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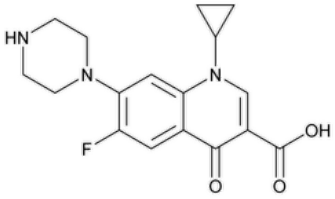
Ciprofloxacin



$C_{17}H_{18}FN_3O_3$ 331.34

3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-;

1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid CAS RN®: 85721-33-1; UNII: 5E8K9I0O4U.

DEFINITION

Ciprofloxacin contains NLT 98.0% and NMT 102.0% of ciprofloxacin ($C_{17}H_{18}FN_3O_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 0.025 M phosphoric acid. Adjust with triethylamine to a pH of 3.0 ± 0.1.

Mobile phase: Acetonitrile and *Buffer* (13:87)

Standard solution: 0.5 mg/mL of USP Ciprofloxacin RS prepared as follows. Transfer 12.5 mg of USP Ciprofloxacin RS to a 25-mL volumetric flask. Add 0.1 mL of 7% phosphoric acid, and dilute with *Mobile phase* to volume.

System suitability stock solution: 0.025 mg/mL of USP Ciprofloxacin Ethylenediamine Analog RS in *Mobile phase*

System suitability solution: Transfer 1.0 mL of the *System suitability stock solution* to a 10-mL volumetric flask, and dilute with *Standard solution* to volume.

Sample solution: Transfer 25 mg of Ciprofloxacin to a 50-mL volumetric flask. Add 0.2 mL of 7% phosphoric acid, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 30 ± 1°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for ciprofloxacin ethylenediamine analog and ciprofloxacin are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6 between ciprofloxacin ethylenediamine analog and ciprofloxacin, *System suitability solution*

Tailing factor: NMT 2.5, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ciprofloxacin ($C_{17}H_{18}FN_3O_3$) in the portion of Ciprofloxacin taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

C_U = concentration of Ciprofloxacin in the *Sample solution* (mg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%, except that where it is intended for use in preparing Ciprofloxacin for Oral Suspension, it is NMT 0.2%.
- **Organic Impurities**

Buffer: Dilute 3.4 mL of phosphoric acid with water to 2000 mL. Adjust with triethylamine to a pH of 3.0 ± 0.1.

Solution A: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Buffer (%)	Solution A (%)
0	87	13
10	87	13
11	50	50
16	50	50
16.1	87	13
20	87	13

Diluent: *Solution A* and *Buffer* (13:87)

System suitability solution: 7.5 µg/mL each of USP Ciprofloxacin Ethylenediamine Analog RS and USP Ciprofloxacin RS in *Diluent*

Standard stock solution: 0.1 mg/mL each of USP Fluoroquinolonic Acid RS and USP Ciprofloxacin RS prepared as follows. Add suitable amounts of USP Fluoroquinolonic Acid RS and USP Ciprofloxacin RS to a suitable volumetric flask. Add 0.1% of the flask volume of 6 M ammonium hydroxide and dilute with water to volume.

Standard solution: 0.7 µg/mL each of USP Fluoroquinolonic Acid RS and USP Ciprofloxacin RS from *Standard stock solution* in *Diluent*

Sample solution: 0.35 mg/mL of Ciprofloxacin prepared as follows. Transfer 35 mg of Ciprofloxacin to a 100-mL volumetric flask, add 0.2 mL of 7% phosphoric acid, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 263 and 278 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 30 µL

System suitability

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

[Note—The relative retention times for ciprofloxacin ethylenediamine analog and ciprofloxacin are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6.0 between ciprofloxacin ethylenediamine analog and ciprofloxacin at 278 nm, *System suitability solution*

Tailing factor: NMT 2.0 for the ciprofloxacin peak at 278 nm, *Standard solution*

Relative standard deviation: NMT 5.0% for ciprofloxacin at 278 nm; NMT 5.0% for fluoroquinolonic acid at 263 nm, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluoroquinolonic acid in the portion of Ciprofloxacin taken:

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

r_U = peak response of fluoroquinolonic acid at 263 nm from the *Sample solution*

r_S = peak response of fluoroquinolonic acid at 263 nm from the *Standard solution*

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

C_U = concentration of Ciprofloxacin in the *Sample solution* (mg/mL)

Calculate the percentage of the ciprofloxacin ethylenediamine analog and any individual unspecified impurity in the portion of Ciprofloxacin taken:

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

r_U = peak response of each impurity at 278 nm from the *Sample solution*

r_S = peak response of ciprofloxacin at 278 nm from the *Standard solution*

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

C_U = concentration of Ciprofloxacin in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Wavelength (nm)	Acceptance Criteria, NMT (%)
Ciprofloxacin ethylenediamine analog	0.70	278	0.2
Ciprofloxacin	1.00	278	—
Fluoroquinolonic acid	1.89	263	0.2
Any individual unspecified impurity	—	278	0.2
Total impurities[a]	—	—	0.5

[a] Total impurities does not include the fluoroquinolonic acid impurity.

SPECIFIC TESTS

• **Clarity of Solution**

Sample solution: Dissolve 0.25 g in 10 mL of 0.1 N hydrochloric acid.

Acceptance criteria: A clear to slightly opalescent solution is obtained.

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** Where it is intended for use in preparing Ciprofloxacin for Oral Suspension, the total microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g. It also meets the requirements for absence of *Salmonella* species and *Escherichia coli*.

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 120° for 6 h.

Acceptance criteria: NMT 1.0%, except that where it is labeled as intended for use in preparing Ciprofloxacin for Oral Suspension, 10%–20%

• **Sterility Tests ⟨71⟩**, *Test for Sterility of the Product to Be Examined, Membrane Filtration***:** Where the label states that it is sterile, it meets the requirements.

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that it is sterile or where the label states that Ciprofloxacin must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.50 USP Endotoxin Units/mg of ciprofloxacin.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°, and avoid excessive heat.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms. Where it is intended for use in preparing Ciprofloxacin for Oral Suspension, it is so labeled.

• **USP Reference Standards ⟨11⟩**

USP Ciprofloxacin RS

USP Ciprofloxacin Ethylenediamine Analog RS

1-Cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-[(2-aminoethyl)amino]-3-quinolinecarboxylic acid hydrochloride.

$C_{15}H_{16}FN_3O_3 \cdot HCl$ 341.77

USP Fluoroquinolonic Acid RS

7-Chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

$C_{13}H_9ClFNO_3$ 281.67

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

Topic/Question	Contact	Expert Committee
CIPROFLOXACIN	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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