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Clemastine Fumarate Tablets

DEFINITION
Clemastine Fumarate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$).

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.** The UV spectrum of the clemastine peak of the *Diluted sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.

ASSAY
• **Procedure**

Solution A: 9.47 g/L of anhydrous dibasic sodium phosphate in water

Solution B: 9.08 g/L of monobasic potassium phosphate in water

Solution C: *Solution A* and *Solution B* (612:388)

Buffer: *Solution C* and water (25:75)

Mobile phase: Methanol and *Buffer* (83:17)

Diluent: Methanol and water (50:50)

Standard solution: 0.14 mg/mL of USP Clemastine Fumarate RS in *Diluent*

Sample solution: Transfer a quantity of NLT 20 finely powdered Tablets, equivalent to 14 mg of clemastine fumarate, to a 200-mL conical flask. Pipet 100 mL of *Diluent* into the flask, shake for 30 min, centrifuge, and filter the supernatant.

Chromatographic system
(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 10-µm packing L7

Flow rate: 4 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$) in the portion of Tablets 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 Clemastine Fumarate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of clemastine fumarate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Buffer: Dissolve 20.0 g of citric acid monohydrate in 1000 mL of water, add 22.0 mL of sodium hydroxide solution (3 in 10) and 8.8 mL of hydrochloric acid, and dilute with water to 2000 mL. Adjust, if necessary, with sodium hydroxide solution (1 in 2) to a pH of 4.0.

Medium: *Buffer*; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: USP Clemastine Fumarate RS in *Medium* with a similar concentration to the *Sample solution*

Sample solution: Centrifuge 60 mL of the solution under test for 20 min at 4000 rpm.

Instrumental conditions

Mode: UV

Analytical wavelength: About 420 nm

Blank: *Medium*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Transfer 50.0 mL of the *Samples* to individual 125-mL separatory funnels, and treat each of the solutions as follows. Add 10 mL of methyl orange solution (2 in 10,000), mix, add 20.0 mL of chloroform, shake simultaneously by mechanical means for 10 min, remove the chloroform layer, and centrifuge the chloroform layer for 10 min at 4000 rpm. Use the *Blank* to set the instrument.

Calculate the percentage of the labeled amount of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$) dissolved.

Tolerances: NLT 75% (*Q*) of the labeled amount of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Buffer: 4.1 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 4.0.

Solution A: Methanol, acetonitrile, and *Buffer* (35:35:30)

Solution B: Methanol, acetonitrile, and *Buffer* (40:37.5:22.5)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
3.1	0	100
18	0	100
18.1	100	0
25	100	0

Standard stock solution 1: 0.14 mg/mL of USP Clemastine Fumarate RS in *Solution A*. Sonicate for NLT 5 min or until dissolved.

Standard stock solution 2: 0.14 mg/mL of USP 4-Chlorobenzophenone RS in methanol. Sonicate for NLT 5 min or until dissolved.

System suitability solution: 2.8 µg/mL each of USP Clemastine Fumarate RS and USP 4-Chlorobenzophenone RS in *Solution A* from *Standard stock solution 1* and *Standard stock solution 2*

Sensitivity solution: 0.14 µg/mL of USP Clemastine Fumarate RS in *Solution A* from *Standard stock solution 1*

Standard solution: 2.8 µg/mL of USP Clemastine Fumarate RS in *Solution A* from *Standard stock solution 1*

Sample solution: Nominally 0.28 mg/mL of clemastine fumarate from Tablets in *Solution A* prepared as follows. Transfer a quantity of NLT 20 finely powdered Tablets, equivalent to 14 mg of clemastine fumarate, to a 50-mL volumetric flask. Add 25 mL of *Solution A*, shake the flask for NLT 30 min, and sonicate for NLT 15 min. Dilute with *Solution A* to volume. Pass an aliquot through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of filtrate.

Diluted sample solution: Nominally 2.8 µg/mL of clemastine fumarate in *Solution A* from *Sample solution*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification* test *B*, use a diode array detector in the range of 200–300 nm.

Column: 4.6-mm × 5-cm; 1.8-µm packing L7

Flow rate: 1.2 mL/min

Injection volume: 50 µL

System suitability

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

[NOTE—The relative retention times for clemastine and 4-chlorobenzophenone are 1.0 and 1.7, respectively.]

Suitability requirements

Resolution: NLT 1.5 between clemastine and 4-chlorobenzophenone, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution*, *Diluted sample solution*, and *Sample solution*

[NOTE—The *Diluted sample solution* is used for *Identification* test *B*.]

Calculate the percentage of any individual unspecified degradation product in the portion of Tablets taken:

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

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

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

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

C_U = nominal concentration of clemastine fumarate in the *Sample solution* (mg/mL)

Acceptance criteria

Any unspecified degradation product: NMT 0.5%

Total impurities: NMT 2.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP 4-Chlorobenzophenone RS

4-Chlorobenzophenone.

$C_{13}H_9ClO$ 216.66

USP Clemastine Fumarate RS

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

Topic/Question	Contact	Expert Committee
CLEMASTINE FUMARATE TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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