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Levofloxacin Tablets

DEFINITION
Levofloxacin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$).

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*.

Add the following:

▲• **B.** The UV absorption spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Diluent: Acetonitrile and water (20:80)

Mobile phase: Transfer 874 mg of cupric sulfate, 918 mg of L-isoleucine, and 5.94 g of ammonium acetate to a suitable container. Add 700 mL of water, and mix until dissolved. Add 300 mL of methanol.

Standard stock solution: 2 mg/mL of USP Levofloxacin RS in *Diluent*. ▲Sonicate, if necessary, to dissolve prior to final dilution.▲ (USP 1-May-2021)

Standard solution: 0.2 mg/mL of USP Levofloxacin RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: Nominally 5 mg/mL of levofloxacin prepared as follows. Transfer intact Tablets (NLT 5) to a volumetric flask, add 75% of the final volume of *Diluent*, and allow to stand for 15 min. Shake for 30 min, and dilute with *Diluent* to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 1–2 mL of the filtrate.

Sample solution: Nominally 0.2 mg/mL of levofloxacin in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 360 nm. ▲For *Identification B*, use a diode array detector in the range of 220–400 nm.▲ (USP 1-May-2021)

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

Column temperature: 45°

Flow rate: 0.8 mL/min

Injection volume: 25 µL

Run time: 2 times the retention time of levofloxacin

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.8

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: 0.56 mg/mL of USP Levofloxacin RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 294 nm

Cell length: 0.1 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) is dissolved.

Test 2

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: L/900 mg/mL of USP Levofloxacin RS in *Medium*. Mix to obtain solutions with known concentrations as indicated in *Table 1*, where L is the label claim in mg/Tablet.

Sample solution: Pass a portion of the solution under test having a concentration similar to that of the *Standard solution* through a suitable filter of 0.45-µm pore size.

Table 1

Tablet Label Claim (mg)	Final Concentration (mg/mL)
250	0.27
500	0.55
750	0.83

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 293 nm

Cell length: 0.1 mm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) is dissolved.

Test 3

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: L/900 mg/mL of USP Levofloxacin RS in *Medium*. Mix to obtain solutions with known concentrations as indicated in *Table 1*, where L is the label claim in mg/Tablet.

Sample solution: Pass a portion of the solution under test having the same concentration as that of the *Standard solution* through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 326 nm

Cell length: 1 mm for a 250-mg Tablet, 0.5 mm for a 500-mg Tablet, and 0.2 mm for a 750-mg Tablet

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) is dissolved.

Test 4

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: 16 µg/mL of USP Levofloxacin RS in *Medium*

Sample solution: Pass a portion of the solution under test having the same concentration as that of the *Standard solution* through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 332 nm

Cell length: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Diluent, Mobile phase, Standard stock solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Standard solution A:** 0.2 mg/mL of USP Levofloxacin RS in *Mobile phase* from the *Standard stock solution*

Standard solution B: 0.001 mg/mL of USP Levofloxacin Related Compound A RS in *Mobile phase*▲ (USP 1-May-2021)

System suitability

Sample: ▲*Standard solution A*▲ (USP 1-May-2021)

Suitability requirements

Tailing factor: NMT 1.8 ▲▲ (USP 1-May-2021)

Relative standard deviation: NMT 2.0% ▲▲ (USP 1-May-2021)

Analysis

Samples: *Sample solution,* ▲*Standard solution A*, and *Standard solution B*▲ (USP 1-May-2021)

Calculate the percentage of levofloxacin related compound A in the portion of Tablets taken:

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

r_U = peak response of levofloxacin related compound A from the *Sample solution*

r_S = peak response of levofloxacin related compound A from ▲*Standard solution B*▲ (USP 1-May-2021)

C_S = concentration of USP Levofloxacin Related Compound A RS in ▲*Standard solution B*▲ (USP 1-May-2021) (mg/mL)

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

Calculate the percentage of any other impurities in the portion of Tablets taken:

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

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

r_S = peak response of levofloxacin from ▲*Standard solution A*▲ (USP 1-May-2021)

C_S = concentration of USP Levofloxacin RS in ▲*Standard solution A*▲ (USP 1-May-2021) (mg/mL)

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Decarboxy levofloxacin[a]	0.38	0.60	0.3
Levofloxacin related compound A[b]	0.47	—	0.7

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Diamine derivative[c]	0.52	0.83	0.3
Levofloxacin *N*-oxide[d]	0.63	▲1.0▲ (USP 1-May-2021)	0.7
9-Desfluoro levofloxacin[e,f]	0.73	—	—
Levofloxacin	1.00	—	—
Dextrofloxacin ▲(D-isomer)▲ (USP 1-May-2021) [g,f]	1.23	—	—
Levofloxacin 9-piperazino isomer[h,f]	1.69	—	—
Any unspecified impurity	—	1.0	0.2
Total impurities	—	—	1

[a] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine.

[b] (*S*)-9-Fluoro-3-methyl-10-(piperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[c] (*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[d] (*S*)-4-(6-Carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7*H*-pyrido-[1,2,3-*de*][1,4]benzoxazine-10-yl)-1-methylpiperazine 1-oxide.

[e] (*S*)-2,3-Dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[f] Process impurity, for information only.

[g] (*R*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

[h] (*S*)-10-fluoro-3-methyl-9-(4-methylpiperazin-1-yl)-7-oxo-3,7-dihydro-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight 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 Levofloxacin RS

USP Levofloxacin Related Compound A RS

(*S*)-9-Fluoro-3-methyl-10-(piperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-pyrido[1,2,3-*de*][1,4]benzoxazine-6-carboxylic acid.

$C_{17}H_{18}FN_3O_4$ 347.34

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

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

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