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Ciprofloxacin for Oral Suspension

DEFINITION

Ciprofloxacin for Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$).

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 major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: Dissolve 13.6 g of sodium acetate in 1000 mL of water and add 1 mL of triethylamine. Adjust with phosphoric acid to a pH of 2.0.

Mobile phase: Methanol and *Solution A* (20:80)

Diluent: 0.1 N hydrochloric acid

Standard stock solution: 1.0 mg/mL of USP Ciprofloxacin RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Ciprofloxacin RS from the *Standard stock solution* in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of ciprofloxacin prepared as follows. Constitute Ciprofloxacin for Oral Suspension as directed in the labeling. Transfer the entire contents to a tube, and centrifuge. Remove the oil from the centrifuge tube and transfer the contents to a 1000-mL volumetric flask. Add 500 mL of *Diluent*, and sonicate for 15 min with constant shaking. Cool to room temperature, add 50 mL of methanol to dissolve the foam, and dilute with *Diluent* to volume. Centrifuge and discard the oil. Transfer an appropriate quantity of the supernatant to a suitable volumetric flask and dilute with *Mobile phase* to volume. Pass through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm. For *Identification B*, use a diode-array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 10°

Column: 40°

Flow rate: 1.2 mL/min

Injection volume: 5 µL

Run time: 1.6 times the retention time of ciprofloxacin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of ciprofloxacin from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 6.8 g/L of sodium acetate in water. Adjust with glacial acetic acid to a pH of 4.5. Add 0.25 g/L of polyoxyethylene (23) lauryl ether and shake well to dissolve; 900 mL.

Apparatus 2: 100 rpm

Time: 30 min

Buffer: Dissolve 13.6 g of sodium acetate in 1000 mL of water and add 1 mL of triethylamine. Adjust with phosphoric acid to a pH of 4.0.

Mobile phase: Methanol and *Buffer* (30:70)

Standard solution: 0.055 mg/mL of USP Ciprofloxacin RS in *Medium*. Sonication may be used to promote dissolution.

Sample solution: Nominally 0.055 mg/mL of ciprofloxacin prepared as follows. Constitute Ciprofloxacin for Oral Suspension as directed in the labeling. Determine the density, *d* (g/mL), of Ciprofloxacin for Oral Suspension using appropriate means. Using a 5-mL syringe, collect approximately 5 mL of constituted Ciprofloxacin for Oral Suspension, and record the weight. With the paddles lowered, gently empty the contents of each syringe into the bottom of each vessel containing *Medium*. Start rotating the paddles. Reweigh each syringe, and determine the weight (g) of Ciprofloxacin for Oral Suspension delivered into each vessel. At the end of 30 min, remove 10 mL of the solution under test from each vessel, and pass through a suitable filter of 0.2-µm pore size. Transfer the appropriate quantity of filtrate to a suitable volumetric flask, and dilute with *Medium* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

Run time: 1.7 times the retention time of ciprofloxacin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (d/W_U) \times D \times (1/L) \times 100$$

r_U = peak response of ciprofloxacin from the *Sample solution*

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

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

V = volume of *Medium*, 900 mL

d = density of constituted Ciprofloxacin for Oral Suspension (g/mL)

W_U = weight of the portion of constituted Ciprofloxacin for Oral Suspension added to the *Medium* (g)

D = dilution factor for the *Sample solution*, if needed

L = label claim for ciprofloxacin (mg/mL)

Tolerances: NLT 85% (*Q*) of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus 2, Time, Buffer, Mobile phase, Standard solution, Sample solution, Chromatographic system, and **Analysis:** Proceed as directed in *Test 1*.

Tolerances: NLT 80% (*Q*) of the labeled amount of ciprofloxacin ($C_{17}H_{18}FN_3O_3$) is dissolved.

• **Deliverable Volume** ⟨698⟩

For multiple-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

• **Organic Impurities**

Solution A and **Mobile phase:** Prepare as directed in the *Assay*.

Diluent: Methanol and 0.1 N hydrochloric acid (70:30)

Standard solution: 0.005 mg/mL of USP Ciprofloxacin RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of ciprofloxacin prepared as follows. Constitute Ciprofloxacin for Oral Suspension as directed in the labeling. Transfer a sufficient quantity of constituted Ciprofloxacin for Oral Suspension to an appropriate volumetric flask. Add *Diluent* to fill about 60% of the flask volume, sonicate for 10 min, and dilute with *Diluent* to volume. Centrifuge and pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

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

Temperatures

Autosampler: 10°

Column: 40°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

Run time: 70 min

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Ciprofloxacin for Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any impurity peaks less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ciprofloxacin ethylenediamine analog[a]	0.75	1.3	0.3
Ciprofloxacin	1.0	—	—
7-Chloro-6-piperazinyl analog[b]	1.15	0.47	0.20
Chlorocipro floxacin[c]	2.20	0.61	0.20
Individual unspecified impurity	—	1.0	0.2
Total impurities	—	—	1.0

[a] 7-(2-Aminoethylamino)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.

[b] 7-Chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

[c] 6-Chloro-1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/mL. The total yeasts and molds count does not exceed 10^2 cfu/mL. It meets the requirements of the test for absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

• **USP Reference Standards ⟨11⟩**

USP Ciprofloxacin RS

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

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

Chromatographic Database Information: Chromatographic Database

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