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Trihexyphenidyl Hydrochloride Tablets

DEFINITION

Trihexyphenidyl Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO \cdot HCl$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** 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: 1.4 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 4.0. Pass the solution through a suitable filter of 0.22-µm pore size.

Solution B: 0.5 mL of phosphoric acid in 1 L of acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
20	60	40
22	60	40
22.1	95	5
24	95	5

Diluent: Methanol and water (80:20)

Standard solution: 0.1 mg/mL of USP Trihexyphenidyl Hydrochloride RS in *Diluent*

Sample stock solution: Nominally 0.5 mg/mL of trihexyphenidyl hydrochloride prepared as follows. Transfer a suitable amount of Tablets (NLT 10), equivalent to 50 mg of trihexyphenidyl hydrochloride, to a 100-mL volumetric flask. Add 10 mL of 0.1 N hydrochloric acid and sonicate. Add another 80 mL of *Solution B* and sonicate again. Dilute with *Solution B* to volume. Centrifuge and use the supernatant.

Sample solution: Nominally 0.1 mg/mL of trihexyphenidyl hydrochloride in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. For *Identification* test *A*, use a diode array detector in the range of 190–300 nm.

Column: 2.1-mm × 10-cm; 2.6-µm packing L1

Column temperature: 30°

Flow rate: 0.3 mL/min

Injection volume: 3.0 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 3.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO \cdot HCl$) in the portion of Tablets taken:

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

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

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

C_S = concentration of USP Trihexyphenidyl Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of trihexyphenidyl hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: pH 4.5 acetate buffer, prepared by mixing 3.0 g of sodium acetate and 1.7 mL of glacial acetic acid with water to obtain 1000 mL of solution with a pH of 4.50 ± 0.05; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: A known concentration of USP Trihexyphenidyl Hydrochloride RS in *Medium*

Sample solution: Filtered portion of the solution under test

Bromocresol green solution: Dissolve 250 mg of bromocresol green in a mixture of 15 mL of water and 5 mL of 0.1 N sodium hydroxide, dilute with *Medium* to 500 mL, and mix. Extract 250 mL portions of this solution with two 100 mL portions of chloroform and discard the chloroform extracts.

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: 415 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Transfer an accurately measured volume of the *Sample solution*, estimated to contain about 50 µg of trihexyphenidyl hydrochloride, to a 50-mL centrifuge tube. Transfer an equal, accurately measured volume of the *Standard solution* to a second 50-mL centrifuge tube. Transfer an equal, accurately measured volume of *Medium* to a third 50-mL centrifuge tube to provide a *Blank*. Add 5 mL of the *Bromocresol green solution* and 10.0 mL of chloroform to each tube, insert the stoppers into the tubes, and shake vigorously for NLT 20 s. Centrifuge the mixtures to separate the layers. Aspirate and discard the upper aqueous layers. Filter each chloroform layer through a separate phase-separating filter paper. Determine the amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO \cdot HCl$) dissolved from the absorbance of the filtrate from the *Sample solution* in comparison with that from the *Standard solution*. The filtrate from the *Blank* is used to set the instrument.

Tolerances: NLT 75% (*Q*) of the labeled amount of trihexyphenidyl hydrochloride ($C_{20}H_{31}NO \cdot HCl$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

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

System suitability solution: 0.1 mg/mL of USP Trihexyphenidyl Hydrochloride RS and 0.01 mg/mL of USP Trihexyphenidyl Related Compound A RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Trihexyphenidyl Hydrochloride RS in *Diluent*

Sample solution: Nominally 1 mg/mL of trihexyphenidyl hydrochloride ▲▲ (ERR 1-Apr-2021) prepared as follows. Transfer a suitable amount of Tablets (NLT 10), equivalent to 100 mg of trihexyphenidyl hydrochloride, to a 100-mL volumetric flask. Add 10 mL of 0.1 N hydrochloric acid and sonicate. Add another 80 mL of *Solution B* and sonicate again. Dilute with *Solution B* to volume. Centrifuge and use the supernatant.

System suitability

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

[NOTE—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 50, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*

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

C_S = concentration of USP Trihexyphenidyl Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of trihexyphenidyl hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.10%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Trihexyphenidyl related compound A[a]	0.4	—
Trihexyphenidyl	1.0	—
Any individual unspecified degradation product	—	1
Total degradation products	—	2

[a] This impurity included for identification only and is not to be included in the calculation of total degradation products.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Trihexyphenidyl Hydrochloride RS

USP Trihexyphenidyl Related Compound A RS

1-Phenyl-3-(piperidin-1-yl)propan-1-one hydrochloride.

$C_{14}H_{19}NO \cdot HCl$ 253.77

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

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

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