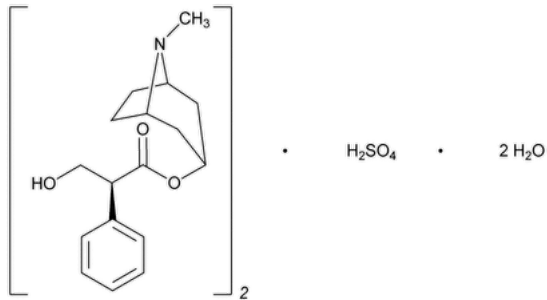


Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-E38B0B89-20D5-4862-AC5F-2AD069398735_6_en-US
DOI: https://doi.org/10.31003/USPNF_M39680_06_01
DOI Ref: n0ug2

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Hyoscyamine Sulfate



$(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot 2H_2O$ 712.85
 $(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4$ 676.83
Benzeneacetic acid, α -(hydroxymethyl)-, 8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester, [3(S)-endo]-, sulfate (2:1), dihydrate;
1 α H,5 α H-Tropan-3 α -ol (-)-tropate (ester) sulfate (2:1) (salt) dihydrate;
(1R,3r,5S)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl (S)-3-hydroxy-2-phenylpropanoate sulfate dihydrate CAS RN®: 6835-16-1; UNII: F2R8V82B84 (dihydrate).

DEFINITION

Hyoscyamine Sulfate contains NLT 98.0% and NMT 102.0% of hyoscyamine sulfate [$(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4$], calculated on the anhydrous basis.

[CAUTION—Handle hyoscyamine sulfate with exceptional care because it is highly potent.**]**

IDENTIFICATION

Change to read:

- A.** **▲** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#), 197A or 197K: **▲** (CN 1-MAY-2020) Meets the requirements.
- B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- C.** [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Sulfate](#)

Sample solution: 50 mg/mL

Acceptance criteria: Meets the requirements

ASSAY

• PROCEDURE

Buffer: 7.0 g/L of [monobasic potassium phosphate](#), adjusted 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*, add 320 mL of acetonitrile, and mix.

Solution B: Acetonitrile

Mobile phase: See [Table 1](#). Return to original conditions and re-equilibrate the system.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2	95	5
20	70	30

Standard solution: 0.24 mg/mL of [USP Hyoscyamine Sulfate RS](#) in *Solution A*

Sample solution: 0.24 mg/mL of Hyoscyamine Sulfate 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: 1.0 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 hyoscyamine sulfate [(C₁₇H₂₃NO₃)₂ · H₂SO₄] in the portion of Hyoscyamine Sulfate 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 Hyoscyamine Sulfate RS](#) in the *Standard solution* (mg/mL)
 C_U = concentration of Hyoscyamine Sulfate in the *Sample solution* (mg/mL)

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

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.1%
- **ORGANIC IMPURITIES**

Buffer, Solution A, Solution B, Mobile phase, Sample solution, and Chromatographic system: Proceed as directed in the Assay.
Standard stock solution: 1.2 mg/mL of [USP Hyoscyamine Sulfate RS](#) in *Solution A*
Standard solution: 0.24 μg/mL of [USP Hyoscyamine Sulfate RS](#) from the *Standard stock solution* in *Solution A*
System suitability stock solution: 2.4 μg/mL of [USP Hyoscyamine Related Compound A RS](#) in *Solution A*
System suitability solution: Transfer 5.0 mL of *System suitability stock solution* to a 50-mL volumetric flask, add 10 mL of the *Standard stock solution*, and dilute with *Solution A* to volume.

System suitability

Samples: *Standard solution* and *System suitability solution*
Suitability requirements
Resolution: NLT 2.0 between hyoscyamine related compound A and hyoscyamine, *System suitability solution*
Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Sample solution* and *Standard solution*
Calculate the percentage of each impurity in the portion of Hyoscyamine Sulfate taken:

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

r_U = peak response of each impurity from the *Sample solution*
 r_S = peak response of hyoscyamine from the *Standard solution*
 C_S = concentration of [USP Hyoscyamine Sulfate RS](#) in the *Standard solution* (μg/mL)
 C_U = concentration of Hyoscyamine Sulfate in the *Sample solution* (μg/mL)
 F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#).

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
DL-Tropic acid	0.2	2.1	0.2
7-Hydroxyhyoscyamine	0.67	1.0	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
6-Hydroxyhyoscyamine	0.72	1.0	0.2
Scopolamine	0.8	1.0	0.2
Norhyoscyamine (hyoscyamine related compound A)	0.9	1.0	0.3
Hyoscyamine	1.0	—	—
Littorine	1.1	1.0	0.2
Apoatropine	1.8	1.7	0.2
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	0.5

SPECIFIC TESTS

- [OPTICAL ROTATION \(781S\)](#), [Procedures](#), [Specific Rotation](#)

Sample solution: 50 mg/mL in [water](#)

Acceptance criteria: -24° to -29°, measured at 20°

- [WATER DETERMINATION \(921\)](#), [Method I](#), [Method Ia](#): 2.0%–5.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

- [USP REFERENCE STANDARDS \(11\)](#).

[USP Hyoscyamine Sulfate RS](#)

[USP Hyoscyamine Related Compound A RS](#)

Norhyoscyamine sulfate;

(1R,3r,5S)-8-Azabicyclo[3.2.1]oct-3-yl(2S)-3-hydroxy-2-phenylpropanoate sulfate (2:1).

$C_{32}H_{44}N_2O_{10}S$ 648.77

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
HYOSCYAMINE SULFATE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. PF 43(4)

Current DocID: GUID-E38B0B89-20D5-4862-AC5F-2AD069398735_6_en-US

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