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Diphenhydramine Hydrochloride Capsules

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

DEFINITION

Diphenhydramine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$).

IDENTIFICATION

- **A. Identification—Organic Nitrogenous Bases ⟨181⟩:** The contents of the Capsules 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**

Buffer: 5.4 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	65	35
4	65	35
7	20	80
9	65	35
13	65	35

Diluent: Acetonitrile and *Buffer* (35:65)

System suitability solution: 0.1 mg/mL each of USP Diphenhydramine Related Compound A RS and USP Diphenhydramine Hydrochloride RS in *Diluent*

Standard solution: Nominally 0.07 mg/mL of USP Diphenhydramine Hydrochloride RS in *Diluent*

Sample stock solution: Weigh and combine the contents of NLT 20 Capsules. Transfer an accurately weighed portion of the combined Capsule contents, equivalent to about 50 mg of diphenhydramine hydrochloride, to a 100-mL volumetric flask. Dissolve in and dilute with water to volume, and filter. Alternatively, dissolve NLT 20 Capsules in water at 50° and pipet the solution equivalent to about 50 mg of diphenhydramine hydrochloride to a 100-mL volumetric flask. Dissolve in and dilute with water to volume, and filter.

Sample solution: 0.07 mg/mL of diphenhydramine hydrochloride in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for diphenhydramine related compound A and diphenhydramine are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between diphenhydramine and diphenhydramine related compound A, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) in the portion of Capsule contents taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Procedure for a pooled sample

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Injection volume: 50 µL

Standard solution: USP Diphenhydramine Hydrochloride RS in *Medium*, at a known concentration similar to that of the *Sample solution*

Sample solution: Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) 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. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Diphenhydramine Hydrochloride RS

USP Diphenhydramine Related Compound A RS

2-(Diphenylmethoxy)-*N*-methylethanamine hydrochloride.

$C_{16}H_{19}NO \cdot HCl$ 277.79

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

Topic/Question	Contact	Expert Committee
DIPHENHYDRAMINE HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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