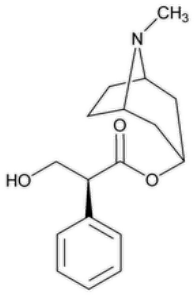
Status: Currently Official on 15-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-313C99E2-03D9-4FE7-98CC-B8535C47903A_1_en-US
DOI: https://doi.org/10.31003/USPNF_M39590_01_01
DOI Ref: bn02k

Hyoscyamine



$C_{17}H_{23}NO_3$ 289.37

Benzeneacetic acid, α-(hydroxymethyl)-, 8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester, [3(*S*)-*endo*-];
1α*H*,5α*H*-Tropan-3α-ol (−)-tropate (ester) CAS RN®: 101-31-5; UNII: PX44XO846X.

DEFINITION

Hyoscyamine contains NLT 98.0% and NMT 101.0% of hyoscyamine ($C_{17}H_{23}NO_3$), calculated on the dried basis.

[**Caution—**Handle Hyoscyamine with exceptional care since it is highly potent.]

IDENTIFICATION

• **A.**

Standard solution: Transfer 36 mg of USP Hyoscyamine Sulfate RS to a 60-mL separator with the aid of 5 mL of water. Add 1.5 mL of 1 N sodium hydroxide and 10 mL of chloroform to the separator. Shake for 1 min, allow the layers to separate, and pass the chloroform extracts through a filter of about 2 g of anhydrous granular sodium sulfate supported on a pledget of glass wool. Extract the aqueous layer with two additional 10-mL portions of chloroform, filtering and combining with the main extract. Evaporate the chloroform solution under reduced pressure to dryness, and dissolve the residue in 10 mL of carbon disulfide.

Sample solution: Prepare as directed in the *Standard solution* using 30 mg of Hyoscyamine.

Acceptance criteria: The IR absorption spectrum (determined in a 1-mm cell) of the *Sample solution* exhibits maxima only at the same wavelengths as those of the *Standard solution*.

• **B.**

Sample: 60 mg

Analysis: Dissolve the *Sample* in 1 mL of 0.2 N hydrochloric acid, and add gold chloride TS, dropwise with shaking, until a definite precipitate separates. Add a small amount of 3 N hydrochloric acid, dissolve the precipitate with the aid of heat, and then allow to cool.

Acceptance criteria: Lustrous golden yellow scales are formed (distinction from atropine and scopolamine).

ASSAY

• **Procedure**

Sample: 500 mg

Analysis: Dissolve the *Sample* in 50 mL of glacial acetic acid, and add 1 drop of crystal violet TS. Titrate with 0.1 N perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 28.94 mg of hyoscyamine ($C_{17}H_{23}NO_3$).

Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Limit of Foreign Alkaloids and Other Impurities**

Standard solution: 24 mg/mL of USP Hyoscyamine Sulfate RS in methanol

Sample solution A: 20 mg/mL of Hyoscyamine in methanol

Sample solution B: 1 mg/mL of Hyoscyamine from *Sample solution A* in methanol

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Adsorbent: 0.5-mm layer of chromatographic silica gel

Developing solvent system: Chloroform, acetone, and diethylamine (5:4:1)

Spray reagent: Potassium iodoplatinate TS

Analysis: Apply 25 µL of *Sample solution A,* 1 µL of *Sample solution B*, and 5 µL of the *Standard solution* to a suitable thin-layer chromatographic plate. Allow the spots to dry, and develop the chromatogram in the *Developing solvent system* until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by spraying with the *Spray reagent*.

Acceptance criteria: The R_F value of the principal spot of each *Sample solution* corresponds to that of the *Standard solution*. No secondary spot of *Sample solution A* exhibits intensity equal to or greater than the principal spot of *Sample solution B* (0.2%).

SPECIFIC TESTS

- **Melting Range or Temperature ⟨741⟩:** 106°–109°
- **Optical Rotation,** *Specific Rotation* ⟨781S⟩

  Sample solution: 10 mg/mL, in dilute alcohol (1 in 2)

  Acceptance criteria: −20° to −23°
- **Loss on Drying ⟨731⟩**

  Analysis: Dry under vacuum over silica gel to constant weight.

  Acceptance criteria: NMT 0.2%

ADDITIONAL REQUIREMENTS

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

  USP Hyoscyamine Sulfate RS

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

Topic/Question	Contact	Expert Committee
HYOSCYAMINE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(6)

Current DocID: GUID-313C99E2-03D9-4FE7-98CC-B8535C47903A_1_en-US

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