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Dimenhydrinate Tablets

DEFINITION
Dimenhydrinate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$).

IDENTIFICATION
• **A.** The relative retention times for the 8-chlorotheophylline and diphenhydramine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.
• **B.** The UV spectra of the 8-chlorotheophylline and diphenhydramine peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Solution A: 10.0 g/L (equivalent to 13.8 mL/L) of triethylamine in water; adjusted with phosphoric acid to a pH of 2.5

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	82	18	1.2
2	82	18	1.2
15	50	50	1.2
20	20	80	2.0
32	20	80	2.0

Return to original conditions, and re-equilibrate the system for NLT 10 min.

Diluent: Acetonitrile and water (18:82)

System suitability solution: 0.114 mg/mL of USP Diphenhydramine Hydrochloride RS and 0.1 mg/mL of USP Diphenhydramine Related Compound A RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.1 mg/mL of USP Dimenhydrinate RS in *Diluent*. Sonicate to dissolve, if necessary.

Sample solution: Nominally 0.1 mg/mL of dimenhydrinate in *Diluent* prepared as follows. Transfer an amount equivalent to 10 mg of dimenhydrinate from finely powdered Tablets (NLT 5) to a 100-mL volumetric flask, and add about 80% of the final volume of *Diluent*. Sonicate for 5 min, and dilute with *Diluent* to volume. Centrifuge a portion of the resulting solution and use the supernatant. [Note—A centrifuge speed of 10,000 rpm for 10 min may be suitable.]

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

Mode: LC

Detector: UV 225 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: See *Table 1*.

Injection volume: 10 µL

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between diphenhydramine related compound A and diphenhydramine, *System suitability solution*

Tailing factor: NMT 2.0 for 8-chlorotheophylline and diphenhydramine, *Standard solution*

Relative standard deviation: NMT 2.0% for 8-chlorotheophylline and diphenhydramine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

Change to read:

• **8-Chlorotheophylline**

Solution A, Solution B, Mobile phase, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.05 mg/mL of USP 8-Chlorotheophylline RS in *Diluent*

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of 8-chlorotheophylline ($C_7H_7ClN_4O_2$) in the portion of Tablets taken:

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

r_U = peak response of 8-chlorotheophylline from the *Sample solution*

r_S = peak response of 8-chlorotheophylline from the *Standard solution*

C_S = concentration of USP 8-Chlorotheophylline RS in the *Standard solution* (mg/mL)

C_U = ▲determined concentration of dimenhydrinate in the *Sample solution*, as obtained in the *Assay* (mg/mL)▲ (ERR 1-Jun-2022)

Acceptance criteria: 43.4%–47.9%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: USP Dimenhydrinate RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium* to a concentration that is similar to the *Standard solution*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 276 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, if applicable

L = label claim (mg/Tablet)

Tolerances: NLT 75% (*Q*) of the labeled amount of dimenhydrinate $C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$ is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 2.28 µg/mL of USP Diphenhydramine Hydrochloride RS in *Diluent*

Sensitivity solution: 1.14 µg/mL of USP Diphenhydramine Hydrochloride RS in *Diluent*, from the *Standard solution*

Sample solution: Nominally 1.0 mg/mL of dimenhydrinate in *Diluent* prepare as follows. Transfer an amount equivalent to 20 mg of dimenhydrinate from finely powdered Tablets (NLT 5) to a 20-mL volumetric flask, and add about 40% of the final volume of *Diluent*. Sonicate for 5 min, and dilute with *Diluent* to volume. Centrifuge a portion of the resulting solution and use the supernatant. [Note—A centrifuge speed of 10,000 rpm for 10 min may be suitable.]

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between diphenhydramine related compound A and diphenhydramine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each individual impurity 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 dimenhydrinate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of diphenhydramine, 255.36

M_{r2} = molecular weight of diphenhydramine hydrochloride, 291.82

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Theophylline[a]	0.3	0.5
8-Chlorotheophylline	0.47	—
Diphenhydramine related compound A	0.95	0.5
Diphenhydramine	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	2.0

[a] 1,3-Dimethyl-3,7-dihydro-1*H*-purine-2,6-dione.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature. Protect from moisture.
- **USP Reference Standards** (11)

USP 8-Chlorotheophylline RS
USP Dimenhydrinate RS
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
DIMENHYDRINATE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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