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Fluoxetine Tablets

DEFINITION

Fluoxetine Tablets 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

Change to read:

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

Sample: Transfer 1 Tablet to a suitable container, dissolve in 10 mL of chloroform, and pass through a suitable filter. Rinse the container with 5 mL of chloroform, and pass the rinsings through a suitable filter. Evaporate the combined filtrate in a hood with the aid of a current of air and mild heat to dryness.

Acceptance criteria: Meet the requirements

• **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**

Solution A: 7.1 g/L of sodium 1-pentane-sulfonate in water. To each L add 2.9 mL of glacial acetic acid, and adjust with 5 N sodium hydroxide solution to a pH of 5.0.

Mobile phase: Methanol and *Solution A* (67:33)

System suitability stock solution: 0.2 mg/mL of 4-trifluoromethylphenol in *Mobile phase*

System suitability solution: 0.02 mg/mL of 4-trifluoromethylphenol from *System suitability stock solution* and 0.11 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Standard solution: 0.1 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sample stock solution: Transfer 10 Tablets to a 1000-mL volumetric flask. Add 500 mL of *Mobile phase*, and shake to disintegrate the Tablets. Dilute with *Mobile phase* to volume, and sonicate for 10 min.

Sample solution: Nominally 0.1 mg/mL of fluoxetine from *Sample stock solution* in *Mobile phase*. Pass through a suitable filter. Use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L7

Column temperature: 38°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 4.0 between fluoxetine and 4-trifluoromethylphenol

Tailing factor: NMT 1.7 for fluoxetine

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 Tablets 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* (mg/mL)

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

M_{r1} = molecular weight of fluoxetine, 309.33

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 1000 mL

Apparatus 1: 100 rpm

Time: 15 min

Solution A, Mobile phase, and **System suitability solution:** Prepare as directed in the *Assay*.

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

Standard solution: USP Fluoxetine Hydrochloride RS in *Medium* having a known concentration similar to that of the *Sample solution*

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm packing L7

Column temperature: 38°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.0 between fluoxetine and 4-trifluoromethylphenol

Tailing factor: NMT 1.7 for fluoxetine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Sample solution* and *Standard solution*

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

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

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* (mg/mL)

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

M_{r1} = molecular weight of fluoxetine, 309.33

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

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

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

IMPURITIES

• **Organic Impurities**

Solution A: 6.5 g/L of sodium 1-octanesulfonate in water. To each L add 2.9 mL of phosphoric acid, and adjust with 5 N sodium hydroxide solution to a pH of 3.0.

Mobile phase: Acetonitrile and *Solution A* (43:57)

Impurity identification solution: Nominally 2.2 mg/mL of fluoxetine hydrochloride from USP Fluoxetine Hydrochloride RS prepared as follows. Transfer 22 mg of USP Fluoxetine Hydrochloride RS to a 10-mL volumetric flask and dilute with 1 N sulfuric acid to volume. Heat the flask to 85° for 3 h, and allow to cool to room temperature. [Note—The resulting solution contains aminomethyl-1-phenylpropanol, which is also known as 3-methylamino-1-phenylpropan-1-ol or α-[2-(methylamino)ethyl]benzenemethanol.]

System suitability solution: 0.001 mg/mL of USP Fluoxetine Related Compound B RS and 0.015 mg/mL of USP Fluoxetine Hydrochloride RS prepared as follows. Transfer suitable quantities of USP Fluoxetine Related Compound B RS and USP Fluoxetine Hydrochloride RS to a 10-mL volumetric flask. Add 0.2 mL of *Impurity identification solution* and dilute with *Mobile phase* to volume.

Standard solution: 0.015 mg/mL of USP Fluoxetine Hydrochloride RS in *Mobile phase*

Sensitivity solution: 0.2 µg/mL of USP Fluoxetine Hydrochloride RS from *Standard solution* in *Mobile phase*

Sample solution: 2 mg/mL of fluoxetine from Tablets prepared as follows. Transfer 10 Tablets to a suitable volumetric flask and add 50% of the final flask volume of *Mobile phase*. Shake to disintegrate and dilute with *Mobile phase* to volume. Sonicate the resulting solution for 10 min, pass a portion through a suitable filter, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of fluoxetine

System suitability

Samples: *Mobile phase*, *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Injection order: *Mobile phase*, *Sensitivity solution*, *System suitability solution*, and *Standard solution*

[NOTE—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 4.5 between aminomethyl-1-phenylpropanol and fluoxetine related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of each impurity 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)

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

M_{r1} = molecular weight of fluoxetine, 309.33

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Aminomethyl-1-phenylpropanol[a]	0.19	0.25
Fluoxetine related compound B	0.26	0.25
Fluoxetine	1.0	—
Any individual unspecified impurity	—	0.25
Total impurities	—	0.80

[a] 3-Methylamino-1-phenylpropan-1-ol; also known as α-[2-(Methylamino)ethyl]benzenemethanol.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Fluoxetine Hydrochloride RS

USP Fluoxetine Related Compound B RS

N-Methyl-3-phenylpropan-1-amine;
also known as *N*-Methyl-3-phenylpropylamine.

$C_{10}H_{15}N$	149.24

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

Topic/Question	Contact	Expert Committee
FLUOXETINE TABLETS	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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