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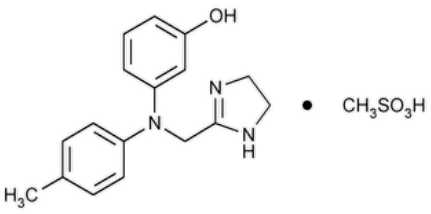
Phentolamine Mesylate

Change to read:



$C_{17}H_{19}N_3O \cdot CH_4O_3S$ 377.46

Phenol, 3-[[(4,5-dihydro-1*H*-imidazol-2-yl)methyl](4-methylphenyl)amino]-, monomethanesulfonate (salt);

m-[*N*-(2-Imidazolin-2-ylmethyl)-*p*-toluidino]phenol monomethanesulfonate (salt);

▲3-{[(4,5-Dihydro-1*H*-imidazol-2-yl)methyl](4-tolyl)amino}phenol methanesulfonate▲ (USP 1-May-2022) CAS RN®: 65-28-1; UNII: Y7543E5K9T.

DEFINITION

Phentolamine Mesylate contains NLT 98.0% and NMT 102.0% of phentolamine mesylate ($C_{17}H_{19}N_3O \cdot CH_4O_3S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M ▲or 197A▲ (USP 1-May-2022)

Change to read:

• **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

Sample solution: 20 µg/mL ▲of Phentolamine Mesylate▲ (USP 1-May-2022) in water

Acceptance criteria: Meets the requirements

Change to read:

• **C.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of *Standard solution A*, as obtained in the *Assay*.▲ (USP 1-May-2022)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** Transfer 10.2 g of monobasic potassium phosphate to a suitable container. Add 3000 mL of water to dissolve. Adjust with phosphoric acid to a pH of 2.5.

Solution A: Methanol and *Buffer* (20:80)

Solution B: Methanol and *Buffer* (70:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
5.0	100	0

Time (min)	Solution A (%)	Solution B (%)
28.0	0	100
44.0	0	100
45	100	0
55	100	0

Diluent: Transfer 1.36 g of sodium acetate and 0.5 g of ethylenediamine tetraacetate disodium dihydrate to a 1000-mL volumetric flask. Add 1000 mL of water to dissolve. Adjust with glacial acetic acid to a pH of 3.8.

Standard solution A: 0.22 mg/mL of USP Phentolamine Mesylate RS in *Diluent*. [NOTE—Sonication may be needed to aid the dissolution.]

Standard solution B: 0.22 mg/mL of USP Phentolamine Related Compound A RS in *Diluent*. [NOTE—Sonication may be needed to aid the dissolution.]

Standard solution C: 0.22 mg/mL of USP Phentolamine Keto Analog RS prepared as follows. Transfer a suitable amount of USP Phentolamine Keto Analog RS to a suitable volumetric flask. Add methanol to 15% of the flask volume, and sonicate. Dilute with *Diluent* to volume.

System suitability solution: 0.22 mg/mL of USP Phentolamine Mesylate RS and 1.1 µg/mL each of USP Phentolamine Related Compound A RS from *Standard solution B* and USP Phentolamine Keto Analog RS from *Standard solution C* in *Diluent*

Sample solution: 0.22 mg/mL of Phentolamine Mesylate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 232 nm

Column: 4.6-mm × 15-cm; 4-µm packing L87

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for phentolamine keto analog, phentolamine, and phentolamine related compound A are about 0.84, 1.00, and 1.09, respectively.]

Suitability requirements

Resolution: NLT 2.0 between phentolamine and phentolamine related compound A, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution A*

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

Analysis

Samples: *Standard solution A* and *Sample solution*

Calculate the percentage of phentolamine mesylate ($C_{17}H_{19}N_3O \cdot CH_4O_3S$) in the portion of Phentolamine Mesylate taken:

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

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

r_S = peak response of phentolamine from *Standard solution A*

C_S = concentration of USP Phentolamine Mesylate RS in *Standard solution A* (mg/mL)

C_U = concentration of Phentolamine Mesylate in the *Sample solution* (mg/mL)▲ (USP 1-May-2022)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Chloride and Sulfate ⟨221⟩, *Sulfate***

Sample: 0.10 g of Phentolamine Mesylate

Acceptance criteria: The *Sample* shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.2%).

Change to read:

• **Organic Impurities**

▲Buffer, Solution A, Solution B, Mobile phase, Diluent, Standard solution B, Standard solution C, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.11 µg/mL of USP Phentolamine Mesylate RS in *Diluent*

Standard solution: 0.22 µg/mL of USP Phentolamine Mesylate RS and 0.33 µg/mL each of USP Phentolamine Related Compound A RS from *Standard solution B* and USP Phentolamine Keto Analog RS from *Standard solution C* in *Diluent*

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between phentolamine and phentolamine related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0% for phentolamine keto analog, phentolamine, and phentolamine related compound A, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phentolamine related compound A and phentolamine keto analog in the portion of Phentolamine Mesylate taken:

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

r_U = peak response of phentolamine related compound A or phentolamine keto analog from the *Sample solution*

r_S = peak response of phentolamine related compound A or phentolamine keto analog from the *Standard solution*

C_S = concentration of USP Phentolamine Related Compound A RS or USP Phentolamine Keto Analog RS in the *Standard solution* (µg/mL)

C_U = concentration of Phentolamine Mesylate in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of Phentolamine Mesylate taken:

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

r_U = peak response of any unspecified impurity from the *Sample solution*

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

C_S = concentration of USP Phentolamine Mesylate RS in the *Standard solution* (µg/mL)

C_U = concentration of Phentolamine Mesylate in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phentolamine keto analog	0.84	0.15
Phentolamine	1.00	—
Phentolamine related compound A	1.09	0.15
Any unspecified impurity	—	0.10
Total impurities	—	1.0▲ (USP 1-May-2022)

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry under vacuum at 60° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at 25°, excursions permitted, 15°–30°.

Change to read:

• **USP Reference Standards** ⟨11⟩

▲ USP Phentolamine Keto Analog RS

N-(3-Hydroxyphenyl)-*N*-(4-tolyl)-4,5-dihydro-1*H*-imidazole-2-carboxamide.

$C_{17}H_{17}N_3O_2$ 295.34▲ (USP 1-May-2022)

USP Phentolamine Mesylate RS

▲ USP Phentolamine Related Compound A RS

N-(2-Aminoethyl)-2-[(3-hydroxyphenyl)(4-tolyl)amino]acetamide.

$C_{17}H_{21}N_3O_2$ 299.37▲ (USP 1-May-2022)

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

Topic/Question	Contact	Expert Committee
PHENTOLAMINE MESYLATE	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:
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