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Propafenone Hydrochloride Extended-Release Capsules

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DEFINITION

Propafenone Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$).

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **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: Dissolve 1.36 g/L of [monobasic potassium phosphate](#) in [water](#), and adjust with [phosphoric acid](#) to a pH of 3.0 ± 0.1 .

Mobile phase: [Methanol](#) and *Buffer* (50:50)

Diluent: 50% [methanol](#) in [water](#)

Standard solution: 0.1 mg/mL of [USP Propafenone Hydrochloride RS](#) in *Diluent*

Sample stock solution: Nominally 1 mg/mL of propafenone hydrochloride prepared as follows. Transfer a suitable amount of finely powdered contents from NLT 20 Capsules to an appropriate volumetric flask. Add about 60% of the final volume of *Diluent*, and sonicate with occasional swirling until the contents are completely disintegrated. Dilute with *Diluent* to volume and pass through a suitable filter of 0.45- μ m pore size.

Sample solution: Nominally 0.1 mg/mL of propafenone hydrochloride in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L7](#)

Flow rate: 1 mL/min

Injection volume: 20 μ L

Run time: NLT 2 times the retention time of propafenone

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 propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the portion of Capsules taken:

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

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

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

C_S = concentration of [USP Propafenone Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Acid stage

Medium: 0.08 N [hydrochloric acid](#); 900 mL

Apparatus 2: 50 rpm

Time: 1 h

Diluent: 6.8 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [sodium hydroxide](#) to a pH of 6.8.

Standard solution: (L/1000) mg/mL of [USP Propafenone Hydrochloride RS](#) in *Diluent*, where L is the label claim in mg/Capsule

Sample solution: At the specified time point, withdraw about 10 mL of the solution and pass through a suitable filter of 0.45-μm pore size.

Discard at least the first 4 mL of the filtrate. Analyze the *Sample solution* immediately.

Instrumental conditions

Mode: UV

Analytical wavelengths: 305 and 375 nm

Cell: 0.2 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Measure and subtract the absorbance at 375 nm from the absorbance at 305 nm to obtain the absorbances for the *Sample solution* and *Standard solution*.

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Propafenone Hydrochloride RS](#) in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: See [Table 1](#).

Buffer stage

Proceed as directed in the *Acid stage*, except for the following parameters.

Buffer: Dissolve 108.88 g of [monobasic potassium phosphate](#) in water, add 14.4 g of [sodium hydroxide](#), mix to dissolve, and dilute with [water](#) to 1 L. Adjust with 2 N [sodium hydroxide](#) to a pH of 6.8.

Solution A: *Buffer* and 2 N [sodium hydroxide](#) (64:36)

Medium: At 2 h of dissolution time, add 100 mL of *Solution A*, preheated at 37°, to 900 mL of 0.08 N [hydrochloric acid](#).

Times: 4 and 12 h

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_2 = C_2 \times V \times (1/L) \times 100$$

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

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (*i*) (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

V_s = volume of *Medium* taken (mL)

Tolerances: See [Table 1](#).

Table 1

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)
1	1	5–25
2	4	40–70
3	12	NLT 75

The percentages of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at the times specified conform to

[Dissolution \(711\)](#), [Acceptance Table 2](#).

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

Acid stage

Acid stage medium: 0.08 N [hydrochloric acid](#); 900 mL

Apparatus 2: 50 rpm, with sinkers

Time: 1 h

Standard stock solution: 0.42 mg/mL of [USP Propafenone Hydrochloride RS](#) prepared as follows. Transfer a suitable amount of [USP Propafenone Hydrochloride RS](#) to a suitable volumetric flask. Add [methanol](#), NMT 10% of the final volume, and sonicate to dissolve. Dilute with *Acid stage medium* to volume.

Standard solution: 0.021 mg/mL of [USP Propafenone Hydrochloride RS](#) in *Acid stage medium* from the *Standard stock solution*

Sample solution: Pass the solution through a suitable filter of 0.45-μm pore size. Dilute with *Acid stage medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 305 nm

Cell: 1 cm

Blank: *Acid stage medium*

Analysis

After 1 h in the *Acid stage medium* and the collection of the *Sample solution*, replace the portion of solution withdrawn with an equal volume of *Acid stage medium*. Continue for an additional 1 h in *Acid stage medium*.

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_u/A_s) \times C_s \times D \times V \times (1/L) \times 100$$

A_u = absorbance of the *Sample solution*

A_s = absorbance of the *Standard solution*

- C_s = concentration of [USP Propafenone Hydrochloride RS](#) in the *Standard solution* (mg/mL)
- D = dilution factor (mL/mL)
- V = volume of *Acid stage medium*, 900 mL
- L = label claim (mg/Capsule)

Tolerances: See [Table 2](#).

Buffer stage

Proceed as directed in the *Acid stage*, except for the following parameters.

Buffer stage medium: After 2 h in the *Acid stage*, add 100 mL of phosphate buffer (68 g of [monobasic potassium phosphate](#) and 42 g of [sodium hydroxide](#) in 1000 mL of [water](#)), preheated at 37°, to 900 mL of *Acid stage medium*; 1000 mL.

Times: 6 and 15 h

Standard stock solution: 0.48 mg/mL of [USP Propafenone Hydrochloride RS](#) prepared as follows. Transfer a suitable amount of [USP Propafenone Hydrochloride RS](#) to a suitable volumetric flask. Add [methanol](#), NMT 10% of the final volume, and sonicate to dissolve. Dilute with *Buffer stage medium* to volume.

Standard solution: 0.048 mg/mL of [USP Propafenone Hydrochloride RS](#) in *Buffer stage medium* from *Standard stock solution*

Sample solution: Withdraw a 10-mL aliquot at each time point. Pass the solution through a suitable filter of 0.45-µm pore size. Dilute with *Buffer stage medium* to a concentration similar to that of the *Standard solution*.

Blank: *Buffer stage medium*

Instrumental conditions: See *Acid stage*.

Analysis

At the specified time points, replace the portion of solution withdrawn with 10 mL of *Buffer stage medium*.

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_1 = (A_U/A_S) \times C_s \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_s = concentration of [USP Propafenone Hydrochloride RS](#) in the *Standard solution* (mg/mL)

D = dilution factor (mL/mL)

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (i):

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

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

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)

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

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

L = label claim (mg/Capsule)

Tolerances: See [Table 2](#).

Table 2

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	