Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Mar-2019
Document Type: USP Monographs
DocId: GUID-7B905C76-4E5A-49C8-9C56-85CCF9EE941E_5_en-US
DOI: https://doi.org/10.31003/USPNF_M17946_05_01
DOI Ref: b0cm8

Citalopram Oral Solution

DEFINITION

Citalopram Oral Solution contains an amount of citalopram hydrobromide equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of citalopram free base ($C_{20}H_{21}FN_2O$). It may contain a suitable preservative.

IDENTIFICATION

• **A.** The retention time of the citalopram peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

Solution A: Methanol and acetonitrile▲(10:90)▲2S *(USP41)*

Buffer: 6.1 g/L of monobasic potassium phosphate in water. Add 1.5 mL of triethylamine per liter of the solution. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: *Solution A* and *Buffer* ▲(28:72)▲2S *(USP41)*

Diluent: Acetonitrile and *Buffer* ▲(25:75)▲2S *(USP41)*

Standard solution: 0.25 mg/mL of USP Citalopram Hydrobromide RS, ▲ equivalent to 0.2 mg/mL of citalopram free base in *Diluent*▲2S *(USP41)*

Sample solution: ▲Nominally equivalent to 0.2 mg/mL of citalopram free base, prepared as follows. Transfer a suitable volume of Oral Solution to a suitable volumetric flask.▲2S *(USP41)* Add 50% of the flask volume of *Diluent*, and sonicate at room temperature for 3 min with intermittent shaking. Allow the solution to cool, and dilute with *Diluent* to volume. [Note—The *Sample solution* may be passed through either a PVDF or nylon membrane filter of suitable pore size.]

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. ▲For *Identification B,* use a diode array detector in the range of 210–400 nm.▲2S *(USP41)*

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: ▲NLT▲2S *(USP41)* 2 times the retention time of citalopram

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: ▲NMT 0.73%▲2S *(USP41)*

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 Oral Solution taken:

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

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

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

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

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

M_{r1} = molecular weight of citalopram free base, 324.39

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

Acceptance criteria: 90.0%–110.0% of citalopram free base ($C_{20}H_{21}FN_2O$)

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: Acetonitrile, *methanol*, and tetrahydrofuran▲(85:5:10)▲2S *(USP41)*

Buffer: Dissolve 3.0 g of ▲octanesulfonic acid sodium salt▲2S *(USP41)* in 1 L of water. Add 2 mL of triethylamine and 5 mL of ▲tetrabutylammonium hydroxide, 40 percent in water.▲2S *(USP41)* Mix, and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: *Solution A* and *Buffer* ▲(25:75)▲2S *(USP41)*

Diluent: Acetonitrile and water▲(25:75)▲2S *(USP41)*

System suitability solution: 6 µg/mL of USP Citalopram Related Compound D RS and 1.3 mg/mL of USP Citalopram Hydrobromide RS in *Diluent*

Standard solution: ▲0.0063 mg/mL▲2S *(USP41)* of USP Citalopram Hydrobromide RS in *Diluent*

Sample solution: ▲Nominally equivalent to 1 mg/mL of citalopram free base, prepared as follows. Transfer a suitable volume of Oral Solution to a suitable volumetric flask.▲2S *(USP41)* Add 60% of the flask volume of *Diluent*, and sonicate at room temperature for 3 min with intermittent shaking. Allow the solution to cool, and dilute with *Diluent* to volume. [Note—The *Sample solution* may be passed through either a PVDF or nylon membrane filter of suitable pore size.]

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: ▲NLT▲2S *(USP41)* 2.6 times the retention time of citalopram for the *System suitability solution* and the *Standard solution*; ▲NLT▲2S *(USP41)* 5.7 times the retention time of citalopram for the *Sample solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.8 between citalopram and citalopram related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲each degradation product▲2S *(USP41)* in the portion of Oral Solution 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▲2S *(USP41)* from the *Sample solution*

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

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

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

F = relative response factor for each ▲degradation product▲2S *(USP41)* (see *Table 1*)

M_{r1} = molecular weight of citalopram free base, 324.39

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citalopram related compound A[a]	0.29	0.86	0.20
Carboxy citalopram[b]	0.47	0.72	0.20
Desfluorocitalopram[c,d]	0.71	—	—
Citalopram related compound C[e]	0.83	1.8	0.20
Citalopram	1.0	—	—
Citalopram related compound D	1.11	0.95	0.20
Citalopram related compound G[d,f]	3.13	—	—
Citalopram related compound H[d,g]	3.75	—	—
Any individual, unspecified degradation product	—	1.0	0.15
Total ▲degradation products▲2S *(USP41)*	—	—	0.50

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

[b] 1-[3-(Dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxylic acid.

[c] 1-[3-(Dimethylamino)propyl]-1-phenyl-1,3-dihydroisobenzofuran-5-carbonitrile.

[d] This process impurity is included in the table for identification only. It is controlled in the drug substance, and is not to be reported or included in the total ▲degradation products▲2S *(USP41)* for the drug product.

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

[f] 3-[5-Chloro-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl]-*N*,*N*-dimethylpropan-1-amine.

[g] 3-[5-Bromo-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl]-*N*,*N*-dimethylpropan-1-amine.

SPECIFIC TESTS

• **Deliverable Volume** ⟨698⟩**:** Meets the requirements

• **pH** ⟨791⟩**:** 3.5–7.0

Change to read:

• **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count does not exceed ▲10^2 cfu/mL.▲2S *(USP41)* The total yeasts and molds count does not exceed 5×10^1 cfu/mL. It meets the requirements of the test for the absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in light-resistant containers at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Citalopram Hydrobromide RS

USP Citalopram Related Compound D RS

[Note—May be available as a hydrochloride or 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

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

Topic/Question	Contact	Expert Committee
CITALOPRAM ORAL SOLUTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(4)

Current DocID: GUID-7B905C76-4E5A-49C8-9C56-85CCF9EE941E_5_en-US
Previous DocID: GUID-7B905C76-4E5A-49C8-9C56-85CCF9EE941E_2_en-US
DOI: https://doi.org/10.31003/USPNF_M17946_05_01
DOI ref: b0cm8