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Citalopram Tablets

DEFINITION

Citalopram Tablets contain an amount of citalopram hydrobromide equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of citalopram free base ($C_{20}H_{21}FN_2O$).

IDENTIFICATION

Change to read:

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

  Sample: Extract finely ground Tablet powder containing 200 mg of citalopram with 30 mL of water, and filter. Add 1 mL of 1 N sodium hydroxide to the filtrate, and extract with 50 mL of cyclohexane by shaking for 10 min. Pass the cyclohexane layer through a silicone-treated filter paper into a beaker. Reduce the filtrate down to 3 mL, using gentle heat as necessary. Transfer the hot solution to a small centrifuge tube. Induce crystallization while cooling by scratching the side of the test tube with a spatula. Centrifuge the mixture, and decant off the cyclohexane. Dry the residue under vacuum in a desiccator. [Note—If crystallization fails to occur in the above procedure, use the following alternative procedure. Extract finely ground Tablet powder containing about 50 mg of citalopram with 10 mL of chloroform in a test tube, and sonicate for 1 min. Centrifuge for 10 min, and filter into a beaker. Evaporate to dryness with nitrogen and, if necessary, induce crystallization by etching the beaker.]

  Mix approximately 2 mg of the residue with approximately 300 mg of potassium bromide, and record the IR spectrum.

  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**

  Buffer: 1.42 g/L of anhydrous dibasic sodium phosphate in water

  Diluent: Methanol and *Buffer* (80:20)

  Mobile phase: 0.77 mg/mL of dodecyltrimethylammonium bromide in *Diluent*

  Internal standard solution: 0.25 mg/mL of USP Citalopram Related Compound F RS in *Diluent*

  Standard stock solution: 1.25 mg/mL of USP Citalopram Hydrobromide RS in *Diluent*

  Standard solution: 0.025 mg/mL of USP Citalopram Related Compound F RS and 0.125 mg/mL of USP Citalopram Hydrobromide RS from the *Internal standard solution* and the *Standard stock solution*, respectively, in *Diluent*

  Sample solution: Transfer 10 Tablets to a 200-mL volumetric flask, add 25 mL of *Buffer*, and shake by mechanical means until disintegrated. Add 100 mL of methanol, and sonicate for about 5 min. Allow to cool to room temperature, and then dilute with *Diluent* to volume. Before taking an aliquot for dilution, allow to stand until the residue settles. Transfer a volume of the clear supernatant to a 50-mL volumetric flask to obtain a final nominal concentration between 0.090 and 0.10 mg/mL of citalopram. Add 5.0 mL of *Internal standard solution*, and dilute with *Diluent* to volume. Pass a portion through a filter (PTFE) having a 0.45-µm or finer pore size.

  Chromatographic system

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

  Mode: LC

  Detector: UV 254 nm

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

  Column temperature: 45°

  Flow rate: 1 mL/min

  Injection volume: 10 µL

  System suitability

  Sample: *Standard solution*

  [Note—The relative retention times for citalopram related compound F and citalopram are about 1.36 and 1.0, respectively.]

  Suitability requirements

  Resolution: NLT 1.5 between citalopram and citalopram related compound F

  Column efficiency: NLT 2000 theoretical plates, calculated from the citalopram peak

  Relative standard deviation: NMT 1.5% for the peak response ratio of citalopram to the internal standard

  Analysis

  Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of citalopram ($C_{20}H_{21}FN_2O$) 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 ratio of citalopram to the internal standard from the *Sample solution*

R_S = peak response ratio of citalopram to the internal standard from the *Standard solution*

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

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

M_{r1} = molecular weight of citalopram, 324.39

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Buffer: pH 1.5 buffer (prepared by transferring 118 mL of 1 N hydrochloric acid and 82 mL of 1 N sodium hydroxide to a 1000-mL volumetric flask, diluting with water to volume, and adjusting with 1 N sodium hydroxide to a pH of 1.5)

Medium: *Buffer*; 800 mL, deaerated

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: 12 µg/mL of USP Citalopram Hydrobromide RS in *Medium*

Sample solution: Sample per *Dissolution ⟨711⟩*. Pass through a PVDF filter having a 0.45-µm pore size, and dilute with *Medium* as needed.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 239 nm

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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*, 800 mL

D = dilution factor of the *Sample solution*

M_{r1} = molecular weight of citalopram, 324.39

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

L = label claim of citalopram (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of citalopram ($C_{20}H_{21}FN_2O$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer: 3.15 g/L of monobasic potassium phosphate and 3.60 g/L of dibasic sodium phosphate dodecahydrate ($Na_2HPO_4 \cdot 12H_2O$) in water

Mobile phase: Methanol, acetonitrile, and *Buffer* (38:7:55). Adjust with phosphoric acid to a pH of 6.5.

Standard stock solution: 0.25 mg/mL of USP Citalopram Hydrobromide RS in *Mobile phase*

System suitability solution: 1 µg/mL each of USP Citalopram Related Compound A RS, USP Citalopram Related Compound B RS, USP Citalopram Related Compound C RS, and USP Citalopram Related Compound E RS in the *Standard stock solution*

Standard solution: 0.625 µg/mL of citalopram hydrobromide from the *Standard stock solution* in *Mobile phase*

Sensitivity solution: 0.05 µg/mL of citalopram hydrobromide from the *Standard solution* in *Mobile phase*

Sample solution: Transfer 10 Tablets to a 200-mL volumetric flask, add 25 mL of *Buffer*, and shake by mechanical means until disintegrated. Add 100 mL of a mixture of methanol and water (1:1), mix, and sonicate for about 5 min. Allow to cool, dilute with a mixture of methanol

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and water (1:1) to volume, and mix thoroughly. Allow the excipients to settle. Dilute with *Mobile phase*, as necessary, to a final concentration of 0.5 mg/mL of citalopram. Pass a portion of this solution through a polytetrafluoroethylene (PTFE) membrane filter having a 0.45-µm or finer pore size, and use the filtrate.

Chromatographic system

(See Chromatography ⟨621⟩, System Suitability.)

Mode: LC

Detector: UV 239 nm

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

Column temperature: 45°

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

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

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

Suitability requirements

Resolution: NLT 3 between citalopram related compound C and citalopram, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

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

Signal-to-noise ratio: NLT 3, *Sensitivity solution*

Analysis

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

Chromatograph the *System suitability solution*, and identify the components on the basis of their relative retention times given in Table 1.

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

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

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

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

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

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

M_{r1} = molecular weight of citalopram, 324.39

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

F = relative response factor (see Table 1)

Acceptance criteria: See Table 1.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citalopram related compound A	0.43	0.77	0.2
Citalopram related compound B	0.60	0.98	0.25
Citalopram related compound C	0.83	0.69	0.25
Citalopram	1.0	—	—
Citalopram related compound E	1.32	0.91	0.1
Any other individual, unidentified impurity	—	1.0	0.2

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Total impurities	—	—	0.8

ADDITIONAL REQUIREMENTS

- **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 A RS

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

$C_{20}H_{23}FN_2O_2$ 342.22

USP Citalopram Related Compound B RS

1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-3-hydroxy-1,3-dihydroisobenzofuran-5-carbonitrile oxalate.

$C_{20}H_{21}FN_2O_2 \cdot C_2H_2O_4$ 430.43

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 Citalopram Related Compound E RS

1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydrobenzofuran-5-carbonitrile-*N*-oxide hydrochloride.

$C_{20}H_{21}FN_2O_2 \cdot HCl$ 376.85

USP Citalopram Related Compound F RS

Dimethyl-(1-methyl-3,3-diphenylallyl)amine hydrochloride.

$C_{18}H_{21}N \cdot HCl$ 287.83

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

Topic/Question	Contact	Expert Committee
CITALOPRAM 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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