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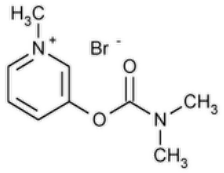
Pyridostigmine Bromide



$C_9H_{13}BrN_2O_2$ 261.12

Pyridinium, 3-[[(dimethylamino)carbonyl]oxy]-1-methyl-, bromide;

3-Hydroxy-1-methylpyridinium bromide dimethylcarbamate CAS RN®: 101-26-8; UNII: KVI301NA53.

DEFINITION

Pyridostigmine Bromide contains NLT 98.0% and NMT 102.0% of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K▲ (CN 1-May-2020)
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Bromide***

  Sample solution: 20 mg/mL of Pyridostigmine Bromide

  Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

  Buffer: 4.3 g/L of sodium dodecyl sulfate in water. Adjust with phosphoric acid to a pH of 2.0.

  Mobile phase: Acetonitrile and *Buffer* (32:68)

  System suitability solution: 2 µg/mL each of USP Pyridostigmine Bromide RS, USP Pyridostigmine Related Compound A RS, and USP Pyridostigmine Related Compound B RS in *Mobile phase*

  Standard solution: 0.3 mg/mL of USP Pyridostigmine Bromide RS in *Mobile phase*

  Sample solution: 0.3 mg/mL of Pyridostigmine Bromide in *Mobile phase*

  Chromatographic system

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

  Mode: LC

  Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

  Column: 4.6-mm × 15-cm; 5-µm packing L1

  Flow rate: 1 mL/min

  Injection volume: 20 µL

  Run time: NLT 2.6 times the retention time of pyridostigmine

  System suitability

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

  Suitability requirements

  Resolution: NLT 1.5 between pyridostigmine related compound A and pyridostigmine, *System suitability solution*

  Tailing factor: NMT 2.0, *Standard solution*

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

  Analysis

  Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pyridostigmine bromide ($C_9H_{13}BrN_2O_2$) in the portion of Pyridostigmine Bromide 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 Pyridostigmine Bromide RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

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

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.2 µg/mL of USP Pyridostigmine Bromide RS in *Mobile phase*

Standard solution: 0.6 µg/mL each of USP Pyridostigmine Bromide RS, USP Pyridostigmine Related Compound A RS, and USP Pyridostigmine Related Compound B RS in *Mobile phase*

Sample solution: 1000 µg/mL of Pyridostigmine Bromide in *Mobile phase*

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between pyridostigmine related compound A and pyridostigmine, *Standard solution*

Relative standard deviation: NMT 5.0% for all the three peaks, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pyridostigmine related compound A and pyridostigmine related compound B in the portion of Pyridostigmine Bromide taken:

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

r_U = peak response of pyridostigmine related compound A or pyridostigmine related compound B from the *Sample solution*

r_S = peak response of pyridostigmine related compound A or pyridostigmine related compound B from the *Standard solution*

C_S = concentration of USP Pyridostigmine Related Compound A RS or USP Pyridostigmine Related Compound B RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of each unspecified impurity in the portion of Pyridostigmine Bromide taken:

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

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

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.02%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pyridostigmine related compound B	0.78	0.06
Pyridostigmine related compound A	0.92	0.06
Pyridostigmine	1.0	—
Any individual unspecified impurity	—	0.06
Total impurities	—	0.5

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 100° for 4 h in a suitable vacuum drying tube, using phosphorus pentoxide as the desiccant.

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Pyridostigmine Bromide RS

USP Pyridostigmine Related Compound A RS

Pyridin-3-yl dimethylcarbamate.

$C_8H_{10}N_2O_2$ 166.18

USP Pyridostigmine Related Compound B RS

3-Hydroxy-1-methylpyridin-1-ium bromide.

C_6H_8BrNO 190.04

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

Topic/Question	Contact	Expert Committee
PYRIDOSTIGMINE BROMIDE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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