

Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2022
Document Type: USP Monographs
DocId: GUID-350307BB-61B2-4090-8CEA-01374092629F_3_en-US
DOI: https://doi.org/10.31003/USPNF_M11815_03_01
DOI Ref: mp6dl

© 2025 USPC
Do not distribute

Diphenhydramine Hydrochloride Oral Powder

DEFINITION

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

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

Change to read:

• **PROCEDURE**

▲ (USP 1-Dec-2022)

Buffer: 5.52 g/L of monobasic potassium hexafluorophosphate in [water](#).▲ (USP 1-Dec-2022)

Solution A: ▲Add 0.5 mL of [phosphoric acid](#) per 1 L of *Buffer*.▲ (USP 1-Dec-2022)

Solution B: ▲For each liter, mix 700 mL of [acetonitrile](#) with 300 mL of *Buffer*. Add 0.5 mL of [phosphoric acid](#) per 1 L of this mixture.▲ (USP 1-Dec-2022)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
0.5	70	30
3.4	45	55
4.3	20	80
4.6	20	80
4.7	70	30
5.3	70	30

Diluent: ▲For each liter, mix 300 mL of [acetonitrile](#), 700 mL of [water](#), and 10 mL of [acetic acid, glacial](#).▲ (USP 1-Dec-2022)

System suitability solution: 0.0025 mg/mL each of [USP Diphenhydramine Hydrochloride RS](#), [USP Diphenhydramine Related Compound A RS](#), and [USP Benzhydrol RS](#) in *Diluent*. ▲Pass the solution through a polytetrafluoroethylene (PTFE) filter of 0.2-µm pore size.▲ (USP 1-Dec-2022)

Standard solution: 0.25 mg/mL of [USP Diphenhydramine Hydrochloride RS](#) in *Diluent*. ▲Pass the solution through a PTFE filter of 0.2-µm pore size.▲ (USP 1-Dec-2022)

Sample solution: Nominally 0.25 mg/mL of diphenhydramine hydrochloride in *Diluent* prepared as follows. Remove the contents of NLT 5 pouches as completely as possible, and weigh. Transfer a portion of the composite powder, equivalent to 50 mg of diphenhydramine hydrochloride, to a 200-mL volumetric flask. Dilute with *Diluent* to volume. ▲Pass the solution through a PTFE filter of 0.2-µm pore size.▲ (USP 1-Dec-2022)

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 2.1-mm × 5-cm; 1.7-μm packing [L1](#)

Column temperature: 40°

Flow rate: 0.9 mL/min

Injection volume: 2.5 μL

System suitability

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

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

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

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT ▲1.0%,▲ (USP 1-Dec-2022) *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 Oral Powder 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

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meets the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Buffer, Solution A, Solution B, Mobile phase, Diluent, System suitability solution, ▲▲ (USP 1-Dec-2022) and **Chromatographic system:** Proceed as directed in the Assay.

Standard solution: 0.5 μg/mL each of [USP Diphenhydramine Hydrochloride RS](#) and [USP Benzophenone RS](#), ▲1.25 μg/mL▲ (USP 1-Dec-2022) of [USP Diphenhydramine Related Compound A RS](#), and ▲2.5 μg/mL▲ (USP 1-Dec-2022) each of [USP Benzhydrol RS](#) and [USP Diphenhydramine N-Oxide RS](#) in *Diluent*

▲**Sample solution:** Nominally 250 μg/mL of diphenhydramine hydrochloride in *Diluent* from Oral Powder, prepared as directed in the Assay▲ (USP 1-Dec-2022)

System suitability

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

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

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

Relative standard deviation: NMT 5.0% for each peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of diphenhydramine related compound A, benzhydrol, benzophenone, or diphenhydramine *N*-oxide in the portion of Oral Powder taken:

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

r_U = peak response of diphenhydramine related compound A, benzhydrol, benzophenone, or diphenhydramine *N*-oxide from the *Sample solution*

r_S = peak response of diphenhydramine related compound A, benzhydrol, benzophenone, or diphenhydramine *N*-oxide from the *Standard solution*