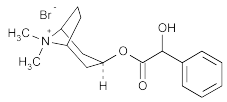
in mg, of $C_{16}H_{21}NO_3 \cdot HBr$ in the portion of Ophthalmic Solution taken by the formula:

$$0.5C(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Homatropine Hydrobromide RS in the *Standard preparation*; and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

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 [80-49-9].

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

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197K⟩**
  [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

Homatropine Methylbromide Tablets

» Homatropine Methylbromide Tablets contain not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of $C_{17}H_{24}BrNO_3$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Homatropine Methylbromide RS

Identification—Shake a quantity of finely powdered Tablets, equivalent to about 10 mg of homatropine methylbromide, with 15 mL of a mixture of equal volumes of methanol and water for 10 minutes, and filter. Evaporate the filtrate on a steam bath to dryness, and dry at 105 ° for 1 hour. The residue of homatropine methylbromide so obtained melts between 190° and 198 ° (see *Class I* under *Melting Range or Temperature* ⟨741⟩), the temperature at which distinct liquefaction of the specimen is first observed being taken as the beginning of melting.

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

*Procedure—*Determine the amount of $C_{17}H_{24}BrNO_3$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 258 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Homatropine Methylbromide RS in the same medium.

*Tolerances—*Not less than 75% *(Q)* of the labeled amount of $C_{17}H_{24}BrNO_3$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—

*Standard preparation—*Transfer about 25 mg of USP Homatropine Methylbromide RS, accurately weighed, to a 50-mL volumetric flask, add water to volume, and mix. Transfer 10.0 mL of this solution to a second 50-mL volumetric flask, dilute with water to volume, and mix. The concentration of USP Homatropine Methylbromide RS in the *Standard preparation* is about 100 µg per mL.

*Test preparation—*Transfer 1 finely powdered Tablet to a volumetric flask, suitably sized such that when the specimen is diluted to volume, the concentration is equivalent to about 100 µg of homatropine methylbromide per mL. Add water to about one-half of the volume of the flask, shake for 10 minutes, dilute with water to volume, mix, and filter, discarding the first 10 mL of filtrate. Use the subsequent filtrate as directed in the *Procedure*.

*Procedure—*Transfer 2.0 mL each of the *Standard preparation* and the *Test preparation* to separate glass-stoppered, 50-mL flasks. To each flask, add 0.1 mL of sodium hydroxide solution (1 in 10), and heat in a water bath at 80 ° for 15 minutes. Cool to room temperature, add 2.0 mL of 0.2 M ceric ammonium sulfate in 1 N sulfuric acid, and mix. To each flask, add 20.0 mL of *n*-hexane, and shake for 15 minutes. Decant the hexane layers into separate 1-cm cells, and concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 242 nm, with a suitable spectrophotometer, using *n*-hexane as the blank. Calculate the quantity, in mg, of $C_{17}H_{24}BrNO_3$ in the Tablet by the formula:

$$(TC / D)(A_U / A_S)$$

in which *T* is the labeled quantity, in mg, of homatropine methylbromide in the Tablet; *C* is the concentration, in µg per mL, of USP Homatropine Methylbromide RS in the *Standard preparation; D* is the concentration, in µg per mL, of the *Test preparation,* based upon the labeled quantity per Tablet and the extent of dilution; and A_U and A_S are the absorbances of the solutions from the *Test preparation* and the *Standard preparation,* respectively.

Assay—

*Standard preparation—*Transfer about 25 mg of USP Homatropine Methylbromide RS, accurately weighed, to a 50-mL volumetric flask, dissolve in water, dilute with water to volume, and mix.

*Assay preparation—*Weigh and finely powder not less than 20 Tablets. Weigh accurately a portion of the powder, equivalent to about 12.5 mg of homatropine methylbromide, and shake with 10 mL of water at frequent intervals during 30 minutes. Filter under reduced pressure through a sintered-glass crucible into a test tube placed in the suction flask under the filtering funnel, and wash under suction with several small portions of water. Transfer the contents of the test tube to a 25-mL volumetric flask, dilute with water to volume, and mix.

*Procedure—*Transfer 10.0 mL each of the *Standard preparation* and the *Assay preparation* to separate test tubes, to each add 1 mL of 5 N sulfuric acid and 2 mL of ammonium reineckate TS, shake gently but well, and allow to stand for 1 hour. Filter through a sintered-glass crucible with suction, using portions of the filtrate to transfer the precipitate completely to the filter, and wash it with three 2-mL portions of ice-cold water. Completely dissolve the precipitate by pouring over it 1-mL portions of acetone with the application of suction, receiving the solution in a 10-mL volumetric flask, add acetone to volume, and mix. Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 525 nm, with a suitable spectrophotometer,