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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