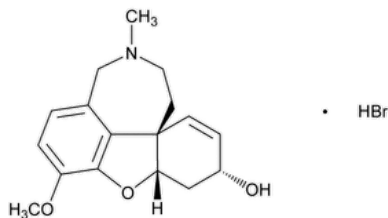


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Galantamine Hydrobromide



$C_{17}H_{21}NO_3 \cdot HBr$ 368.27
6*H*-Benzofuro[3a,3,2-*ef*][2]benzazepin-6-ol, 4a,5,9,10,11,12-hexahydro-3-methoxy-11-methyl-, hydrobromide, (4a*S*,6*R*,8a*S*)-;
(4a*S*,6*R*,8a*S*)-3-Methoxy-11-methyl-4a,5,9,10,11,12-hexahydro-6*H*-benzofuro[3a,3,2-*ef*][2]benzazepin-6-ol hydrobromide;
(4a*S*,6*R*,8a*S*)-3-Methoxy-11-methyl-4a,5,9,10,11,12-hexahydro-6*H*-benzo[2,3]benzofuro[4,3-*cd*]azepin-6-ol hydrobromide CAS RN[®]: 1953-04-4.

DEFINITION
Galantamine Hydrobromide contains NLT 98.0% and NMT 102.0% of galantamine hydrobromide ($C_{17}H_{21}NO_3 \cdot HBr$), calculated on the dried basis.

IDENTIFICATION

- A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** 197K
[NOTE—Specimens are to be prepared using undried [USP Galantamine Hydrobromide RS](#) and the test article.]
- B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the Assay.
- C. [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Bromide](#)**
Sample solution: 7 mg/mL of Galantamine Hydrobromide in [water](#)
Acceptance criteria: Meets the requirements of test *B*

ASSAY

- PROCEDURE**
Diluent: [Methanol](#) and [water](#) (5:95)
Buffer: 0.79 g/L of [dibasic sodium phosphate dihydrate](#) and 2.46 g/L of [monobasic sodium phosphate anhydrous](#) in [water](#)
Solution A: [Methanol](#) and *Buffer* (5:95)
Solution B: [Acetonitrile](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
6.0	100	0
20.0	95	5
35.0	85	15
50.0	80	20

Time (min)	Solution A (%)	Solution B (%)
51.0	40	60
55.0	40	60
56.0	100	0
60.0	100	0

System suitability solution: 1 mg/mL of [USP Galantamine Hydrobromide Related Compounds Mixture RS](#) in *Diluent*

Standard solution: 1.0 mg/mL of [USP Galantamine Hydrobromide RS](#) in *Diluent*

Sample solution: 1.0 mg/mL of Galantamine Hydrobromide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 10-cm; 3.5-μm packing [L1](#)

Column temperature: 55°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

System suitability

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

[NOTE—For relative retention times, see [Table 2](#).]

Suitability requirements

Resolution: NLT 4.5 between galantamine and 6S-galantamine, *System suitability solution*

Tailing factor: NMT 2.0 for galantamine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of galantamine hydrobromide ($C_{17}H_{21}NO_3 \cdot HBr$) in the portion of Galantamine Hydrobromide 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 Galantamine Hydrobromide RS](#) in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Delete the following:

▲ **LIMIT OF PALLADIUM:** Proceed as directed below or in [Elemental Impurities—Procedures \(233\)](#).

[NOTE—Perform this test only if palladium is a known inorganic impurity of the manufacturing process.]

Standard stock solution: 20 mg/L of palladium reference stock solution (NIST traceable) in [water](#)

Aqua regia: Under a hood, carefully mix [hydrochloric acid](#) and [nitric acid](#) (3:1).

[NOTE—To obtain each of the required Standard solutions, it is recommended that the required volume of *Standard stock solution* be mixed with a volume of *Aqua regia* equivalent to 5% of the final volume, followed by [water](#).]

Standard solution A: 0.2 mg/L of palladium from the *Standard stock solution* in [water](#)

Standard solution B: 1.0 mg/L of palladium from the *Standard stock solution* in [water](#)

Standard solution C: 2.0 mg/L of palladium from the *Standard stock solution* in [water](#)

System suitability solution: Prepare a solution having a known concentration of 1.6 mg/L of palladium, as directed for the Standard solutions.

Sample solution: Weigh 1 g of Galantamine Hydrobromide. Transfer the sample to an appropriate digestion system, and digest using appropriate acids (e.g., [nitric acid](#) or mixtures of [nitric acid](#) and [sulfuric acid](#) and mixtures of [nitric acid](#) and [hydrogen peroxide](#)). After digestion, heat to dryness. Add 0.5 mL of *Aqua regia* and 2 mL of [water](#). Warm gently to dissolve any residue. Allow to cool. Transfer quantitatively to a 10-mL volumetric flask, and dilute with [water](#) to volume.

Digestion blank solution: Prepare this solution following the procedure for the *Sample solution*, without the test article.

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectroscopy (flame)

Analytical wavelength: 247.6 nm (0.2-nm slit width)

Lamp: Palladium hollow-cathode

Blank solution: Dilute 5 mL of *Aqua regia* with [water](#) to 100 mL.

System suitability

Samples: *Standard solution A, Standard solution B, Standard solution C, System suitability solution, and Blank solution*

Using the Standard solutions and *Blank solution*, construct a calibration curve.

Suitability requirements

Correlation coefficient: NLT 0.99

Recovery: 87.5%–112.5%, *System suitability solution*. [NOTE—Recovery is calculated using the calibration curve.]

Analysis

Samples: *Sample solution and Digestion blank solution*

Calculate the concentration of palladium in the *Sample solution*, using the calibration curve, corrected for the *Digestion blank solution* and the sample weight. Calculate the amount of palladium in the Galantamine Hydrobromide taken to prepare the *Sample solution*.

Acceptance criteria: NMT 10 ppm▲ (USP 1-May-2022)

• ORGANIC IMPURITIES

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

Sensitivity solution: 0.5 µg/mL of [USP Galantamine Hydrobromide RS](#) in *Diluent*

Standard solution: 5.0 µg/mL of [USP Galantamine Hydrobromide RS](#) in *Diluent*

Sample solution: 1000 µg/mL of Galantamine Hydrobromide in *Diluent*

System suitability

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

[NOTE—For relative retention times, see [Table 2](#).]

Suitability requirements

Resolution: NLT 4.5 between galantamine and 6S-galantamine, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

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

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of each impurity in the portion of Galantamine Hydrobromide taken, on the dried basis:

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

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

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

C_S = concentration of [USP Galantamine Hydrobromide RS](#) in the *Standard solution* (µg/mL)

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

F = relative response factor (see [Table 2](#))

LOD = loss on drying (%)

Acceptance criteria: See [Table 2](#). Disregard the bromide peak near the void volume. The reporting threshold is 0.05%.

Table 2