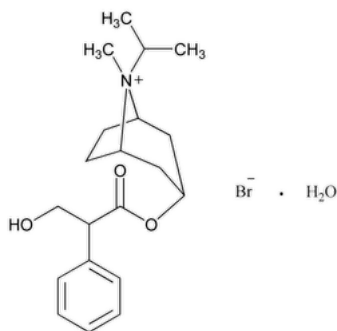


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Ipratropium Bromide

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-ipratropium-br-20230728.



$C_{20}H_{30}BrNO_3 \cdot H_2O$ 430.38

$C_{20}H_{30}BrNO_3$ 412.37

8-Azoniabicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, bromide, monohydrate(*endo,syn*)-, (±)-; (8*r*)-3*α*-Hydroxy-8-isopropyl-1*αH*,5*αH*-tropanium bromide (±)-tropate monohydrate;

(1*R*,3*r*,5*S*,8*r*)-3-[(3-Hydroxy-2-phenylpropanoyl)oxy]-8-isopropyl-8-methyl-8-azabicyclo[3.2.1]octan-8-ium bromide monohydrate CAS RN®: 66985-17-9; UNII: J697UZ2A9J..

Anhydrous CAS RN®: 22254-24-6; UNII: VJV4X1P2Z1..

DEFINITION

Ipratropium Bromide contains NLT 98.0% and NMT 102.0% of ipratropium bromide ($C_{20}H_{30}BrNO_3$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197M
- **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Bromide**

Sample solution: 10 mg/mL of Ipratropium Bromide in [water](#)

Acceptance criteria: Meets the requirements

- **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Solution A: 89 g/L of [dibasic sodium phosphate dihydrate](#) in [water](#)

Buffer: 14.3 g/L of [monobasic sodium phosphate dihydrate](#) and 2.0 g/L of [tetrapropylammonium chloride](#) in [water](#). Adjust with *Solution A* to a pH of 5.5.

Mobile phase: [Methanol](#) and *Buffer* (13:87). [NOTE—Do not use the *Mobile phase* after 36 h.]

System suitability solution: 0.5 mg/mL of [USP Ipratropium Bromide RS](#) and 0.1 mg/mL of [USP Ipratropium Bromide Related Compound C RS](#) in *Mobile phase*

Standard solution: 0.5 mg/mL of [USP Ipratropium Bromide RS](#) in *Mobile phase*

Sample solution: 0.5 mg/mL of Ipratropium Bromide in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 220 nm

Column: 3.9-mm × 15-cm; 4-μm packing [L1](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 5 μL

Run time: NLT 6 times the retention time of ipratropium

System suitability

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

[NOTE—The relative retention times for ipratropium bromide related compound C and ipratropium are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4 between ipratropium bromide related compound C and ipratropium, *System suitability solution*

Tailing factor: NMT 2.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ipratropium bromide ($C_{20}H_{30}BrNO_3$) in the portion of Ipratropium Bromide taken:

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

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

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

C_S = concentration of [USP Ipratropium Bromide RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Ipratropium Bromide 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 IPRATROPIUM BROMIDE RELATED COMPOUND A**

Buffer: 3.9 g/L of [ammonium acetate](#) in [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (90:10)

Diluent: 0.01 N [hydrochloric acid](#)

Standard stock solution: 10 µg/mL of [USP Ipratropium Bromide Related Compound A RS](#) in *Diluent*

Standard solution: 0.1 µg/mL of [USP Ipratropium Bromide Related Compound A RS](#) from *Standard stock solution* in *Diluent*

Sensitivity solution: 0.01 µg/mL of [USP Ipratropium Bromide Related Compound A RS](#) from *Standard solution* in *Diluent*

Sample solution: 100 µg/mL of Ipratropium Bromide in *Diluent*

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: Mass spectrometer

Ionization: Electrospray positive ion. [NOTE—Adjustments to the electrospray source parameters including the probe temperature, cone voltage, and capillary voltage may be necessary to meet *Suitability requirements*.]

Acquisition mode: Selected ion monitoring (SIM) mode with m/z of 184.2 for the ipratropium related compound A cation

Column: 3.0-mm × 5-cm; 5-µm packing [L9](#)

Column temperature: 20°

Flow rate: 0.6 mL/min

Injection volume: 5 µL

Run time: NLT 1.5 times the retention time of ipratropium bromide related compound A

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 10.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ipratropium bromide related compound A in the portion of Ipratropium Bromide taken:

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

r_U = peak response of ipratropium bromide related compound A from the *Sample solution*

r_S = peak response of ipratropium bromide related compound A from the *Standard solution*

C_S = concentration of [USP Ipratropium Bromide Related Compound A RS](#) in the *Standard solution* (µg/mL)

C_U = concentration of Ipratropium Bromide in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.10%

• **ORGANIC IMPURITIES**

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