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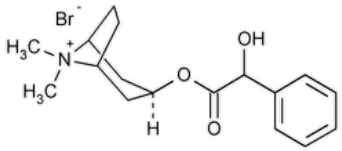
Homatropine Methylbromide



$C_{17}H_{24}BrNO_3$ 370.28

8-Azoniabicyclo[3.2.1]octane, 3-(hydroxyphenylacetyl)oxy-8,8-dimethyl-, bromide, *endo*-(±)-;
3α-Hydroxy-8-methyl-1α*H*,5α*H*-tropanium bromide mandelate;
(1*R*,3*s*,5*S*)-3-[[(2*RS*)-2-Hydroxy-2-phenylacetyl]oxy]-8,8-dimethyl-8-azoniabicyclo[3.2.1]octane bromide CAS RN®: 80-49-9; UNII: 68JRS2HC1C.

DEFINITION

Homatropine Methylbromide contains NLT 98.0% and NMT 102.0% of $C_{17}H_{24}BrNO_3$, calculated on the dried basis.

IDENTIFICATION

Change to read:

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

[Note—If differences are observed, dissolve the specimen and the Reference Standard separately in methanol, and recrystallize by adding dioxane to each solution.]

• **B.** **Identification Tests—General**, *Bromide* ⟨191⟩

Sample solution: 50 mg/mL in water

Acceptance criteria: Meets the requirements

ASSAY

Procedure

Solution A: 3.4 g/L of monobasic potassium phosphate and 5 g/L of 1-pentanesulfonic acid sodium salt in water. Adjust with a 330-g/L solution of phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile and *Solution A* (3:2)

Diluent: Acetonitrile and *Solution A* (9:41)

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	70	30
2	70	30
15	30	70
15.1	70	30
20	70	30

System suitability solution: 0.01 mg/mL each of USP Homatropine Methylbromide RS and USP Homatropine Hydrobromide RS in *Diluent*

Standard solution: 2.0 mg/mL of USP Homatropine Methylbromide RS in *Diluent*

Sample solution: 2.0 mg/mL of Homatropine Methylbromide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1.4 mL/min

Injection size: 5 µL

System suitability

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

[NOTE—The relative retention times for homatropine methylbromide and homatropine hydrobromide are 1.0 and 1.14, respectively.]

Suitability requirements

Resolution: NLT 2.5 between homatropine methylbromide and homatropine hydrobromide, *System suitability solution*

Tailing factor: NMT 1.5 for homatropine methylbromide peak, *System suitability solution*

Relative standard deviation: NMT 1%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{17}H_{24}BrNO_3$ in the portion of Homatropine Methylbromide taken:

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

r_U = peak response of Homatropine Methylbromide from the *Sample solution*

r_S = peak response of homatropine methylbromide from the *Standard solution*

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

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

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

IMPURITIES

Inorganic Impurities

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

Organic Impurities

- **Procedure**

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

Standard solution: 0.01 mg/mL of USP Homatropine Methylbromide RS in *Diluent*

Chromatographic system: Proceed as directed in the *Assay*, except for injection size.

Injection size: 10 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.5 between homatropine methylbromide and homatropine hydrobromide

Tailing factor: NMT 1.5 for the homatropine methylbromide peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Homatropine Methylbromide taken:

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

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

r_S = peak response of homatropine methylbromide from the *Standard solution*

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

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

[NOTE—Reporting level for impurities is 0.05%.]

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%

[NOTE—Disregard the peak due to the bromide ion that elutes close to the solvent peak at about 1 min.]

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Methyldehydrohomatropine bromide[a]	0.94	0.5
Homatropine methylbromide	1.0	—
Homatropine hydrobromide	1.1	0.5
Any other individual impurity	—	0.1

[a] (1*R*,3*s*,5*S*)-3-[[(2*RS*)-2-Hydroxy-2-phenylacetyl]oxy]-8,8-dimethyl-8-azoniabicyclo[3.2.1]oct-6-ene.

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 50 mg/mL in carbon dioxide-free water

  Acceptance criteria: 4.5–6.5

- **Loss on Drying** ⟨731⟩**:** Dry a sample at 105° to constant weight: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

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

  USP Homatropine Methylbromide RS

  USP Homatropine Hydrobromide RS

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

Topic/Question	Contact	Expert Committee
HOMATROPINE METHYLBROMIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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