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Atropine Sulfate Ophthalmic Solution

DEFINITION

Atropine Sulfate Ophthalmic Solution is a sterile, aqueous solution of Atropine Sulfate. It contains NLT 93.0% and NMT 107.0% of the labeled amount of atropine sulfate monohydrate $[(C_{17}H_{23}NO_3)_2 \cdot H_2SO_4 \cdot H_2O]$. It may contain suitable stabilizers and antimicrobial agents.

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.

Delete the following:

B. [IDENTIFICATION TESTS—GENERAL \(191\), Chemical Identification Tests, Sulfate](#)

Sample solution: Evaporate to dryness a quantity of Ophthalmic Solution. Prepare a solution from the residue that contains the equivalent of 50 mg of atropine sulfate/mL.

Acceptance criteria: Meets the requirements

Add the following:

- ▲ **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.▲ (IRA 1-Nov-2019)

ASSAY

Change to read:

PROCEDURE

▲ **Buffer A:** 6.8 g/L of [sodium acetate](#) in [water](#). To each liter add 3.5 mL of [triethylamine](#) and 6.6 mL of [glacial acetic acid](#). Adjust with [glacial acetic acid](#), if needed, to a pH of 4.5.

Buffer B: 6.8 g/L of [sodium acetate](#) in [water](#). To each liter add 4 mL of [glacial acetic acid](#). Adjust with [glacial acetic acid](#), if needed, to a pH of 4.5.

Mobile phase: [Methanol](#) and *Buffer A* (15:85)

Diluent: [Methanol](#) and *Buffer B* (15:85)

Standard solution: 0.5 mg/mL of [USP Atropine Sulfate RS](#) in *Diluent*

Sample solution: Nominally 0.5 mg/mL of atropine sulfate monohydrate from a volume of Ophthalmic Solution prepared as follows. Rinse a 100-mL volumetric flask with *Diluent*. Transfer about 33 mL of *Diluent* to the flask and then add a 5.0-mL aliquot of Ophthalmic Solution using a "to contain" pipet (see [Volumetric Apparatus \(31\)](#)) to the flask. Shake vigorously. Dilute with *Diluent* to volume. Additional shaking may be needed to obtain a uniform solution.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 225 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

Column: 4.6-mm × 15-cm; 5-μm packing [L10](#)

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 20 μL

Run time: NLT 3 times the retention time of atropine

System suitability

Sample: *Standard solution*

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

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 Solution 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
- M_{r2} = molecular weight of anhydrous atropine sulfate, 676.82▲ (IRA 1-Nov-2019)

Acceptance criteria: 93.0%–107.0%

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

▲ **Buffer A, Buffer B, Mobile phase, Diluent, Standard solution, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.

System suitability solution: 0.005 mg/mL of [atropic acid](#) and 0.5 mg/mL of [USP Atropine Sulfate RS](#) in *Diluent*

System suitability

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

[NOTE—See [Table 1](#) for the relative response factors.]

Suitability requirements

Resolution: NLT 1.5 between atropic acid and atropine, *System suitability solution*

Relative standard deviation: NMT 1.0%, *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 Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

- 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* (mg/mL)
- C_U = nominal concentration of atropine sulfate in the *Sample solution* (mg/mL)
- F = relative response factor (see [Table 1](#))
- M_{r1} = molecular weight of atropine sulfate monohydrate, 694.84
- M_{r2} = molecular weight of anhydrous atropine sulfate, 676.82

Acceptance criteria: See [Table 1](#).

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tropic acid ^a	0.69	2.0	7.0
Atropic acid ^b	0.87	12.2	1.0
Atropine	1.0	—	—
Apoatropine ^c	2.1	4.3	1.0
Any individual unspecified degradation product	—	1.0	1.0
Total impurities	—	—	7.0

- a 3-Hydroxy-2-phenylpropanoic acid.
- b 2-Phenylacrylic acid.
- c (1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl 2-phenylacrylate.▲ (IRA 1-Nov-2019)

SPECIFIC TESTS

- [pH \(791\)](#): 3.5–6.0
- [STERILITY TESTS \(71\)](#): Meets the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and 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 SOLUTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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