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Propranolol Hydrochloride Tablets

DEFINITION
Propranolol Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$).

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*.

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*.▲ (USP 1-Aug-2021)

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Dissolve 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 stock solution: Nominally 1.0 mg/mL of propranolol hydrochloride in *Mobile phase* prepared as follows. Transfer a suitable amount of powdered Tablets (NLT 20) to a suitable volumetric flask, and add *Mobile phase* to 60% of the flask volume. Sonicate and dilute with *Mobile phase* to volume. Centrifuge a portion for 10 min, and pass the solution through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally 0.2 mg/mL of propranolol hydrochloride in *Mobile phase* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 292 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Flow rate: 1.8 mL/min

Injection volume: 20 µL

Run time: NLT 11 times the retention time of propranolol

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) in the portion of Tablets 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 = nominal concentration of propranolol hydrochloride in the *Sample solution* (mg/mL)

▲ (USP 1-Aug-2021)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Dilute hydrochloric acid (1 in 100); 1000 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: USP Propranolol Hydrochloride RS at a known concentration in *Medium*

Sample solution: Filtered portions of the solution under test. Dilute with *Medium* as needed.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 289 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) dissolved:

$$\text{▲Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

▲ (USP 1-Aug-2021)

Tolerances: NLT 75% (Q) of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

▲▲ (USP 1-Aug-2021)

Add the following:

▲IMPURITIES

• **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: 0.004 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: Nominally 2 mg/mL of propranolol hydrochloride in *Mobile phase* prepared as follows. Transfer a suitable amount of powdered Tablets (NLT 20) to a suitable volumetric flask, and add *Mobile phase* to 60% of the flask volume. Sonicate and dilute with *Mobile phase* to volume. Centrifuge a portion of the solution for 10 min, and pass the solution through a suitable filter of 0.45-µm pore size.

System suitability

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

[Note—The relative retention times for propranolol related compound A and propranolol are 0.6 and 1.0, respectively.]

Suitability requirements

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

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified or any unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of any specified or 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 = nominal concentration of propranolol hydrochloride in the *Sample solution* (mg/mL)

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Propranolol related compound A	0.6	1.4	0.2
Propranolol	1.0	1.0	—
Propranolol dimer[a]	4.7	1.4	0.2
Dinaphthyl glycerol[b]	6.1	1.9	0.2
Any unspecified impurity	—	1.0	0.2
Total impurities	—	—	1.0

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

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

▲ (USP 1-Aug-2021)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2021)

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-Aug-2021)

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

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

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