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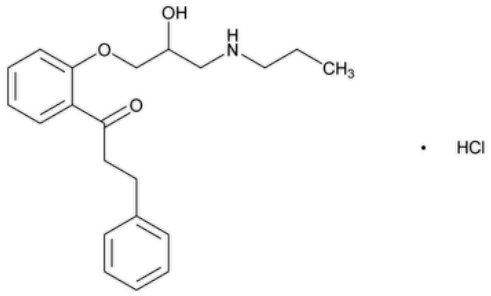
Propafenone Hydrochloride



$C_{21}H_{27}NO_3 \cdot HCl$ 377.90

1-Propanone, 1-[2-[2-hydroxy-3-(propylamino)propoxy] phenyl]-3-phenyl-, hydrochloride;

2'-[2-Hydroxy-3-(propylamino)propoxy]-3-phenylpropiophenone hydrochloride CAS RN®: 34183-22-7; UNII: 33XCH0HOCD.

DEFINITION

Propafenone Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{21}H_{27}NO_3 \cdot HCl$, calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** Dissolve 0.5 g of Propafenone Hydrochloride in 50 mL of water with heating. Adjust with 0.1 N sodium hydroxide to a pH of 9.5–10.0: a precipitate is formed. Cool the mixture, and filter. Add 1 mL of 6 N nitric acid and 2–3 drops of 0.1 N silver nitrate to the filtrate: a precipitate is formed, which dissolves upon the addition of a few drops of ammonium hydroxide.

ASSAY

• **Procedure**

Sample solution: Transfer 250 mg of Propafenone Hydrochloride to a 125-mL flask. Dissolve in 30 mL of methanol, and add 15 mL of mercuric acetate TS.

Analysis: Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 37.79 mg of $C_{21}H_{27}NO_3 \cdot HCl$.

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

IMPURITIES

Inorganic Impurities

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Organic Impurities

• **Procedure**

Solvent A: 3.42 g/L of dipotassium hydrogen phosphate trihydrate. Adjust with phosphoric acid to a pH of 2.5.

Solvent B: Acetonitrile

Mobile phase: See the gradient table below.

Time (min)	Solvent A (%)	Solvent B (%)
0	65	35
8	65	35

Time (min)	Solvent A (%)	Solvent B (%)
20	30	70
30	30	70
31	65	35
36	65	35

Diluent: *Solvent A* and *Solvent B* (13:7)

System suitability solution: 0.1 mg/mL of USP Propafenone Hydrochloride RS and USP Propafenone Related Compound B RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Propafenone Hydrochloride RS in *Diluent*

Sample solution: 1 mg/mL of Propafenone Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection size: 20 µL

Run time: NLT six times the retention time of propafenone

Suitability requirements

Resolution: NLT 3 between propafenone and propafenone related compound B

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Propafenone Hydrochloride taken:

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

r_U = peak response for each impurity 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*

C_U = concentration of Propafenone Hydrochloride in the *Sample solution*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.3%. [NOTE—Disregard any peak below 0.03%.]

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Propafenone related compound B[a]	0.8	0.1
Impurity D[b]	2.3	0.1
Impurity G[c]	3.6	0.1
Impurity C[d]	4.1	0.1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Impurity F[e]	5.3	0.1
Individual unspecified impurities	—	0.1

[a] (2*E*)-1-[2-[(2*RS*)-2-Hydroxy-3-(propylamino)propoxy]phenyl]-3-phenylprop-2-en-1-one.

[b] 1-[2-[(2*RS*)-2,3-Dihydroxypropoxy]phenyl]-3-phenylpropan-1-one.

[c] 1,1'[Propyliminobis(2-hydroxypropane-3,1-diyl)oxy-2,1-phenylene]bis(3-phenylpropan-1-one.

[d] 1-[2-[[(2*RS*)-Oxiranyl]methoxy]phenyl]-3-phenylpropan-1-one.

[e] 1,1'-[2-Hydroxypropane-1,3-diylbis(oxy-2,1-phenylene)]bis(3-phenylpropan-1-one).

SPECIFIC TESTS

- **Clarity of Solution:** Dissolve 1.0 g in 30 mL of hot water, and observe without delay: the solution initially is clear.
- **Melting Range or Temperature ⟨741⟩:** 171°–175°
- **pH ⟨791⟩:** 5.0–6.2, in a solution (1 in 200)
- **Loss on Drying ⟨731⟩:** Dry a sample at 105° to constant weight: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at a temperature between 15° and 30°.
- **USP Reference Standards ⟨11⟩**

USP Propafenone Hydrochloride RS

USP Propafenone Related Compound B RS

(*RS*,*E*)-1-[2-[2-Hydroxy-3-(propylamino)propoxy]phenyl]-3-phenylprop-2-en-1-one.

$C_{21}H_{25}NO_3$ 339.43

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

Topic/Question	Contact	Expert Committee
PROPAFENONE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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