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Escitalopram Tablets

DEFINITION

Escitalopram Tablets contain an amount of Escitalopram Oxalate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of escitalopram ($C_{20}H_{21}FN_2O$).

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

Change to read:

- **Procedure**

Buffer: 1.5 g of anhydrous sodium acetate and 0.4 mL of glacial acetic acid in 1 L of water. Adjust with 1 N sodium hydroxide▲ (ERR 1-May-2023) to a pH of 5.2.

Mobile phase: Methanol, acetonitrile, and *Buffer* (33:7:60)

System suitability solution: 6.4 µg/mL of USP Escitalopram Oxalate RS (equivalent to 5 µg/mL of escitalopram) and 1 µg/mL of USP Citalopram Related Compound C RS in *Mobile phase*

Standard solution: 510 µg/mL of USP Escitalopram Oxalate RS (equivalent to 400 µg/mL of escitalopram) in *Mobile phase*

Sample solution: Nominally 400 µg/mL of escitalopram from Tablets prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask, add *Buffer* to 10% of the total volume, and shake vigorously for 10 min. Add methanol to 50% of the total volume, shake for 1 additional min, sonicate for 10 min, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 239 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 10-cm; 3-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of escitalopram

System suitability

Samples: *System suitability solution* and *Standard solution*

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

Suitability requirements

Resolution: NLT 3.0 between escitalopram and citalopram related compound C, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of escitalopram ($C_{20}H_{21}FN_2O$) 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 Escitalopram Oxalate RS in the *Standard solution* (µg/mL)

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

M_{r1} = molecular weight of escitalopram, 324.39

M_{r2} = molecular weight of escitalopram oxalate, 414.43

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

[Note—USP Citalopram Hydrobromide RS is used as a quantitative standard with an appropriate molecular weight correction. Escitalopram is an optical isomer of citalopram.]

Medium: 0.1 N hydrochloric acid▲ (ERR 1-May-2023) ; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution 1: 3 µg/mL of USP Citalopram Hydrobromide RS (equivalent to 2.4 µg/mL of citalopram) in *Medium*

Standard solution 2: 15 µg/mL of USP Citalopram Hydrobromide RS (equivalent to 12 µg/mL of citalopram) in *Medium*

Standard solution 3: 30 µg/mL of USP Citalopram Hydrobromide RS (equivalent to 24 µg/mL of citalopram) 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-Vis

Analytical wavelength: 239 nm

Cell: 0.5 cm

Blank: *Medium*

System suitability

Samples: *Standard solution 1*, *Standard solution 2*, and *Standard solution 3*

Suitability requirements

Correlation coefficient: NLT 0.995, determined using *Standard solution 1*, *Standard solution 2*, and *Standard solution 3*, three replicates of each solution

Relative standard deviation: NMT 2.0%, determined using *Standard solution 3*, six replicates

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, *Standard solution 3*, and *Sample solution*

Calculate the concentration, in µg/mL, of citalopram for each *Standard solution* (*i*):

$$\text{Result}_i = C_{Si} \times (M_{r1}/M_{r2})$$

C_{Si} = concentration of USP Citalopram Hydrobromide RS in the *Standard solution* (*i*) (µg/mL)

M_{r1} = molecular weight of citalopram, 324.39

M_{r2} = molecular weight of citalopram hydrobromide, 405.30

Plot the absorbances of *Standard solution 1*, *Standard solution 2*, and *Standard solution 3* versus the corresponding citalopram concentrations.

Determine the concentration, C_U, in µg/mL, of escitalopram in the *Sample solution* using the calibration curve.

Calculate the percentage of the labeled amount of escitalopram ($C_{20}H_{21}FN_2O$) dissolved:

$$\text{Result} = C_U \times V \times (1/L) \times F \times 100$$

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

F = conversion factor, 0.001 mg/µg

Tolerances: NLT 80% (*Q*) of the labeled amount of escitalopram ($C_{20}H_{21}FN_2O$) 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▲ (ERR 1-May-2023) ; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Buffer: 3.4 g/L of monobasic potassium phosphate in water. To each 1 L of the mixture, add 1.0 mL of *triethylamine*, and adjust with 1.5 M phosphoric acid TS to a pH of 3.8.

Mobile phase: Acetonitrile, methanol, and *Buffer* (28:5:67)

Standard solution: (*L*/900) mg/mL of escitalopram from USP Escitalopram Oxalate RS in *Medium*, where *L* is the label claim of escitalopram

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

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 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 escitalopram ($C_{20}H_{21}FN_2O$) 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 of escitalopram from the *Sample solution*

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

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

M_{r1} = molecular weight of escitalopram, 324.39

M_{r2} = molecular weight of escitalopram oxalate, 414.43

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of escitalopram is dissolved.

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

IMPURITIES

- **Organic Impurities**

Buffer, Mobile phase, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1.0 µg/mL of USP Escitalopram Oxalate RS (equivalent to 0.8 µg/mL of escitalopram) in *Mobile phase*

System suitability

Samples: *System suitability solution* and *Standard solution*

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

Suitability requirements

Resolution: NLT 3.0 between escitalopram and citalopram related compound C, *System suitability solution*

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

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak response of each degradation product from the *Sample solution*

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

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

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

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

M_{r1} = molecular weight of escitalopram, 324.39

M_{r2} = molecular weight of escitalopram oxalate, 414.43

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citalopram related compound A[a]	0.33	0.84	0.3
Citalopram related compound B[b]	0.56	0.78	0.5
Citalopram related compound C	0.80	0.51	0.5
Escitalopram	1.0	—	—
Citalopram related compound E[c]	1.4	0.94	0.2
Any other individual, unspecified degradation product	—	1.0	0.20
Total degradation products	—	—	2.0

[a] 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide.

[b] 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-3-hydroxy-1,3-dihydroisobenzofuran-5-carbonitrile.

[c] 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile-*N*-oxide.

ADDITIONAL REQUIREMENTS

- **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.
- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Citalopram Hydrobromide RS

USP Citalopram Related Compound C RS

3-(3-Dimethylaminopropyl)-3-(4-fluorophenyl)-6-cyano-1(3*H*)-isobenzofuranone oxalate.

$C_{20}H_{19}FN_2O_2 \cdot C_2H_2O_4$ 428.42

USP Escitalopram Oxalate RS

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

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

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