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Promethazine Hydrochloride Tablets

DEFINITION

Promethazine Hydrochloride Tablets contain NLT 95.0% and NMT 110.0% of the labeled amount of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$).

[NOTE—Throughout the following procedures, protect the samples, the Reference Standards, and the solutions containing them, by conducting the procedures without delay under subdued light or using low-actinic glassware.]

IDENTIFICATION

• A.

Standard solution: In a separator, dissolve 50 mg of [USP Promethazine Hydrochloride RS](#) in 40 mL of dilute hydrochloric acid (1 in 1000).

Sample solution: Shake a quantity of powdered Tablets, equivalent to 50 mg of promethazine hydrochloride, with 30 mL of chloroform, and filter into a beaker. Evaporate the chloroform, dissolve the residue in 40 mL of dilute hydrochloric acid (1 in 1000), and transfer the liquid to a separator.

Analysis: Separately treat the *Sample solution* and the *Standard solution* as follows. Add 2 mL of [1 N sodium hydroxide](#) and 15 mL of carbon disulfide to the separators, and shake for 2 min. Centrifuge if necessary to clarify the lower phase, and pass through a dry filter, collecting the filtrate from each separator in a small flask provided with a glass stopper. Reduce the volume of the carbon disulfide extracts to 4–5 mL, and proceed as directed in [Identification—Organic Nitrogenous Bases \(181\)](#), beginning with “Determine the absorption spectra”.

Acceptance criteria: Meet the requirements

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

ASSAY

• PROCEDURE

Diluent: Dissolve 8.2 mL of [hydrochloric acid](#) in 1000 mL of water.

Mobile phase: Acetonitrile, water, and [triethylamine](#) (850:270:1)

System suitability stock solution: 1.2 mg/mL of [USP Promethazine Related Compound B RS](#) in *Diluent*. Sonicate to dissolve.

Standard solution: 0.1 mg/mL of [USP Promethazine Hydrochloride RS](#) in *Diluent*. Sonicate to dissolve.

System suitability solution: 0.09 mg/mL of [USP Promethazine Hydrochloride RS](#) and 0.12 mg/mL of [USP Promethazine Related Compound B RS](#) in *Diluent* from the *Standard solution* and *System suitability stock solution*, respectively

Sample stock solution: Nominally 2.5–5.0 mg/mL of promethazine hydrochloride prepared as follows. Transfer 20 Tablets to a volumetric flask of an appropriate size and add 50% of the flask volume of *Diluent*. Sonicate with swirling for NLT 20 min, or until the Tablets have fully disintegrated. Shake the flask for NLT 15 min and dilute with *Diluent* to volume.

Sample solution: Nominally 0.1 mg/mL of promethazine hydrochloride in *Diluent* from the *Sample stock solution*. Pass a portion through a filter of 0.45-μm pore size and use the clear filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-μm packing L1

Flow rate: 2.5 mL/min

Injection volume: 20 μL

Run time: NLT 2.5 times the retention time of promethazine

System suitability

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

[NOTE—The relative retention times for promethazine related compound B and promethazine are 0.82 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between promethazine and promethazine related compound B, *System suitability solution*



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Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Promethazine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of promethazine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: Prepare a solution with a known concentration of [USP Promethazine Hydrochloride RS](#) in *Medium*.

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium*

Instrumental conditions

Mode: UV

Analytical wavelength: Absorption maximum at about 249 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Promethazine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of promethazine hydrochloride in the *Sample solution* (mg/mL)

D = dilution factor for the *Sample solution*

Tolerances: NLT 75% (Q) of the labeled amount of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$) is dissolved.

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

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 15 min

Standard solution: (L/900) mg/mL of [USP Promethazine Hydrochloride RS](#) in *Medium*, where L is the label claim (mg/Tablet)

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

Instrumental conditions

Mode: UV

Analytical wavelength: Absorption maximum at about 249 nm

Cell: 0.2 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*