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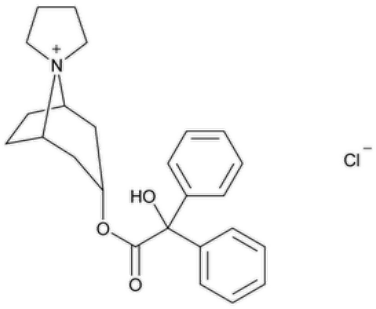
Trospium Chloride



$C_{25}H_{30}ClNO_3$ 427.96

Spiro [8-azoniabicyclo[3.2.1]octane-8,1'-pyrrolidinium], 3-[(hydroxydiphenylacetyl)oxy]-, chloride, (1*R*,3*r*,5*S*);

(1*R*,3*r*,5*S*)-3-[(Hydroxydiphenylacetyl)oxy]spiro[8-azoniabicyclo[3.2.1]octane-8,1'-pyrrolidinium] chloride CAS RN®: 10405-02-4; UNII: 1E6682427E.

DEFINITION

Trospium Chloride contains NLT 98.0% and NMT 102.0% of trospium chloride ($C_{25}H_{30}ClNO_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** **Identification Tests—General, *Chloride* ⟨191⟩:** 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**

Mobile phase: Acetonitrile, triethylamine, phosphoric acid, and water (300:1:3:700)

System suitability solution: 0.01 mg/mL of USP Trospium Chloride RS and 0.003 mg/mL each of USP Trospium Chloride Related Compound A RS and USP Trospium Chloride Related Compound B RS in *Mobile phase*

Standard solution: 0.6 mg/mL of USP Trospium Chloride RS in *Mobile phase*

Sample solution: 0.6 mg/mL of Trospium Chloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1. (Alternatively, a 4.6-mm × 25-cm column that contains 5-µm packing L7 may be used.)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 3 between trospium chloride related compound B and trospium, *System suitability solution*

Relative standard deviation: NMT 0.85% for six replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of trospium chloride ($C_{25}H_{30}ClNO_3$) in the portion of Trospium Chloride 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 Trospium Chloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Trospium Chloride in the *Sample solution* (mg/mL)

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

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Sample: 1 g

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: 0.01 mg/mL of USP Trospium Chloride RS and 0.003 mg/mL each of USP Trospium Chloride Related Compound A RS and USP Trospium Chloride Related Compound B RS in *Mobile phase*

Sample solution: 3.0 mg/mL of Trospium Chloride in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*, except for the following parameters.

Injection volume: 20 µL

Run time: NLT 3 times the retention time of trospium

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3 between trospium chloride related compound B and trospium

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of trospium chloride related compound A and trospium chloride related compound B in the portion of Trospium Chloride taken:

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

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

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

C_S = concentration of trospium chloride related compound A or trospium chloride related compound B in the *Standard solution* (mg/mL)

C_U = concentration of Trospium Chloride in the *Sample solution* (mg/mL)

Calculate the percentage of any other individual impurity in the portion of Trospium Chloride 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 trospium chloride related compound B from the *Standard solution*

C_S = concentration of USP Trospium Chloride Related Compound B RS in the *Standard solution* (mg/mL)

C_U = concentration of Trospium Chloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. The reporting level for impurities is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Trospium chloride related compound B[a]	0.7–0.8	0.15
Trospium	1.0	—
Benzilic acid (trospium chloride related compound A)	1.9–2.8	0.15
Any other individual impurity	—	0.10
Total impurities	—	0.5

[a] (1*R*,3*r*,5*S*)-8-Azabicyclo[3.2.1]octan-3-yl hydroxydiphenylacetate.

- **Limit of Trospium Chloride Related Compound C**

Mobile phase: Acetonitrile, anhydrous formic acid, and water (20:0.2:80)

Diluent: Water

Standard solution: 0.1 mg/mL of USP Trospium Chloride Related Compound C RS in *Diluent*, using sonication to dissolve

Sample solution: 100.0 mg/mL of Trospium Chloride in *Diluent*, using sonication to dissolve. [Note—The solution is stable for 12 h.]

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 0.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0% for six replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of trospium chloride related compound C in the portion of Trospium Chloride taken:

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

r_U = peak response of trospium chloride related compound C from the *Sample solution*

r_S = peak response of trospium chloride related compound C from the *Standard solution*

C_S = concentration of USP Trospium Chloride Related Compound C RS in the *Standard solution* (mg/mL)

C_U = concentration of Trospium Chloride in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.1%

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry the sample at 105° to constant weight.

Acceptance criteria: NMT 0.5%

- **pH ⟨791⟩**

Sample solution: 10 mg/mL of Trospium Chloride in carbon dioxide-free water

Acceptance criteria: 5.0–7.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Protect from light. Store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Trospium Chloride RS

USP Trospium Chloride Related Compound A RS

Benzilic acid.

$C_{14}H_{12}O_3$ 228.24

USP Trospium Chloride Related Compound B RS

Nortropane benzilate;
(1*R*,3*r*,5*S*)-8-Azabicyclo[3.2.1]octan-3-yl hydroxydiphenylacetate.

$C_{21}H_{23}NO_3$ 337.41

USP Trospium Chloride Related Compound C RS

Azoniaspironortropanol chloride;
(1*R*,3*r*,5*S*)-3-Hydroxyspiro[8-azoniabicyclo[3.2.1]octane-8,1'-pyrrolidinium] chloride, or (1*R*,3*r*,5*S*)-3-Hydroxyspiro[bicyclo[3.2.1]octane-8,1'-pyrrolidin]-1'-ium chloride.

$C_{11}H_{20}ClNO$ 217.74

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

Topic/Question	Contact	Expert Committee
TROSPIUM CHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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