

Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2022
Document Type: USP Monographs
DocId: GUID-E004F593-4C53-4E2C-B3D3-D771BB6E8822_3_en-US
DOI: https://doi.org/10.31003/USPNF_M70920_03_01
DOI Ref: zd4c1

© 2025 USPC
Do not distribute

Propranolol Hydrochloride and Hydrochlorothiazide Tablets

DEFINITION

Propranolol Hydrochloride and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION

Change to read:

- **A.** ▲The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay. ▲

(USP 1-Aug-2022)

Change to read:

- **B.** ▲The UV spectrum of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay. ▲ (USP 1-Aug-2022)

ASSAY

Change to read:

• PROCEDURE

Solution A: ▲Tetrabutylammonium hydroxide, 40% in [water](#) ▲ (USP 1-Aug-2022)

Buffer: Dissolve 6.8 g of [monobasic potassium phosphate](#) in 1000 mL of [water](#). Add 3.4 mL of [phosphoric acid](#) and a volume of *Solution A* equivalent to 2.6 g of tetrabutylammonium hydroxide, and dilute with [water](#) to 2000 mL. Adjust, if necessary, with [phosphoric acid](#) or 10 N [potassium hydroxide](#) to a pH of 2.5. ▲ (USP 1-Aug-2022)

Mobile phase: [Methanol](#) and *Buffer* (15:85) ▲ (USP 1-Aug-2022)

Standard solution A: 0.25 mg/mL of [USP Hydrochlorothiazide RS](#) prepared as follows. Transfer 25 mg of [USP Hydrochlorothiazide RS](#) to a 100-mL volumetric flask. Add 15 mL of [methanol](#), and dilute with *Buffer* to volume.

Standard solution B: Dissolve a quantity of [USP Propranolol Hydrochloride RS](#) in *Mobile phase* to obtain a solution having a known concentration of 0.25J mg/mL, with J being the ratio of the labeled quantity, in milligrams, of propranolol hydrochloride to the labeled quantity, in milligrams, of hydrochlorothiazide per Tablet.

Standard solution: 50 µg/mL of [USP Hydrochlorothiazide RS](#) and 50J µg/mL of [USP Propranolol Hydrochloride RS](#) in *Mobile phase* prepared as follows. Mix 5.0 mL of *Standard solution A* and 5.0 mL of *Standard solution B* in a 25-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 50 µg/mL of hydrochlorothiazide prepared as follows. Transfer an equivalent to 25 mg of hydrochlorothiazide, from finely powdered Tablets (NLT 20), to a 500-mL volumetric flask. Add 5 mL of [water](#), mix, and allow to stand for 5 min, with occasional swirling. Add 75 mL of [methanol](#), mix, and sonicate for 10 min, with occasional swirling, adding ice to the bath, if necessary, to maintain the temperature at NMT 20°. Add about 350 mL of *Buffer* to the flask, and sonicate for 10 min, with occasional swirling, maintaining the temperature of the bath at NMT 20°. Dilute with *Buffer* to volume. Centrifuge a portion of this solution, if necessary, to obtain a clear solution.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm. ▲ (USP 1-Aug-2022)

Column: 4-mm × 15-cm; 5-µm packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 50 µL

▲**Run time:** NLT 3 times the retention time of propranolol ▲ (USP 1-Aug-2022)

System suitability**Sample:** *Standard solution*

[NOTE—The relative retention times for ▲ (USP 1-Aug-2022) hydrochlorothiazide and propranolol are about ▲ (USP 1-Aug-2022) 0.4 and 1.0, respectively.]

Suitability requirements

▲ (USP 1-Aug-2022)

Tailing factor: NMT 1.5 for the propranolol and hydrochlorothiazide peaks**Relative standard deviation:** NMT ▲ 1.0% for the propranolol and hydrochlorothiazide peaks ▲ (USP 1-Aug-2022)**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) 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 or hydrochlorothiazide from the *Sample solution*
 r_S = peak response of propranolol or hydrochlorothiazide from the *Standard solution*
 C_S = concentration of [USP Propranolol Hydrochloride RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (µg/mL)

 C_U = nominal concentration of propranolol hydrochloride or hydrochlorothiazide in the *Sample solution* (µg/mL)
Acceptance criteria: 90.0%–110.0%**PERFORMANCE TESTS****Change to read:**• [DISSOLUTION \(711\)](#)**Medium:** 0.01 N [hydrochloric acid](#); 900 mL**Apparatus 1:** 100 rpm**Time:** 30 min▲ [NOTE—Analyze the sample under test using either the *Instrumental procedure* or *Chromatographic procedure*.]**Instrumental procedure** ▲ (USP 1-Aug-2022)

Standard solution: Transfer a mixture of 5.0 mL of an aqueous solution having a known concentration of [USP Propranolol Hydrochloride RS](#) and 5.0 mL of a 0.005 N sodium hydroxide solution having a known concentration of [USP Hydrochlorothiazide RS](#) to a suitable capped bottle, and add 5.0 mL of [water](#), 1.0 mL of 5 N [sodium hydroxide](#), and 25.0 mL of [n-heptane](#). Cap the bottle, shake by mechanical means for 5 min, and allow the layers to separate, centrifuging if necessary, to obtain clear upper (*n*-heptane) and lower (aqueous) extracts.

Sample solution: Filter a portion of the solution under test, transfer 10.0 mL of the filtrate to a suitable capped bottle, and add 5.0 mL of [water](#), 1.0 mL of 5 N [sodium hydroxide](#), and 25.0 mL of [n-heptane](#). Cap the bottle, shake by mechanical means for 5 min, and allow the layers to separate, centrifuging if necessary, to obtain clear upper (*n*-heptane) and lower (aqueous) extracts.

Blank solution: Transfer 10.0 mL of [water](#) to a suitable capped bottle, and add 5.0 mL of [water](#), 1.0 mL of 5 N [sodium hydroxide](#), and 25.0 mL of [n-heptane](#). Cap the bottle, shake by mechanical means for 5 min, and allow the layers to separate, centrifuging if necessary, to obtain clear upper (*n*-heptane) and lower (aqueous) extracts.

Instrumental conditions**Mode:** UV**Analytical wavelength:** 293 nm for *n*-heptane layer (propranolol hydrochloride); 273 nm for aqueous layer (hydrochlorothiazide)**Analysis****Samples:** *Standard solution*, *Sample solution*, and *Blank solution*▲ Calculate the percentage of the labeled amount of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) dissolved:

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

 A_U = absorbance from the *Sample solution*
 A_S = absorbance from the *Standard solution*