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Fluoxetine Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-fluoxetine-caps-20230224.

DEFINITION

Fluoxetine Capsules contain an amount of Fluoxetine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

Sample: Nominally 10 mg of fluoxetine from Capsules prepared as follows. Transfer a portion of Capsule contents, equivalent to 10 mg of fluoxetine, to a suitable container. Dissolve in 10 mL of methanol and pass through a suitable filter. Rinse the container and filter with 5 mL of methanol, and evaporate with the aid of a current of air and mild heat to dryness.

Acceptance criteria: Meet the requirements

ASSAY

• **Procedure**

Buffer: Triethylamine and water (1:98), adjusted with phosphoric acid to a pH of 6.0

Mobile phase: Stabilizer-free tetrahydrofuran, methanol, and *Buffer* (30:10:60)

Standard solution: 0.11 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of fluoxetine from Capsules prepared as follows. Remove, as completely as possible, the contents of NLT 20 Capsules and mix. Transfer a suitable portion of the contents to an appropriate volumetric flask and dissolve in *Mobile phase*. Dilute with *Mobile phase* to volume. Pass the resulting solution through a suitable filter, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 25-cm; 5-µm base-deactivated packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

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 fluoxetine ($C_{17}H_{18}F_3NO$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Fluoxetine Hydrochloride RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of fluoxetine in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of fluoxetine, 309.33

M_{r2} = molecular weight of fluoxetine hydrochloride, 345.79

Acceptance criteria: 90.0%–110.0%

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PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

▲**Test 1**▲ (RB 1-Mar-2023)

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: Transfer 250 mL of acetonitrile to a suitable container, add 1.0 mL of diethylamine, mix, and adjust with phosphoric acid to a pH of 3.5. [Note—Diethylamine phosphate will precipitate; therefore, keep it well-mixed.]

Mobile phase: Acetonitrile, diethylamine, and water (400:4:600), adjusted with phosphoric acid to a pH of 3.5

Standard stock solution: USP Fluoxetine Hydrochloride RS having a concentration similar to that of the *Sample stock solution* passed through a suitable filter. Use the filtrate.

Standard solution: Transfer 5.0 mL of *Standard stock solution* to a suitable container, add 2.0 mL of *Solution A*, and mix.

Sample stock solution: Pass 20 mL of the solution under test through a suitable filter. Use the filtrate.

Sample solution: Transfer 5.0 mL of *Sample stock solution* to a suitable container, add 2.0 mL of *Solution A*, and mix.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; packing L10

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

M_{r1} = molecular weight of fluoxetine, 309.33

M_{r2} = molecular weight of fluoxetine hydrochloride, 345.79

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$) is dissolved.

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

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm, with sinkers

Time: 30 min

Solution A: Transfer 250 mL of acetonitrile to a suitable container, add 1.0 mL of diethylamine, mix, and adjust with phosphoric acid to a pH of 3.5. [Note—Diethylamine phosphate will precipitate; therefore, keep it well-mixed.]

Mobile phase: Acetonitrile and water (40:60). Add 4 mL of diethylamine to each liter of the solution. Adjust with phosphoric acid to a pH of 3.5.

Standard stock solution: 0.027 mg/mL of USP Fluoxetine Hydrochloride RS prepared as follows. Transfer 27 mg of USP Fluoxetine Hydrochloride RS to a 50-mL volumetric flask, add 30 mL of *Mobile phase*, and sonicate for NLT 5 min. Cool and dilute with methanol to volume. Transfer 5 mL of the solution to a 100-mL volumetric flask and dilute with *Medium* to volume. Pass the solution through a suitable filter of 0.45-µm pore size, discard NLT 3 mL, and use the filtrate.

Standard solution: Transfer 5.0 mL of *Standard stock solution* to a suitable container, add 2.0 mL of *Solution A*, and mix.

Sample stock solution: Withdraw and pass 10 mL of the solution under test through a suitable filter, discarding NLT 3 mL. Dilute the filtrate with *Medium* to a concentration similar to that of the *Standard stock solution*, if necessary.

Sample solution: Transfer 5.0 mL of *Sample stock solution* to a suitable container, add 2.0 mL of *Solution A*, and mix.

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Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 2 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of fluoxetine

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times D \times (1/L) \times 100$$

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

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

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

M_{r1} = molecular weight of fluoxetine, 309.33

M_{r2} = molecular weight of fluoxetine hydrochloride, 345.79

V = volume of *Medium*, 500 mL

D = dilution factor for the *Sample stock solution*

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of fluoxetine ($C_{17}H_{18}F_3NO$) is dissolved. ▲(RB 1-Mar-2023)

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

IMPURITIES

• **Organic Impurities**

Buffer: Triethylamine and water (1:98), adjusted with phosphoric acid to a pH of 6.0

Mobile phase: Acetonitrile and *Buffer* (35:65)

System suitability solution: 0.01 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 2 mg/mL of fluoxetine from Capsules prepared as follows. Remove, as completely as possible, the contents of NLT 20 Capsules and mix. Transfer a suitable portion of the contents to an appropriate volumetric flask and dissolve in *Mobile phase*. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 22 min

System suitability

Sample: *System suitability solution*

Suitability requirements

Column efficiency: NLT 1100 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules taken:

$$\text{Result} = (r_i/r_T) \times 100$$

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

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r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria

Any individual impurity: NMT 0.25%

Total impurities: NMT 0.80%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Mar-2023)

• **USP Reference Standards** ⟨11⟩

USP Fluoxetine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
FLUOXETINE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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