Propranolol Hydrochloride Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	25-Aug-2023
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 2

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 2 Expert Committee intends to revise the Propranolol Hydrochloride Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Propranolol Hydrochloride Tablets monograph to add *Dissolution Test 2*.

- *Dissolution Test 2* was validated using the Zorbax Eclipse XDB C18 brand of column with L1 packing. The typical retention time for propranolol is 5 min.

Labeling information has been incorporated to support the inclusion of *Dissolution Test 2*.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact V. Durga Prasad, Senior Scientist II (+91-40-4448-8723 or durgaprasad.v@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

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*.

● **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

● **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)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

▲**Test 1**▲ (TBD)

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)

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

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

Medium: 0.1 N hydrochloric acid; deaerated, if necessary, 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Solution A: Acetonitrile, sulfuric acid, and water (55: 0.1: 45)

Mobile phase: Dissolve 1.6 g of sodium dodecyl sulfate and 0.31 g of tetrabutylammonium phosphate in 1 L of *Solution A*. Adjust with 2 N sodium hydroxide to a pH of 3.3.

Standard solution: (*L*/500) mg/mL of USP Propranolol Hydrochloride RS in *Medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system:

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

Mode: LC

Detector: UV 289 nm

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

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.6 times the retention time of propranolol

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 propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) dissolved:

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

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)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) is dissolved.▲ (TBD)

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

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.

ADDITIONAL REQUIREMENTS

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

Add the following:

▲● **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.▲ (TBD)

- **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

Page Information:

Not Applicable

Current DocID: