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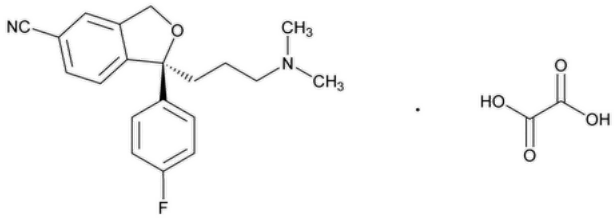
Escitalopram Oxalate



$C_{20}H_{21}FN_2O \cdot C_2H_2O_4$ 414.43

S-(+)-5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, oxalate;

S-(+)-1-[3-(Dimethylamino)propyl]-1-(*p*-fluorophenyl)-5-phthalancarbonitrile oxalate CAS RN®: 219861-08-2; UNII: 5U85DBW7LO.

DEFINITION

Escitalopram Oxalate contains NLT 98.0% and NMT 102.0% of escitalopram oxalate ($C_{20}H_{21}FN_2O \cdot C_2H_2O_4$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **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**

Buffer: 3.4 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid or sodium hydroxide solution to a pH of 3.0 before final dilution.

Solution A: Acetonitrile and *Buffer* (10:90)

Solution B: Acetonitrile and *Buffer* (65:35)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	95	5	1
35	65	35	1
45	0	100	1
45.1	0	100	2
60	0	100	2
60.1	95	5	1
68	95	5	1

[Note—The gradient was established on an HPLC system with a dwell volume of approximately 1.6 mL.]

System suitability solution: 2 µg/mL each of USP Escitalopram Oxalate RS and USP Citalopram Related Compound D RS in *Solution A*

Standard solution: 0.5 mg/mL of USP Escitalopram Oxalate RS in *Solution A*

Sample solution: 0.5 mg/mL of Escitalopram Oxalate in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 237 nm

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

Column temperature: 45°

Flow rate: See *Table 1*.

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between escitalopram and citalopram related compound D, *System suitability solution*

Tailing factor: 0.8–3, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of escitalopram oxalate ($C_{20}H_{21}FN_2O \cdot C_2H_2O_4$) in the portion of Escitalopram Oxalate taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Enantiomeric Purity**

Buffer: Dissolve 6.8 g of monobasic potassium phosphate in 250 mL of water, add 150 mL of 0.2 N sodium hydroxide, adjust with phosphoric acid or sodium hydroxide solution to a pH of 7.0, and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Buffer* (15:85)

System suitability solution: 125 µg/mL each of USP R-Citalopram Oxalate RS and USP Escitalopram Oxalate RS in *Mobile phase*

Sample solution: 125 µg/mL of Escitalopram Oxalate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 15-cm; 5-µm packing L57

Column temperature: 30°

Flow rate: 0.6 mL/min

Injection volume: 15 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.3 between *R*-citalopram and escitalopram

Tailing factor: 0.8–2.5 for escitalopram

Analysis

Sample: *Sample solution*

Calculate the percentage of *R*-citalopram oxalate in the portion of Escitalopram Oxalate taken:

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

r_U = peak response of *R*-citalopram from the *Sample solution*

r_T = sum of peak responses of *R*-citalopram and escitalopram from the *Sample solution*

Acceptance criteria: NMT 3.0%

- **Organic Impurities**

Buffer, Solution A, Solution B, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution A: 2 µg/mL each of USP Escitalopram Oxalate RS and USP Citalopram Related Compound D RS in *Solution A*

System suitability solution B: 0.5 mg/mL of USP Escitalopram Oxalate RS in *Solution A*

System suitability

Samples: *System suitability solution A* and *System suitability solution B*

Suitability requirements

Resolution: NLT 1.5 between escitalopram and citalopram related compound D, *System suitability solution A*

Tailing factor: 0.8–3, *System suitability solution B*

Relative standard deviation: NMT 2.0%, *System suitability solution B*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Escitalopram Oxalate taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

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

r_T = peak response of escitalopram from the *Sample solution*

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxalic acid[a]	0.075	—	—
5-Dimethylamino butyryl citalopram[b]	0.40	0.34	0.2
Citalopram related compound A[c]	0.50	0.79	0.1
Citalopram related compound B (3-hydroxycitalopram)[d]	0.74	1.0	0.1
Citalopram related compound C (3-oxocitalopram)[e]	0.90	0.79	0.1
Citalopram related compound D (desmethyl citalopram)	0.97	1.0	0.1
Escitalopram	1.0	—	—
Citalopram related compound E (citalopram *N*-oxide)[f]	1.1	1.0	0.1
Any other individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.5

[a] Included for identification only. This peak is due to the oxalate counterion and hence is not an impurity.

[b] 1-(3-Dimethylaminopropyl)-1-(4'-fluorophenyl)-5-(4-dimethylaminobutyryl)-1,3-dihydroisobenzofuran.

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

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

[e] 3-(3-Dimethylaminopropyl)-3-(4-fluorophenyl)-6-cyano-1(3*H*)-isobenzofuranone.

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

SPECIFIC TESTS

• **Water Determination,** *Method Ia* ⟨921⟩**:** NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP R-Citalopram Oxalate RS

(*R*)-1-[3-(Dimethylamino)propyl]-1-(*p*-fluorophenyl)-5-phthalancarbonitrile oxalate.
$C_{20}H_{21}FN_2O \cdot C_2H_2O_4$ 414.43

USP Citalopram Related Compound D RS. [Note—May be available as a hydrochloride or a hydrobromide salt.]

1-(4-Fluorophenyl)-1-(3-methylaminopropyl)-1,3-dihydroisobenzofuran-5-carbonitrile hydrochloride.
$C_{19}H_{19}FN_2O \cdot HCl$ 346.83

1-(4-Fluorophenyl)-1-(3-methylaminopropyl)-1,3-dihydroisobenzofuran-5-carbonitrile hydrobromide. $C_{19}H_{19}FN_2O \cdot HBr$ 391.28

USP Escitalopram Oxalate RS

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

Topic/Question	Contact	Expert Committee
ESCITALOPRAM OXALATE	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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