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Methscopolamine Bromide Tablets

DEFINITION

Methscopolamine Bromide Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of methscopolamine bromide ($C_{18}H_{24}BrNO_4$).

IDENTIFICATION

• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

pH 7.3 dye–buffer solution: Prepare a solution containing, in each 500 mL, 200 mg of bromothymol blue, 3.2 mL of 0.1 N sodium hydroxide, 577.5 mg of citric acid monohydrate, and 6.3 mg of anhydrous dibasic sodium phosphate.

Standard solution: Prepare 0.025 mg/mL of USP Methscopolamine Bromide RS in water. Transfer 10 mL of this solution to a vessel containing 10 mL of chloroform and 10 mL of *pH 7.3 dye–buffer solution*. Shake vigorously for 3 min, centrifuge, and transfer 8 mL of the chloroform layer to a suitable container. Evaporate to dryness, and dissolve the residue in 1 mL of chloroform.

Sample solution: Finely powder 1 Tablet, and transfer an amount equivalent to 0.5 mg of methscopolamine bromide to a suitable container. Add 20 mL of water, heat for 5 min on a steam bath with frequent agitation, and centrifuge to obtain a clear supernatant. Transfer 10 mL of the supernatant to a vessel containing 10 mL of chloroform and 10 mL of *pH 7.3 dye–buffer solution*. Shake vigorously for 3 min, centrifuge, and transfer 8 mL of the chloroform layer to a suitable container. Evaporate to dryness, and dissolve the residue in 1 mL of chloroform.

Application volume: 50 µL

Developing solvent system: Butyl alcohol, water, and glacial acetic acid (4:5:1). Transfer a measured volume of the upper organic layer to a suitable container, and mix with a volume of alcohol equivalent to 20% of the volume of the organic layer.

Spray reagent: Potassium–bismuth iodide TS

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the solvent front to move three-fourths of the length of the plate, remove the plate from the developing chamber, mark the solvent front, and dry the plate under a current of air for 30 min. Spray the plate evenly with *Spray reagent*.

Acceptance criteria: The chromatogram of the *Sample solution* shows a bright orange spot on a yellow background corresponding in R_F value (0.25) to that of the *Standard solution*. [Note—Bromothymol blue produces a dark yellow spot at an R_F value of 0.8.]

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** A solution containing 5.16 g/L of sodium 1-hexanesulfonate monohydrate and 3.40 g/L of monobasic potassium phosphate in water, adjusted with 1 M phosphoric acid to a pH of 2.8

Solution A: *Buffer*

Solution B: Acetonitrile

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	87	13
3	87	13
10	81	19
12	81	19

Diluent: Acetonitrile and *Buffer* (13:87)

Standard solution: 0.125 mg/mL of USP Methscopolamine Bromide RS in *Diluent*

Sample solution: Place 10 Tablets in a 200-mL volumetric flask. Add about 180 mL of *Diluent*, and sonicate for 30 min. Shake by mechanical means for 30 min, dilute with *Diluent* to volume, and mix. Further dilute with *Diluent*, if needed, to obtain the solution with a nominal concentration of 0.125 mg/mL of methscopolamine bromide. Centrifuge for about 10 min and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 10.0-cm; monolithic packing L1

Column temperature: 40°

Flow rate: 3 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.0%▲2S *(USP41)*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of methscopolamine bromide ($C_{18}H_{24}BrNO_4$) in the portion of Tablets 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 Methscopolamine Bromide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

pH 3.0 phosphate buffer: 5.44 g/L of monobasic potassium phosphate in water, adjusted with 1 N phosphoric acid to a pH of 3.0

Mobile phase: Methanol and *pH 3.0 phosphate buffer* (1:3)

Standard solution: Solution of USP Methscopolamine Bromide RS in *Medium* having a known concentration similar to the one expected in the *Sample solution*

Sample solution: Use portions of the *Sample solution* that have been passed through a 0.45-µm PTFE filter.

Chromatographic system

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

Mode: LC

Detector: UV 204 nm

Column: 4.6-mm × 15-cm; packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of methscopolamine bromide ($C_{18}H_{24}BrNO_4$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of the *Medium*, 500 mL

L = label claim (mg/Tablet)

Acceptance criteria: NLT 80% (Q) of the labeled amount of methscopolamine bromide ($C_{18}H_{24}BrNO_4$) is dissolved.

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

IMPURITIES

Add the following:

▲• **Organic Impurities**

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

Scopolamine hydrobromide solution: 0.05 mg/mL of USP Scopolamine Hydrobromide RS in *Diluent*

System suitability solution: 1.0 mg/mL of USP Methscopolamine Bromide RS and 1.0 µg/mL of USP Scopolamine Hydrobromide RS in *Diluent*, from the *Scopolamine hydrobromide solution*

Standard stock solution: Prepare as directed for the *Standard solution* in the *Assay*.

Standard solution: 2.0 µg/mL of USP Methscopolamine Bromide RS in *Diluent* from the *Standard stock solution*

Sample solution

For Tablets that contain 2.5 mg of methscopolamine bromide: Place 20 Tablets in a 50-mL volumetric flask. Add 40–45 mL of *Diluent*, and sonicate for 30 min. Shake by mechanical means for 30 min, dilute with *Diluent* to volume, and mix. Centrifuge for about 10 min and use the clear supernatant.

For Tablets that contain 5 mg of methscopolamine bromide: Place 20 Tablets in a 100-mL volumetric flask. Add 80 mL of *Diluent*, and sonicate for 30 min. Shake by mechanical means for 30 min, dilute with *Diluent* to volume, and mix. Centrifuge for about 10 min and use the clear supernatant.

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1 between methscopolamine and scopolamine

Analysis

Samples: *Sample solution* and *Standard solution*

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

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

r_U = peak area of any impurity from the *Sample solution*

r_S = peak area of methscopolamine from the *Standard solution*

C_S = concentration of USP Methscopolamine Bromide RS in the *Standard solution* (µg/mL)

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tropic acid	0.4	2.4	0.2
Scopolamine hydrobromide[a]	0.9	—	—
Methscopolamine bromide	1.0	—	—
Methylatropine bromide[a,b]	1.2	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Apomethscopolamine bromide[a,c]	3.5	—	—
Any other individual impurity	—	1.0	0.2
Total impurities	—	—	0.5

[a] These impurities are controlled in the drug substance and are included in the table for identification only. They are not to be reported for the drug product and should not be included in the total impurities.

[b] (1*R*,3*r*,5*S*)-3-[(3-Hydroxy-2-phenylpropanoyl)oxy]-8,8-dimethyl-8-azabicyclo[3.2.1]octan-8-ium bromide.

[c] (1*R*,2*R*,4*S*,5*S*,7*s*)-9,9-Dimethyl-7-[(2-phenylacryloyl)oxy]-3-oxa-9-azatricyclo[3.3.1.$0^{2,4}$]nonan-9-ium bromide.

▲2S *(USP41)*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Methscopolamine Bromide RS

▲ USP Scopolamine Hydrobromide RS▲2S *(USP41)*

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

Topic/Question	Contact	Expert Committee
METHSCOPOLAMINE BROMIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

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