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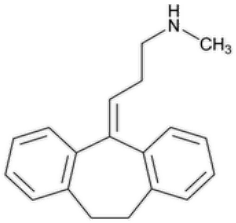
Nortriptyline Hydrochloride



• HCl

$C_{19}H_{21}N \cdot HCl$ 299.84

1-Propanamine, 3-(10,11-dihydro-5*H*-dibenzo[*a,d*] cyclohepten-5-ylidene)-*N*-methyl-, hydrochloride;

10,11-Dihydro-*N*-methyl-5*H*-dibenzo[*a,d*]cycloheptene-Δ^{5},γ-propylamine hydrochloride CAS RN®: 894-71-3; UNII: 00FN6IH15D.

DEFINITION

Nortriptyline Hydrochloride contains NLT 97.0% and NMT 101.5% of nortriptyline hydrochloride ($C_{19}H_{21}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B.** The retention time 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, Chloride*:** Meets the requirements of the test for amine hydrochlorides

ASSAY

• **Procedure**

Solution A: Phosphoric acid and water (1:10)

Buffer: Dissolve 1.4 g of dibasic sodium phosphate in 1 L of water, and adjust with *Solution A* to a pH of 7.7.

Mobile phase: Methanol and *Buffer* (70:30)

Standard solution: 0.2 mg/mL of USP Nortriptyline Hydrochloride RS in *Mobile phase*

Sample solution: 0.2 mg/mL of Nortriptyline Hydrochloride 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 L7

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 1.3 times the retention time of nortriptyline

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nortriptyline hydrochloride ($C_{19}H_{21}N \cdot HCl$) in the portion of Nortriptyline Hydrochloride 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 Nortriptyline Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Nortriptyline Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–101.5% on the dried basis

IMPURITIES

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

Solution A: 400 mg/mL of tetrabutylammonium hydroxide in water

Solution B: Phosphoric acid and water (1:7)

Buffer: Dissolve 0.7 g of potassium dihydrogen phosphate in 900 mL water. Add 3.25 mL of *Solution A*, and adjust with *Solution B* to a pH of 7.5. Dilute with water to 1 L.

Mobile phase: Methanol and *Buffer* (75:25). [Note—The *Mobile phase* ratio can be adjusted to 70:30 to meet the system suitability requirements.]

System suitability solution: 2.0 µg/mL each of USP Amitriptyline Related Compound B RS, USP Cyclobenzaprine Related Compound B RS, and USP Nortriptyline Hydrochloride RS in *Mobile phase*

Standard solution: 0.002 mg/mL of USP Nortriptyline Hydrochloride RS in *Mobile phase*

Sample solution: 2.0 mg/mL of Nortriptyline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 35°. [Note—The *Column temperature* can be adjusted to 45° to meet the system suitability requirements.]

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of nortriptyline

System suitability

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

Suitability requirements

Resolution: NLT 1.4 between the amitriptyline related compound B and cyclobenzaprine related compound B peaks; NLT 2.0 between the cyclobenzaprine related compound B and nortriptyline peaks, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Nortriptyline Hydrochloride taken:

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

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

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

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

C_U = concentration of Nortriptyline Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Amitriptyline related compound A[a]	0.5	1.0	0.05
Amitriptyline related compound B	0.8	0.58	0.15
Cyclobenzaprine related compound B	0.9	1.0	0.10
Nortriptyline	1.0	—	—
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	0.2

[a] Dibenzosuberone.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Amitriptyline Related Compound B RS

5-[3-(Dimethylamino)propyl]-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepten-5-ol.

$C_{20}H_{25}NO$ ▲295.43▲ (ERR 1-Jul-2021)

USP Cyclobenzaprine Related Compound B RS

3-(5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*-methyl-1-propanamine hydrochloride.

$C_{19}H_{19}N \cdot HCl$ 297.81

USP Nortriptyline Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
NORTRIPTYLINE HYDROCHLORIDE	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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