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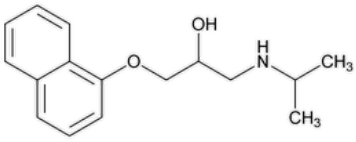
Propranolol Hydrochloride



• HCl

$C_{16}H_{21}NO_2 \cdot HCl$ 295.80

2-Propanol, 1-[(1-methylethyl)amino]-3-(1-naphthalenyloxy)-, hydrochloride, (±)-;

(±)-1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol hydrochloride CAS RN®: 318-98-9; UNII: F8A3652H1V.

DEFINITION

Change to read:

Propranolol Hydrochloride contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-May-2020) of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

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

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Mix 1.6 g of sodium dodecyl sulfate and 0.31 g of tetrabutylammonium phosphate in a mixture of 1 mL of sulfuric acid, 450 mL of water, and 550 mL of acetonitrile. Adjust with 2 N sodium hydroxide solution to a pH of 3.3.

Standard solution: 0.2 mg/mL of USP Propranolol Hydrochloride RS in *Mobile phase*. Sonication may be needed to aid dissolution.

Sample solution: 0.2 mg/mL of Propranolol Hydrochloride in *Mobile phase*. Sonication may be needed to aid dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 292 nm

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

Flow rate: 1.8 mL/min

Injection volume: 20 µL

Run time: NLT 7 times the retention time of propranolol

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) in the portion of Propranolol Hydrochloride taken:

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

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

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

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

C_U = concentration of Propranolol Hydrochloride in the *Sample solution* (mg/mL)

▲ (USP 1-May-2020)

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-May-2020) on the dried basis

IMPURITIES

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

Change to read:

• **▲Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.002 mg/mL of USP Propranolol Related Compound A RS and 2 mg/mL of USP Propranolol Hydrochloride RS in *Mobile phase*

Standard solution: 0.002 mg/mL of USP Propranolol Hydrochloride RS in *Mobile phase*

Sensitivity solution: 0.001 mg/mL of USP Propranolol Hydrochloride RS in *Mobile phase* from *Standard solution*

Sample solution: 2 mg/mL of Propranolol Hydrochloride in *Mobile phase*. Sonication may be needed to aid dissolution.

System suitability

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

[Note—The relative retention times for the impurities are listed in *Table 1*.]

Suitability requirements

Resolution: NLT 3.0 between propranolol and propranolol related compound A, *System suitability solution*

Relative standard deviation: NMT ▲5.0%,▲ (ERR 1-May-2020) *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified and unspecified impurity in the portion of Propranolol Hydrochloride taken:

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

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

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

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

C_U = concentration of Propranolol Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Propranolol related compound A	0.6	1.4	0.1
Propranolol	1.0	1.0	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Propranolol dimer[a]	4.8	1.3	0.1
Dinaphthyl glycerol[b]	5.7	1.9	0.1
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.4

[a] 3,3′-(Isopropylazanediyl)bis[1-(naphthalen-1-yloxy)propan-2-ol].

[b] 1,3-Bis(naphthalen-1-yloxy)propan-2-ol.

▲ (USP 1-May-2020)

SPECIFIC TESTS

Delete the following:

▲• **Melting Range or Temperature**, *Class Ia* ⟨741⟩**:** 162°–165°▲ (USP 1-May-2020)

Delete the following:

▲• **Optical Rotation** ⟨781S⟩, *Specific Rotation*

Sample solution: 40 mg/mL in water

Acceptance criteria: −1.0° to +1.0°▲ (USP 1-May-2020)

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Propranolol Hydrochloride RS

▲ USP Propranolol Related Compound A RS

3-(Naphthalen-1-yloxy)propane-1,2-diol.

$C_{13}H_{14}O_3$ 218.25▲ (USP 1-May-2020)

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

Topic/Question	Contact	Expert Committee
PROPRANOLOL 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

Most Recently Appeared In:
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