compound D RS in *Diluent*

Sample solution: 1.0 mg/mL of timolol maleate from NLT 20 finely ground Tablets (ground with a mortar and pestle) in *Diluent* with sonication if necessary, and filtration with 0.2-µm syringe filters, discarding the first 2 mL

System suitability

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

[Note—The relative retention times are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 3 between timolol and timolol related compound D, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of timolol maleate related compound B and timolol maleate related compound D the portion of Tablets taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of each impurity from the *Standard solution*

C_S = concentration of each impurity in the *Standard solution* (mg/mL)

C_U = nominal concentration of timolol maleate in the *Sample solution* (mg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of any impurity 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*

C_U = nominal concentration of timolol maleate in the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Timolol related compound B	0.5	0.4
Timolol related compound D	0.8	0.4
Timolol	1.0	—
Any individual impurity	—	0.2
Total impurities	—	1.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Timolol Maleate RS

USP Timolol Related Compound B RS

3-(*tert*-Butylamino)-2-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-1-ol.

$C_{13}H_{24}N_4O_3S$ 316.42

USP Timolol Related Compound D RS

4-Morpholino-1,2,5-thiadiazol-3-ol.

$C_6H_9N_3O_2S$ 187.22

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

Topic/Question	Contact	Expert Committee
TIMOLOL MALEATE 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 41(2)

Current DocID: GUID-343578EA-85D7-477F-8DB3-1979D5D0F640_4_en-US
Previous DocID: GUID-343578EA-85D7-477F-8DB3-1979D5D0F640_2_en-US
DOI: https://doi.org/10.31003/USPNF_M83685_04_01

DOI ref: j15vp