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Atropine Sulfate Ophthalmic Ointment

DEFINITION

Atropine Sulfate Ophthalmic Ointment is Atropine Sulfate in a suitable ophthalmic ointment base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of atropine sulfate monohydrate $[(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot H_2O]$. It is sterile.

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sulfate*

Sample solution: Transfer 5 g of Ophthalmic Ointment to a separator, dissolve in 50 mL of ether, and extract with 20 mL of water.

Acceptance criteria: Meets the requirements

ASSAY

Change to read:

- **Procedure**

Solution A: Stronger ammonia water and water (1:100), adjusted with perchloric acid to a pH of 3.0

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
3	95	5
14	75	25
19	60	40
21	60	40
22	95	5
25	95	5

Diluent: Acetonitrile and *Solution A* (25:75)

System suitability solution: 1.0 µg/mL each of USP Atropine Sulfate RS and littorine hydrochloride in *Diluent*

Standard solution: 0.1 mg/mL of USP Atropine Sulfate RS in *Diluent*

Sample stock solution: Nominally 0.5 mg/mL of atropine sulfate from a portion of Ophthalmic Ointment prepared as follows. Transfer 10 mg of atropine sulfate from a portion of Ophthalmic Ointment to a stoppered 250-mL flask, add 20 mL of *Diluent*, and shake at 40° for 60 min. Centrifuge and use the lower layer clear solution. [Note—The use of a centrifuge speed of 4000 rpm for 10 min may be suitable.]

Sample solution: Nominally 0.1 mg/mL of atropine sulfate from the *Sample stock solution* in *Diluent*

Chromatographic system

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

[Note—Rinse the system with water after each set of analysis.]

Mode: LC

Detector: UV 210 nm

Column: 2.1-mm × 10-cm; 1.8-µm packing L96

Column temperature: 30°

Flow rate: 0.4 mL/min

Injection volume: 3 µL

System suitability

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

[NOTE—The relative retention times for atropine and littorine are 1.0 and 1.04, respectively.]

Suitability requirements

Resolution: NLT 2.0 between atropine and littorine, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of atropine sulfate monohydrate $[(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot H_2O]$ in the portion of Ophthalmic Ointment taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

C_U = nominal concentration of atropine sulfate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of atropine sulfate monohydrate, ▲694.84▲ (ERR 1-Jul-2020)

M_{r2} = molecular weight of anhydrous atropine sulfate, 676.82

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **ORGANIC IMPURITIES**

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

Standard solution: 1.0 µg/mL of USP Atropine Sulfate RS in *Diluent*

Sample solution: Nominally 500 µg/mL of atropine sulfate from a portion of Ophthalmic Ointment prepared as follows. Transfer a portion of Ophthalmic Ointment equivalent to 25 mg of atropine sulfate to a stoppered 250-mL flask, add 50 mL of *Diluent*, and shake at 40° for 60 min. Centrifuge and use the lower layer clear solution. [NOTE—The use of a centrifuge speed of 4000 rpm for 10 min may be suitable.]

System suitability

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

[NOTE—The relative retention times for atropine and littorine are 1.0 and 1.04, respectively.]

Suitability requirements

Resolution: NLT 2.0 between atropine and littorine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified and any unspecified degradation product in the portion of Ophthalmic Ointment taken:

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

r_U = peak response of each specified and any unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of atropine sulfate in the *Sample solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tropic acid[a]	0.35	2.1	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Scopolamine[b]	0.74	1.0	0.2
Hyoscyamine related compound A[c]	0.92	1.0	0.3
Atropine	1.0	—	—
Apoatropine[d]	1.46	2.1	0.2
Any individual unspecified degradation product	—	1.0	0.2

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

[b] (*S*)-(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 3-hydroxy-2-phenylpropanoate.

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

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

SPECIFIC TESTS

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Other Requirements:** It meets the requirements for *Particulate and Foreign Matter* in *Ophthalmic Products—Quality Tests ⟨771⟩, Drug Product Quality, Universal Tests, Particulate and Foreign Matter.*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in collapsible ophthalmic ointment tubes. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Atropine Sulfate RS

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

Topic/Question	Contact	Expert Committee
ATROPINE SULFATE OPHTHALMIC OINTMENT	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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