Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Nov-2021
Document Type: USP Monographs
DocId: GUID-69AD0099-857D-44C1-B637-4B56CE13D780_3_en-US
DOI: https://doi.org/10.31003/USPNF_M8167_03_01
DOI Ref: b6tbv

Diphenhydramine and Phenylephrine Hydrochlorides Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-diphenhydramine-phenylephrine-hcl-tabs-20211029.

DEFINITION

Diphenhydramine and Phenylephrine Hydrochlorides Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and phenylephrine hydrochloride ($C_9H_{13}NO_2 \cdot HCl$).

IDENTIFICATION

• **A.** The UV absorption spectra of the diphenhydramine and phenylephrine peaks of the *Sample solutions* and those of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the *Assay*.

• **B.** The retention times of the diphenhydramine and phenylephrine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

It is suggested to use plastic vials for analysis.

Buffer: 3.45 g/L of monobasic ammonium phosphate in water. Adjust with phosphoric acid to a pH of 3.5 ± 0.05 if necessary.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Solution A: Dilute 10 mL of glacial acetic acid with 1000 mL of water.

Diluent: Methanol and *Solution A* (30:70)

Standard solution: 0.25 mg/mL of USP Diphenhydramine Hydrochloride RS and 0.1 mg/mL of USP Phenylephrine Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.25 mg/mL of diphenhydramine hydrochloride and 0.1 mg/mL of phenylephrine hydrochloride prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask, add 50% final volume of *Solution A*, and stir for NLT 30 min. Add 30% final volume of methanol, and stir additionally for NLT 90 min. To ensure that particles do not collect above the solvent level, periodically rinse particulate into solution with *Solution A*. Allow the resulting solution to cool to room temperature, and dilute with *Solution A* to volume. Pass a portion through a suitable filter of 0.45-µm pore size. Discard the first 2–3 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm. For *Identification A*, use a diode-array detector in the range of 200–350 nm.

Column: 4.6-mm × 10-cm; 5-µm packing L9

Flow rate: 2.0 mL/min

Injection volume: 15 µL

Run time: NLT 3 times the retention time of phenylephrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.5–3.0 for both phenylephrine and diphenhydramine

Relative standard deviation: NMT 2.0% for both phenylephrine and diphenhydramine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and phenylephrine hydrochloride ($C_9H_{13}NO_2 \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of diphenhydramine or phenylephrine from the *Sample solution*

r_S = peak response of diphenhydramine or phenylephrine from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

It is suggested to use plastic vials for analysis.

Medium: Simulated gastric fluid without pepsin; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: (L_1/900) mg/mL of USP Diphenhydramine Hydrochloride RS and (L_2/900) mg/mL of USP Phenylephrine Hydrochloride RS in *Medium*, where L_1 is the label claim of diphenhydramine hydrochloride in mg/Tablet; and L_2 is the label claim of phenylephrine hydrochloride in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 10–20 µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 10-cm; 5-µm packing L9

Flow rate: 2.0 mL/min

Injection volume: 100 µL

Run time: NLT 3 times the retention time of phenylephrine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.5–3.0 for both phenylephrine and diphenhydramine

Relative standard deviation: NMT 2.0% for both phenylephrine and diphenhydramine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of phenylephrine hydrochloride ($C_9H_{13}NO_2 \cdot HCl$) and diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) dissolved:

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

r_U = peak response of diphenhydramine or phenylephrine from the *Sample solution*

r_S = peak response of diphenhydramine or phenylephrine from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim of diphenhydramine hydrochloride (L_1) or phenylephrine hydrochloride (L_2) (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and phenylephrine hydrochloride ($C_9H_{13}NO_2 \cdot HCl$) is dissolved.

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

Delete the following:

▲▲ (RB 1-Nov-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at 20°–25°.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Diphenhydramine Hydrochloride RS

▲▲ (RB 1-Nov-2021)

USP Phenylephrine Hydrochloride RS

▲▲ (RB 1-Nov-2021)

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

Topic/Question	Contact	Expert Committee
DIPHENHYDRAMINE AND PHENYLEPHRINE HYDROCHLORIDES TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(5)

Current DocID: GUID-69AD0099-857D-44C1-B637-4B56CE13D780_3_en-US

DOI: https://doi.org/10.31003/USPNF_M8167_03_01

DOI ref: b6tbv