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Phenoxybenzamine Hydrochloride Capsules

DEFINITION

Phenoxybenzamine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of phenoxybenzamine hydrochloride ($C_{18}H_{22}ClNO \cdot HCl$).

IDENTIFICATION

• **A.** The UV absorption spectra of the phenoxybenzamine peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the corresponding peak from the *Standard solution*, as obtained in the *Assay*.

• **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

Change to read:

• **Procedure**

Solution A: 2.2 mg/mL of anhydrous monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: ▲▲ (USP 1-May-2022) *Solution A* and acetonitrile (45:55)

System suitability solution: ▲0.2 mg/mL of USP Phenoxybenzamine Hydrochloride RS, 1 µg/mL of USP Phenoxybenzamine Alcohol RS, and 50 µg/mL of USP Phenoxybenzamine Nitrile RS in acetonitrile. [Note—USP Phenoxybenzamine Alcohol RS is used for retention time verification.]▲ (USP 1-May-2022)

Standard solution: 0.2 mg/mL of USP Phenoxybenzamine Hydrochloride RS in acetonitrile. [Note—Sonicate, if necessary.]

Sample solution: Nominally 0.2 mg/mL of phenoxybenzamine hydrochloride in acetonitrile prepared as follows. Remove, as completely as possible, the contents of Capsules (NLT 20). Transfer a portion of the mixed powder, equivalent to about 10 mg of phenoxybenzamine hydrochloride, to a 50-mL volumetric flask. Add about 40 mL of acetonitrile, and sonicate for 15 min with occasional swirling. Cool, and dilute with acetonitrile to volume to obtain the concentration, based on the label claim. Allow the sample to stand undisturbed for 30 min such that the undissolved material settles to the bottom. Transfer the top clear solution into HPLC vials, and use as the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: UV 268 nm. For *Identification A*, use a diode array detector in the range of 240–340 nm.

Column: 4.6-mm × ▲15▲ (USP 1-May-2022) -cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

▲[Note—The relative retention times for phenoxybenzamine alcohol, phenoxybenzamine, and phenoxybenzamine nitrile are about 0.2, 1.0, and 1.4, respectively.]▲ (USP 1-May-2022)

Suitability requirements

Resolution: NLT 4 between phenoxybenzamine and ▲phenoxybenzamine nitrile,▲ (USP 1-May-2022) *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenoxybenzamine hydrochloride ($C_{18}H_{22}ClNO \cdot HCl$) in the portion of Capsules taken:

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

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

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

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

C_U = nominal concentration of phenoxybenzamine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer: 2.2 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 3.00 ± 0.05.

Mobile phase: *Buffer* and acetonitrile (45:55)

Standard solution: 0.02 mg/mL of USP Phenoxybenzamine Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 268 nm

Column: 4.6-mm × ▲15▲ (USP 1-May-2022) -cm; packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2%

▲Analysis

Samples: *Standard solution* and *Sample solution*▲ (USP 1-May-2022)

Calculate the percentage of the labeled amount of phenoxybenzamine hydrochloride ($C_{18}H_{22}ClNO \cdot HCl$) dissolved:

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

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

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

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 500 mL

Tolerances: NLT 75% (Q) of the labeled amount of phenoxybenzamine hydrochloride ($C_{18}H_{22}ClNO \cdot HCl$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A, Mobile phase, System suitability solution, **▲Standard solution,▲** (USP 1-May-2022) and **Chromatographic system:** Proceed as directed in the *Assay*.

▲Sensitivity solution: 0.4 µg/mL of USP Phenoxybenzamine Hydrochloride RS from *Standard solution* in acetonitrile

Sample solution: Nominally 0.4 mg/mL of phenoxybenzamine hydrochloride in acetonitrile prepared as follows. Transfer a portion of the mixed powder that is used for the *Sample solution* preparation in the *Assay*, equivalent to about 20 mg of phenoxybenzamine hydrochloride,

to a 50-mL volumetric flask. Add about 40 mL of acetonitrile, and sonicate to dissolve. Dilute with acetonitrile to volume. Allow the sample to stand undisturbed for 30 min such that the undissolved material settles to the bottom. Transfer the top clear solution into HPLC vials, and use as the *Sample solution*.▲ (USP 1-May-2022)

System suitability

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

[NOTE—The relative retention times for phenoxybenzamine alcohol, phenoxybenzamine, and phenoxybenzamine nitrile are about 0.2, 1.0, and 1.4, respectively.]▲ (USP 1-MAY-2022)

Suitability requirements

Resolution: NLT 4 between phenoxybenzamine and ▲phenoxybenzamine nitrile,▲ (USP 1-May-2022) *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-May-2022)

Analysis

Sample: *Sample solution*

Calculate the percentage of ▲phenoxybenzamine alcohol or any unspecified degradation product▲ (USP 1-May-2022) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response of ▲phenoxybenzamine alcohol or any unspecified degradation product▲ (USP 1-May-2022) from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
▲Phenoxybenzamine alcohol▲ (USP 1-May-2022) (phenoxybenzamine tertiary amine)▲▲ (USP 1-May-2022)	▲0.2▲ (USP 1-May-2022)	1.1	1.5
Phenoxybenzamine	1.0	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products▲▲ (USP 1-May-2022)	—	—	2.0

ADDITIONAL REQUIREMENTS

Change to read:

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. ▲Store at controlled room temperature.▲ (USP 1-May-2022)

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

▲ USP Phenoxybenzamine Alcohol RS

2-[Benzyl(1-phenoxypropan-2-yl)amino]ethan-1-ol.

$C_{18}H_{23}NO_2$ 285.39▲ (USP 1-May-2022)

USP Phenoxybenzamine Hydrochloride RS

▲ USP Phenoxybenzamine Nitrile RS

3-[Benzyl(1-phenoxypropan-2-yl)amino]propanenitrile.

$C_{19}H_{22}N_2O$ 294.40▲ (USP 1-May-2022)

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

Topic/Question	Contact	Expert Committee
PHENOXYBENZAMINE HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

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