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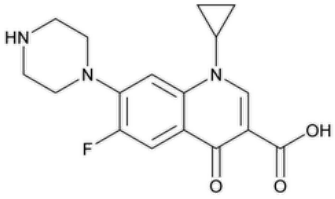
Ciprofloxacin Hydrochloride



• HCl • $x\ H_2O$

$C_{17}H_{18}FN_3O_3 \cdot HCl \cdot xH_2O$

Sesquihydrate 394.83
Monohydrate 385.82
Anhydrous 367.81

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

Monohydrate CAS RN®: 86393-32-0; UNII: 4BA73M5E37.

DEFINITION

Ciprofloxacin Hydrochloride contains NLT 98.0% and NMT 102.0% of ciprofloxacin hydrochloride ($C_{17}H_{18}FN_3O_3 \cdot HCl$), calculated on the anhydrous basis. It contains a variable quantity of water.

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*.

• **C.** Identification Tests—General ⟨191⟩, *Chloride*

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 Hydrochloride RS in *Mobile phase*

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: 0.5 mg/mL of Ciprofloxacin Hydrochloride in *Mobile phase*

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 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 hydrochloride ($C_{17}H_{18}FN_3O_3 \cdot HCl$) in the portion of Ciprofloxacin Hydrochloride 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 Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **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 Hydrochloride RS in *Diluent*

Standard stock solution: 0.1 mg/mL each of USP Fluoroquinolonic Acid RS and USP Ciprofloxacin Hydrochloride RS prepared as follows. Add suitable amounts of USP Fluoroquinolonic Acid RS and USP Ciprofloxacin Hydrochloride 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 Hydrochloride RS from *Standard stock solution* in *Diluent*

Sample solution: 0.35 mg/mL of Ciprofloxacin Hydrochloride in *Diluent*

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 Hydrochloride 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 Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of ciprofloxacin ethylenediamine analog and any individual unspecified impurity in the portion of Ciprofloxacin Hydrochloride 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 Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Ciprofloxacin Hydrochloride 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 fluoroquinolonic acid impurity.

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 25-mg/mL solution in water

  Acceptance criteria: 3.0–4.5

- **Water Determination** ⟨921⟩, *Method I*: 4.7%–6.7%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°.
- **USP Reference Standards** ⟨11⟩

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 Ciprofloxacin Hydrochloride RS

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 HYDROCHLORIDE	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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