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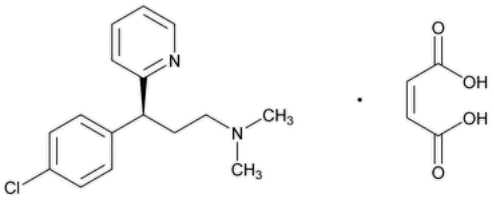
Dexchlorpheniramine Maleate



$C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$ 390.86

2-Pyridinepropanamine, γ-(4-chlorophenyl)-*N*,*N*-dimethyl-, (*S*)-, (*Z*)-2-butenedioate (1:1);

(+)-2-[*p*-Chloro-α-[2-(dimethylamino)ethyl]benzyl]pyridine maleate (1:1) CAS RN®: 2438-32-6; UNII: B10YD955QW.

DEFINITION

Dexchlorpheniramine Maleate, dried at 65° for 4 h, contains NLT 98.0% and NMT 102.0% of dexchlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

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

ASSAY

• **Procedure**

Solution A: 5.44 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0 ± 0.1.

Solution B: Acetonitrile

Diluent: Acetonitrile and *Solution A* (5:95)

System suitability stock solution: 0.02 mg/mL each of USP Pheniramine Maleate RS, USP Chlorpheniramine Related Compound B RS, and USP Chlorpheniramine Related Compound C RS in *Diluent*. Sonicate for 1 min.

System suitability solution: 0.5 mg/mL of USP Dexchlorpheniramine Maleate RS and 2 µg/mL each of USP Pheniramine Maleate RS, USP Chlorpheniramine Related Compound B RS, and USP Chlorpheniramine Related Compound C RS in *Diluent*, prepared as follows. Transfer 5.0 mg of USP Dexchlorpheniramine Maleate RS to a 10-mL volumetric flask, add 5 mL of *Diluent* and 1.0 mL of the *System suitability stock solution*, and dilute with *Diluent* to volume. Sonicate for 1 min.

Standard solution: 0.5 mg/mL of USP Dexchlorpheniramine Maleate RS in *Diluent*. Sonicate for 1 min.

Sample solution: 0.5 mg/mL of Dexchlorpheniramine Maleate in *Diluent*. Sonicate for 1 min.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
1	95	5
20	70	30
30	70	30
31	95	5
40	95	5

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times of maleic acid, chlorpheniramine related compound C, and dexchlorpheniramine are 0.18, 0.94, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between chlorpheniramine related compound C and dexchlorpheniramine; NLT 2.0 between chlorpheniramine related compound B and pheniramine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dexchlorpheniramine maleate ($C_{16}H_{19}ClN_2 \cdot C_4H_4O_4$) in the portion of Dexchlorpheniramine Maleate taken:

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

r_U = peak response for dexchlorpheniramine from the *Sample solution*

r_S = peak response for dexchlorpheniramine from the *Standard solution*

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

C_U = concentration of Dexchlorpheniramine Maleate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0%, previously dried at 65° for 4 h

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.2%

• **ORGANIC IMPURITIES**

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

Standard solution: 2.8 µg/mL of USP Dexchlorpheniramine Maleate RS in *Diluent*, equivalent to 2.0 µg/mL of dexchlorpheniramine. Sonicate for 1 min.

Sensitivity solution: 0.74 µg/mL of USP Pheniramine Maleate RS in *Diluent*

Sample solution: 0.5 mg/mL of Dexchlorpheniramine Maleate in *Diluent*. Sonicate for 1 min.

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between chlorpheniramine related compound C and dexchlorpheniramine; NLT 2.0 between chlorpheniramine related compound B and pheniramine, *System suitability solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Dexchlorpheniramine Maleate taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

C_S = concentration of dexchlorpheniramine in the *Standard solution* (mg/mL)

C_U = concentration of Dexchlorpheniramine Maleate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks having areas less than 0.05% of dexchlorpheniramine.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Maleic acid[a]	0.18	—	—
Chlorpheniramine related compound B[b]	0.49	—	—
Pheniramine	0.57	0.40	0.4
Chlorpheniramine related compound C[c]	0.97	—	—
Dexchlorpheniramine	1.0	—	—
Any other unspecified impurity	—	1.0	0.10
Total impurities	—	—	1

[a] Salt counter ion is included in the table for identification purposes only.

[b] Di(pyridin-2-yl)amine. Used only to establish system suitability.

[c] 3-(4-Chlorophenyl-*N*-methyl-3-(pyridin-2-yl)propan-1-amine. Used only to establish system suitability.

• **Enantiomeric Purity**

System suitability solution: 0.7 mg/mL of chlorpheniramine in 2-propanol prepared as follows. Dissolve 10.0 mg of USP Chlorpheniramine Maleate RS in 3 mL of water. Make the solution basic by adding a few drops of concentrated ammonium hydroxide, and shake with 5 mL of methylene chloride. Separate the layers and evaporate the lower, methylene chloride layer on a water bath until an oily residue is obtained. Dissolve the residue, and dilute with 2-propanol to 10.0 mL.

Standard stock solution: 0.7 mg/mL of dexchlorpheniramine in 2-propanol prepared as follows. Dissolve 10.0 mg of USP Dexchlorpheniramine Maleate RS in 3 mL of water. Make the solution basic by adding a few drops of concentrated ammonium hydroxide, and shake with 5 mL of methylene chloride. Separate the layers and evaporate the lower, methylene chloride layer on a water bath until an oily residue is obtained. Dissolve the residue, and dilute with 2-propanol to 10.0 mL.

Standard solution: 0.014 mg/mL of dexchlorpheniramine in 2-propanol from the *Standard stock solution*

Sample solution: 0.7 mg/mL of dexchlorpheniramine in 2-propanol prepared as follows. Dissolve 10.0 mg of Dexchlorpheniramine Maleate in 3 mL of water. Make the solution basic by adding a few drops of concentrated ammonium hydroxide, and shake with 5 mL of methylene chloride. Separate the layers and evaporate the lower, methylene chloride layer on a water bath until an oily residue is obtained. Dissolve the residue, and dilute with 2-propanol to 10.0 mL.

Mobile phase: *n*-Hexane, 2-propanol, and diethylamine (980:20:3)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 10-µm packing L51

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

[Note—Under these conditions the dexchlorpheniramine (*S*-enantiomer) elutes first.]

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between the *R*-enantiomer and dexchlorpheniramine (*S*-enantiomer)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the *R*-enantiomer in the portion of dexchlorpheniramine taken:

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

r_U = peak response of the *R*-enantiomer from the *Sample solution*

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

C_S = concentration of dexchlorpheniramine in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 2%

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation*⟨781S⟩

Sample solution: 50 mg/mL, in dimethylformamide

Acceptance criteria: +39.5° to +43.0°

- **pH** ⟨791⟩

Sample solution: 10 mg/mL

Acceptance criteria: 4.0–5.0

ADDITIONAL REQUIREMENTS

- **Loss on Drying** ⟨731⟩

Analysis: Dry a sample at 65° for 4 h.

Acceptance criteria: NMT 0.5%

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **USP Reference Standards** ⟨11⟩

USP Chlorpheniramine Maleate RS

USP Chlorpheniramine Related Compound B RS

Di(pyridin-2-yl)amine.

$C_{10}H_9N_3$ 171.20

USP Chlorpheniramine Related Compound C RS

3-(4-Chlorophenyl-*N*-methyl-3-(pyridin-2-yl)propan-1-amine maleate.

$C_{15}H_{17}ClN_2 \cdot C_4H_4O_4$ 376.83

USP Dexchlorpheniramine Maleate RS

USP Pheniramine Maleate RS

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

Topic/Question	Contact	Expert Committee
DEXCHLORPHENIRAMINE MALEATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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