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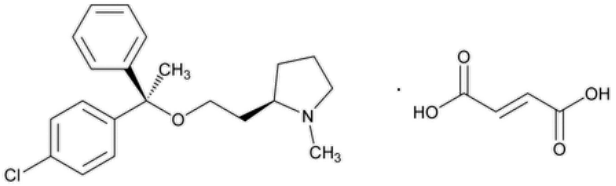
Clemastine Fumarate



$C_{21}H_{26}ClNO \cdot C_4H_4O_4$ 459.96

Pyrrolidine, 2-[2-[1-(4-chlorophenyl)-1-phenylethoxy]ethyl]-1-methyl-, [*R*-(*R**,*R**)]-, (*E*)-2-butenedioate (1:1);

(+)-(2*R*)-2-[2-[[[(*R*)-*p*-Chloro-α-methyl-α-phenylbenzyl]-oxy]ethyl]-1-methylpyrrolidine fumarate (1:1) CAS RN®: 14976-57-9; UNII: 19259EGQ3D.

DEFINITION

Clemastine Fumarate contains NLT 98.0% and NMT 102.0% of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)

• **B.** The retention times of the fumarate and clemastine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

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

Mobile phase: Methanol, acetonitrile, and *Buffer* (35:35:30)

Standard solution: 0.28 mg/mL of USP Clemastine Fumarate RS in *Mobile phase*

Sample solution: 0.28 mg/mL of Clemastine Fumarate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Flow rate: 1.2 mL/min

Injection volume: 5 µL

Run time: 3 min

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.8 for clemastine

Relative standard deviation: NMT 0.73% for clemastine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clemastine fumarate ($C_{21}H_{26}ClNO \cdot C_4H_4O_4$) in the portion of Clemastine Fumarate taken:

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

r_U = peak response of clemastine 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 = concentration of Clemastine Fumarate in the *Sample solution* (mg/mL)

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

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*. Sonication may be needed to aid dissolution.

Standard stock solution 2: 0.14 mg/mL of USP 4-Chlorobenzophenone RS in methanol. Sonication may be needed to aid dissolution.

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

Standard solution: 0.28 µg/mL of USP Clemastine Fumarate RS and 0.36 µg/mL of USP 4-Chlorobenzophenone RS in *Solution A* from *Standard stock solution 1* and *Standard stock solution 2*, respectively

Sample solution: 0.28 mg/mL of Clemastine Fumarate in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 220 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: *Sensitivity solution* and *Standard solution*

Suitability requirements

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

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

Signal-to-noise ratio: NLT 50 for clemastine, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 4-chlorobenzophenone in the portion of Clemastine Fumarate taken:

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

r_U = peak response of 4-chlorobenzophenone from the *Sample solution*

r_S = peak response of 4-chlorobenzophenone from the *Standard solution*

C_S = concentration of USP 4-Chlorobenzophenone RS in the *Standard solution* (µg/mL)

C_U = concentration of Clemastine Fumarate in the *Sample solution* (µg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Clemastine Fumarate taken:

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

r_U = peak response of each individual unspecified impurity 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 = concentration of Clemastine Fumarate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard peaks having areas less than 0.05% of clemastine.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fumaric acid[a]	0.5	—
Clemastine	1.0	—
4-Chlorobenzophenone	1.7	0.15
Any individual unspecified impurity	—	0.10
Total impurities	—	1.0

[a] Salt counter ion is included in this table for identification purposes only.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩
  Sample solution: 10 mg/mL in methanol
  Acceptance criteria: +15.0° to +18.0° (*T* = 20°)
- **pH** ⟨791⟩
  Sample solution: 100 mg/mL suspension
  Acceptance criteria: 3.2–4.2
- **Loss on Drying** ⟨731⟩
  Analysis: Dry at 105° to constant weight.
  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers at a temperature not exceeding 25°.
- **USP Reference Standards** ⟨11⟩

USP 4-Chlorobenzophenone RS

4-Chlorobenzophenone.
$C_{13}H_9ClO$ 216.66

USP Clemastine Fumarate RS

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

Chromatographic Database Information: Chromatographic Database

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