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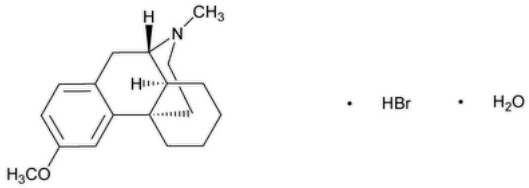
Dextromethorphan Hydrobromide



• HBr • H_2O

$C_{18}H_{25}NO \cdot HBr \cdot H_2O$ 370.32

Morphinan, 3-methoxy-17-methyl-, (9α,13α,14α)-, hydrobromide, monohydrate;

3-Methoxy-17-methyl-9α,13α,14α-morphinan hydrobromide monohydrate CAS RN®: 6700-34-1; UNII: 9D2RTI9KYH.

Anhydrous CAS RN®: 125-69-9; UNII: Z0CG3115FG. 352.32

DEFINITION

Dextromethorphan Hydrobromide contains NLT 98.0% and NMT 102.0% of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

Sample: Dry under vacuum over silica for 4 h.

Acceptance criteria: Meets the requirements

• **B.**

Buffer: 1.54 g of ammonium acetate in 1 L of water, adjusted with phosphoric acid to a pH of 4.1

Mobile phase: Methanol and *Buffer* (90:10)

Diluent: Methanol and water (90:10)

System suitability solution: 10 µg/mL of levomethorphan from USP Levomethorphan Solution RS and 10 mg/mL of USP Dextromethorphan Hydrobromide RS in *Diluent*

Standard solution: 10 µg/mL of USP Dextromethorphan Hydrobromide RS in *Diluent*

Sample solution: 10.0 mg/mL of Dextromethorphan Hydrobromide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: 225 nm

Column: 4.6-mm × 25-cm; 5-µm packing L88

Flow rate: 1 mL/min

Injection volume: 4 µL

System suitability

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

[Note—The relative retention times for dextromethorphan and levomethorphan are 1.0 and 1.28, respectively.]

Suitability requirements

Resolution: NLT 2.0 between dextromethorphan and levomethorphan, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of levomethorphan in the portion of Dextromethorphan Hydrobromide taken:

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

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

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

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

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

M_{r1} = molecular weight of dextromethorphan, 271.40

M_{r2} = molecular weight of dextromethorphan hydrobromide, 352.32

Acceptance criteria: NMT 0.10%

ASSAY

• **Procedure**

Mobile phase: 0.007 M docusate sodium and 0.007 M ammonium nitrate in acetonitrile and water (70:30), filtered and degassed. Dissolve the docusate sodium in the acetonitrile and water mixture before adding the ammonium nitrate. Adjust the solution with glacial acetic acid to a pH of 3.4.

Standard stock solution: 1 mg/mL of USP Dextromethorphan Hydrobromide RS in water

Standard solution: 0.1 mg/mL of USP Dextromethorphan Hydrobromide RS from *Standard stock solution* in *Mobile phase*

Sample stock solution: 1 mg/mL of Dextromethorphan Hydrobromide in water

Sample solution: 0.1 mg/mL of Dextromethorphan Hydrobromide from *Sample stock solution* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr$) in the portion of Dextromethorphan Hydrobromide taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Limit of Phenolic Compounds**

Sample: 5 mg of Dextromethorphan Hydrobromide

Analysis: To the *Sample* add 1 drop of 3 N hydrochloric acid, 1 mL of water, and 2 drops of ferric chloride TS. Add 2 drops of potassium ferricyanide TS, and observe after 2 min.

Acceptance criteria: No blue-green color develops.

• **Limit of *N,N*-Dimethylaniline**

Standard solution: Transfer 50 mg of *N,N*-dimethylaniline to a 100-mL volumetric flask. Add 70.0 mL of water, insert the stopper tightly, shake for 20 min using a mechanical wrist-action shaker or equivalent, and dilute with water to volume. Transfer 1.0 mL to a 100-mL volumetric flask, and dilute with water to volume. Transfer 1.0 mL of the resulting solution to a 25-mL volumetric flask, and add 19 mL of water.

Sample solution: Transfer 500 mg of Dextromethorphan Hydrobromide to a 25-mL volumetric flask. Add 19 mL of water and 1 mL of 3 N hydrochloric acid. Dissolve by warming on a steam bath, and cool.

Analysis: Add 2 mL of 1 N acetic acid and 1 mL of sodium nitrite solution (1 in 100) to the *Sample solution*, and dilute with water to volume. This solution shows no more color than the straw yellow to greenish yellow color of the *Standard solution* similarly treated.

Acceptance criteria: NMT 0.001% of *N,N*-dimethylaniline

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 10 mg/mL

  Acceptance criteria: 5.2–6.5

- **Water Determination** ⟨921⟩, *Method I, Method Ia*: 3.5%–5.5%

ADDITIONAL REQUIREMENTS

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

  USP Dextromethorphan Hydrobromide RS

  USP Levomethorphan Solution RS

  3-Methoxy-17-methylmorphinan.

  $C_{18}H_{25}NO$ 271.40

This solution contains 0.1 mg/mL of levomethorphan in methanol.

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

Topic/Question	Contact	Expert Committee
DEXTROMETHORPHAN HYDROBROMIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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