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Paroxetine Extended-Release Tablets

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DEFINITION

Paroxetine Extended-Release Tablets contain paroxetine hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$).

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.

ASSAY

• PROCEDURE

Buffer: 3.9 g/L of [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.5.

Mobile phase: [Acetonitrile](#), *Buffer*, and [triethylamine](#) (40:60:1). Adjust with [glacial acetic acid](#) to a pH of 5.5.

Standard solution: 0.5 mg/mL of [USP Paroxetine Hydrochloride RS](#) in methanol

System suitability solution: 0.5 mg/mL of [USP Paroxetine Related Compound B RS](#) in *Standard solution*

Sample solution: Nominally 0.5 mg/mL of paroxetine from NLT 10 Tablets prepared as follows. Transfer the required number of Tablets to a suitable volumetric flask. Add 80% of the flask volume of [methanol](#). Sonicate for 30 min followed by stirring for 30 min. Dilute with [methanol](#) to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 295 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L13](#)

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

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

[NOTE—The relative retention times for paroxetine related compound B and paroxetine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between paroxetine related compound B and paroxetine, *System suitability solution*

Tailing factor: NMT 2.0 for paroxetine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) 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 Paroxetine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Test 1

Acid stage medium: 0.1 N [hydrochloric acid](#); 750 mL

Buffer stage medium: 0.05 M tris buffer prepared as follows. Dissolve 6.06 g of [tris\(hydroxymethyl\)aminomethane](#) in 1 L of [water](#). Add 1.8 mL of [hydrochloric acid](#) to the resulting solution. Adjust with [hydrochloric acid](#) to a pH of 7.5; 1000 mL deaerated.

Apparatus 1: 100 rpm

Times: 2 h in *Acid stage*; 2, 4, and 12 h in *Buffer stage*

Buffer and Mobile phase: Proceed as directed in the Assay.

Acid stage standard stock solution: 0.33 mg/mL of paroxetine prepared as follows. Transfer a suitable amount of [USP Paroxetine Hydrochloride RS](#) to a suitable volumetric flask. Dissolve in 5% of the flask volume of [methanol](#). Dilute with *Acid stage medium* to volume.

Acid stage standard solution: Dilute the *Acid stage standard stock solution* with *Acid stage medium* to obtain a final concentration of (L/7500) mg/mL, where L is the label claim in mg.

Buffer stage standard stock solution: 0.25 mg/mL of paroxetine prepared as follows. Transfer a suitable amount of [USP Paroxetine Hydrochloride RS](#) to a suitable volumetric flask. Dissolve in 5% of the flask volume of [methanol](#). Dilute with *Buffer stage medium* to volume.

Buffer stage standard solution: Dilute the *Buffer stage standard stock solution* with *Buffer stage medium* to obtain a final concentration of (L/1000) mg/mL, where L is the label claim in mg.

Acid stage sample solution: Run the *Acid stage* for 2 h. Withdraw 10 mL of the solution under test and centrifuge. Use the centrifugate for analysis.

Buffer stage sample solution: Remove the *Acid stage medium* from the vessel and replace it with the *Buffer stage medium*. At the times specified, remove 10 mL of the solution under test and centrifuge. Use the centrifugate for analysis.

Chromatographic system: Proceed as directed in the Assay. For *Injection volume*, use 100 μ L for the *Acid stage* analysis and 10 μ L for the *Buffer stage* analysis.

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0, *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 3.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage*:

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

r_U = peak response from the *Acid stage sample solution*

r_S = peak response from the *Acid stage standard solution*

C_S = concentration of [USP Paroxetine Hydrochloride RS](#) in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

V = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point in the *Buffer stage*:

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



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r_i = peak response from the *Buffer stage sample solution* at each time point i

r_s = peak response from the *Buffer stage standard solution*

C_s = concentration of [USP Paroxetine Hydrochloride RS](#) in the *Buffer stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Calculate the percentage of the labeled amount (Q_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage medium*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_s)] + (C_1 \times V_s)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_s)]] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

C_i = concentration of paroxetine in the *Buffer stage medium* in the portion of sample withdrawn at time point i (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

L = label claim (mg/Tablet)

V_s = volume of the *Sample solution* withdrawn from the *Buffer stage medium* (mL)

Tolerances

Acid stage: NMT 10% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) is dissolved in 2 h.

Buffer stage: See [Table 1](#).

Table 1

Time Point (i)	Time (h)	Amount Dissolved (Tablets labeled to contain 12.5 mg of paroxetine)	Amount Dissolved (Tablets labeled to contain 25 mg of paroxetine)	Amount Dissolved (Tablets labeled to contain 37.5 mg of paroxetine)
1	2	15%–35%	10%–30%	20%–45%
2	4	40%–70%	40%–70%	60%–85%
3	12	NLT 80%	NLT 80%	NLT 80%

The percentages of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2](#).

Test 2

If the product complies with this procedure, the labeling indicates that it meets USP *Dissolution Test 2*.

Acid stage medium: 0.1 N [hydrochloric acid](#); 750 mL

Buffer stage medium: 0.05 M tris buffer prepared as follows. Dissolve 6.06 g of [tris\(hydroxymethyl\)aminomethane](#) in 900 mL of [water](#). Add 40 mL of 1.0 M [hydrochloric acid](#) to the resulting solution. Adjust with either 1.0 M [hydrochloric acid](#) or 1.0 M [sodium hydroxide](#) to a pH of 7.5. Dilute with [water](#) to 1 L; 1000 mL deaerated.

Apparatus 2: 150 rpm with suitable sinkers

Times: 2 h in *Acid stage*; 1, 2, 4, and 6 h in *Buffer stage*

Acid stage standard stock solution: 0.04 mg/mL of [USP Paroxetine Hydrochloride RS](#) prepared as follows. Transfer a suitable amount of [USP Paroxetine Hydrochloride RS](#) to a suitable volumetric flask. Dissolve in 2 mL of [methanol](#). Dilute with *Acid stage medium* to volume.

Acid stage standard solution: Dilute the *Acid stage standard stock solution* with *Acid stage medium* to obtain a final concentration of $(L/7500)$ mg/mL of paroxetine, where L is the label claim in mg.

Buffer stage standard solution: $(L/1000)$ mg/mL of paroxetine, where L is the label claim in mg prepared as follows. Transfer a suitable amount of [USP Paroxetine Hydrochloride RS](#) to a suitable volumetric flask. Dissolve in 2 mL of [methanol](#). Dilute with *Buffer stage medium* to volume.

Acid stage sample solution: Run the *Acid stage* for 2 h. Withdraw 10 mL of the solution under test, and filter. Use the filtrate for analysis.

Buffer stage sample solution: Remove the Tablet and sinker from the acid stage vessel and pat them dry. Introduce the Tablet and sinker into the dissolution vessel with 1000 mL of the *Buffer stage medium*. At the times specified, remove 10 mL of the solution under test and filter. Use the filtrate for analysis.

Acid stage analysis

Buffer: Add 2.9 mL of [phosphoric acid](#) to 800 mL of [water](#). Adjust with 1 M [sodium hydroxide](#) to a pH of 6.0. Dilute with [water](#) to 1000 mL.

Mobile phase: [Acetonitrile](#) and *Buffer* (40:60)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 50 μL for 12.5-mg Tablet; 20 μL for 25- and 37.5-mg Tablets

Run time: 2 times the retention time of paroxetine

System suitability

Sample: *Acid stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage*:

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

r_U = peak response from the *Acid stage sample solution*

r_S = peak response from the *Acid stage standard solution*

C_S = concentration of [USP Paroxetine Hydrochloride RS](#) in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

V = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Buffer stage analysis

Instrumental conditions

Mode: UV

Analytical wavelength: 294 nm with 340 nm for background correction

Blank: *Buffer stage medium*

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage*:

$$\text{Result} = (A_i/A_S) \times C_S \times (M_{r1}/M_{r2})$$

A_i = absorbance of the *Buffer stage sample solution* at time point i