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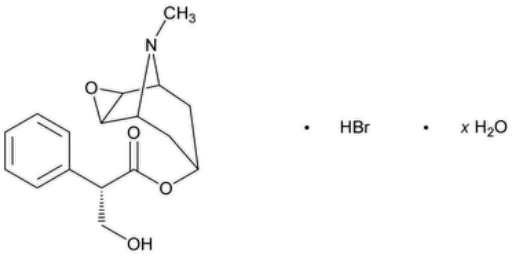
Scopolamine Hydrobromide

Change to read:

▲



▲ (USP 1-Dec-2021)

$C_{17}H_{21}NO_4 \cdot HBr \cdot$ ▲xH_2O▲ (USP 1-Dec-2021)

Benzeneacetic acid, α-(hydroxymethyl)-, 9-methyl-3-oxa-9-azatricyclo[3.3.1.0.^{2,4}]non-7-yl ester, hydrobromide,▲hydrate,▲ (USP 1-Dec-2021) [7(*S*)-(1α,2β,4β,5α,7β)]-;

6β,7β-Epoxy-1α*H*,5α*H*-tropan-3α-ol (−)-tropate (ester) hydrobromide▲hydrate;

(1*R*,2*R*,4*S*,5*S*,7*s*)-9-Methyl-3-oxa-9-azatricyclo[3.3.1.0.^{2,4}]nonan-7-yl (*S*)-3-hydroxy-2-phenylpropanoate hydrobromide hydrate▲ (USP 1-Dec-2021)

Anhydrous 384.27 CAS RN®: 114-49-8; UNII: R3K67DRL3J.

DEFINITION

Scopolamine Hydrobromide contains NLT 98.0% and NMT 102.0% of scopolamine hydrobromide ($C_{17}H_{21}NO_4 \cdot HBr$), calculated on the anhydrous basis.

[**Caution—**Handle scopolamine hydrobromide with exceptional care, because it is highly potent.]

IDENTIFICATION

Change to read:

- **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

  ▲**Sample:**▲ (USP 1-Dec-2021) Dissolve 3 mg in 1 mL of alcohol, and evaporate the solution on a steam bath to dryness. Dissolve the residue in 0.5 mL of chloroform, add 200 mg of potassium bromide previously dried at 105° for 30 min, and stir frequently for 5 min. Allow the chloroform to evaporate to dryness, and stir frequently to obtain a flowing powder residue. Dry the residue ▲as directed in the test for *Water Determination*,▲ (USP 1-Dec-2021) and then immediately compress the residue to a disk.

  ▲**Standard solution:** Proceed as directed in the *Sample* using USP Scopolamine Hydrobromide RS.▲ (USP 1-Dec-2021)

  Acceptance criteria: Meets the requirements

- **B.**

  Sample solution: 50 mg/mL of Scopolamine Hydrobromide in water

  Analysis: To 1 mL of the *Sample solution* add a few drops of chlorine TS, and shake the mixture with 1 mL of chloroform.

  Acceptance criteria: A brownish color forms in the chloroform layer.

- **C.** The retention time of the scopolamine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

  Buffer solution: 7.0 g/L of monobasic potassium phosphate in water. Adjust with 0.05 M phosphoric acid to a pH of 3.3.

  Solution A: Dissolve 3.5 g of sodium dodecyl sulfate in 606 mL of *Buffer solution*. Add 320 mL of acetonitrile and mix.

  Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.0	95	5
20.0	70	30
20.1	95	5
25.0	95	5

Standard solution: 0.2 mg/mL of USP Scopolamine Hydrobromide RS in *Solution A*

Sample solution: 0.2 mg/mL of Scopolamine Hydrobromide in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of scopolamine hydrobromide ($C_{17}H_{21}NO_4 \cdot HBr$) in the portion of Scopolamine Hydrobromide taken:

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

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

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

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

C_U = concentration of Scopolamine Hydrobromide in the *Sample solution* (mg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Sample: 1 g

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

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

System suitability solution: 0.2 mg/mL of USP Scopolamine Hydrobromide RS and 0.001 mg/mL of USP Norscopolamine RS in *Solution A*

Standard solution: 0.002 mg/mL of USP Scopolamine Hydrobromide RS in *Solution A*

Sample solution: 2.0 mg/mL of Scopolamine Hydrobromide in *Solution A*

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between the norscopolamine and scopolamine peaks, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Scopolamine Hydrobromide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

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

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

C_U = concentration of Scopolamine Hydrobromide in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%. Disregard any peak due to the bromide ion at a relative retention time of 0.1 that appears close to the solvent peak.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tropic acid[a]	0.19	2.4	0.20
Norscopolamine	0.89	1.4	0.5
Scopolamine	1.0	—	—
Hyoscyamine[b]	1.3	1.3	0.20
Apohyoscine[c]	1.8	2.2	0.20
Apoatropine[d]	2.4	2.3	0.20
Any other individual impurity	—	—	0.10
Total impurities	—	—	0.7

[a] 3-Hydroxy-2-phenylpropanoic acid.

[b] (1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl (*S*)-3-hydroxy-2-phenylpropanoate.

[c] (1*R*,2*R*,4*S*,5*S*,7*s*)-9-Methyl-3-oxa-9-azatricyclo[3.3.1.$0^{2,4}$]nonan-7-yl 2-phenylacrylate.

[d] (1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl 2-phenylacrylate.

SPECIFIC TESTS

- **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 50 mg/mL of anhydrous Scopolamine Hydrobromide in water

Acceptance criteria: −24° to −26°

- **pH** ⟨791⟩

Sample solution: 50 mg/mL of Scopolamine Hydrobromide in water

Acceptance criteria: 4.0–5.5

- **Water Determination** ⟨921⟩, *Method III*

Analysis: Dry in two stages (see *Loss on Drying* ⟨731⟩): first at 80° for 2 h, and then at 105° for an additional 3 h.

Acceptance criteria: NMT 13.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **USP Reference Standards** ⟨11⟩

USP Norscopolamine RS

(1*R*,2*R*,4*S*,5*S*,7s)-3-Oxa-9-azatricyclo[3.3.1.$0^{2,4}$]nonan-7-yl (*S*)-3-hydroxy-2-phenylpropanoate.
$C_{16}H_{19}NO_4$ 289.33

USP Scopolamine Hydrobromide RS

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

Topic/Question	Contact	Expert Committee
SCOPOLAMINE HYDROBROMIDE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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