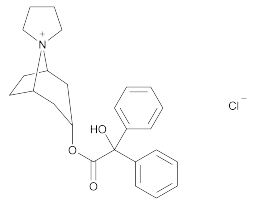
Trospium Chloride



$C_{25}H_{30}ClNO_3$ 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 [10405-02-4].

DEFINITION

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

IDENTIFICATION

- **A. Infrared Absorption** ⟨**197K**⟩
- **B. Identification Tests—General,** *Chloride* ⟨**191**⟩**:** Meets the requirements

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 size: 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 $C_{25}H_{30}ClNO_3$ 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

Inorganic Impurities

- **Residue on Ignition** ⟨**281**⟩

Sample: 1 g

Acceptance criteria: NMT 0.1%

Organic Impurities

- **Procedure 1**

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 size: 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)

[NOTE—Reporting level for impurities is 0.05%.]

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.5%

Impurity 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

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

- **PROCEDURE 2: LIMIT OF TROSPIUM CHLORIDE RELATED COMPOUND C**

System suitability solution: 0.5 mg/mL of USP Trospium Chloride RS and 0.5 mg/mL of USP Trospium Chloride Related Compound C RS in methanol
Standard solution: 0.1 mg/mL of USP Trospium Chloride Related Compound C RS in methanol
Sample solution: 100 mg/mL of Trospium Chloride in methanol
Chromatographic system
(See *Chromatography* ⟨621⟩*, Thin-Layer Chromatography*.)
Mode: TLC
Plate: 0.25-mm layer of chromatographic silica gel mixture
Application volume: 10 µL
Developing distance: Two-thirds of the length of the plate
Developing solvent system: Acetonitrile, glacial acetic acid, and hydrochloric acid (45: 1: 3.5)
Spray reagent 1: Use Dragendorff's TS.
Spray reagent 2: 5 g/L of sodium nitrite in water
System suitability
Sample: *System suitability solution*
Suitability requirements
Resolution: The chromatogram shows two clearly visible and separated spots.
Analysis
Samples: *Standard solution* and *Sample solution*
Allow the spots to dry in a current of warm air until the odor of acetic acid is no longer perceptible. Spray the plate with *Spray reagent 1*, and subsequently with *Spray reagent 2*.
Acceptance criteria: Any spot from the *Sample solution* corresponding to trospium chloride related compound C is not more intense than the corresponding spot from the *Standard solution* (0.1%).

SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry the sample at 105° to constant weight: it loses NMT 0.5% of its weight.
- **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 [76-93-7]
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.
$C_{11}H_{20}ClNO$ 217.74

Crystallized Trypsin

» Crystallized Trypsin is a proteolytic enzyme crystallized from an extract of the pancreas of healthy bovine or porcine animals, or both. When assayed as directed herein, it contains not less than 2500 USP Trypsin Units in each mg, calculated on the dried basis, and not less than 90.0 percent and not more than 110.0 percent of the labeled potency.

NOTE—Determine the suitability of the substrates and check the adjustment of the spectrophotometer by performing the *Assay* using USP Crystallized Trypsin Reference Standard.

Packaging and storage—Preserve in tight containers, and avoid exposure to excessive heat.

USP Reference standards ⟨11⟩**—**
USP Trypsin Crystallized RS

Solubility test—An amount, equivalent to 500,000 USP Trypsin Units, is soluble in 10 mL of water and in 10 mL of saline TS.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Salmonella* species.

Loss on drying ⟨731⟩**—**Dry it in vacuum at 60° for 4 hours: it loses not more than 5.0% of its weight.

Residue on ignition ⟨281⟩: not more than 2.5%.

Limit of chymotrypsin—

0.067 M Phosphate buffer, pH 7.0—Dissolve 4.54 g of monobasic potassium phosphate in water to make 500 mL of solution. Dissolve 4.73 g of anhydrous dibasic sodium phosphate in water to make 500 mL of solution. Mix 38.9 mL of the monobasic potassium phosphate solution with 61.1 mL of dibasic sodium phosphate solution. Adjust dropwise, if necessary, with dibasic sodium phosphate solution to a pH of 7.0.

Substrate solution—Dissolve 23.7 mg of N-acetyl-L-tyrosine ethyl ester, suitable for use in determining chymotrypsin, in about 50 mL of *0.067 M Phosphate buffer, pH 7.0* with warming. When cool, dilute with additional pH 7.0 buffer to 100 mL. (*Substrate solution* may be stored in the frozen state and used after thawing; it is important, however, to freeze immediately after preparation.)

Crystallized Trypsin solution—Dissolve a sufficient quantity of Crystallized Trypsin, accurately weighed, in 0.0010 N hydrochloric acid to obtain a solution containing 650 USP Trypsin Units per mL.

Procedure—Conduct the test in a suitable spectrophotometer equipped to maintain a temperature of 25 ± 0.1° in the cell compartment. Determine the temperature in the reaction cell before and after the measurement of absorbance to ensure that the temperature does not change by more than 0.5°. Pipet 200 µL of 0.0010 N hydrochloric acid and 3.0 mL of the *Substrate solution* into a 1-cm cell. Place this cell in the spectrophotometer, and adjust the instrument so that the absorbance reads 0.200 at 237 nm. Pipet 200 µL of *Crystallized Trypsin solution*