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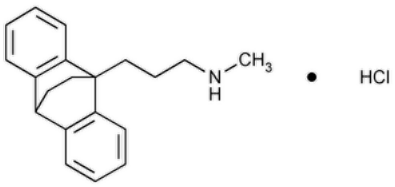
Maprotiline Hydrochloride



$C_{20}H_{23}N \cdot HCl$ 313.86

9,10-Ethanoanthracene-9(10*H*)-propanamine, *N*-methyl-, hydrochloride;

N-Methyl-9,10-ethanoanthracene-9(10*H*)-propylamine hydrochloride CAS RN®: 10347-81-6; UNII: 7C8J54PVFI.

DEFINITION

Maprotiline Hydrochloride contains NLT 98.0% and NMT 102.0% of maprotiline hydrochloride ($C_{20}H_{23}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

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

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample solution: 5 mg/mL

Acceptance criteria: Responds to ▲the tests for amine hydrochloride▲ (USP 1-May-2021)

ASSAY

• **Procedure**

Ammonia solution: 70 g/L of ammonium hydroxide solution

Mobile phase: Dissolve 0.58 g of ammonium acetate in 200 mL of water, and add 2 mL of *Ammonia solution*, 150 mL of 2-propanol, and 650 mL of methanol. Adjust with drops of glacial acetic acid to a pH of 8.1.

System suitability solution: 1 mg/mL of USP Maprotiline Hydrochloride RS and 0.1 mg/mL of USP Maprotiline Related Compound D RS in *Mobile phase*

Standard solution: 1.0 mg/mL of USP Maprotiline Hydrochloride RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Maprotiline Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 272 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Autosampler temperature: 4°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of maprotiline

System suitability

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

[Note—The relative retention times for maprotiline related compound D and maprotiline are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: 1.8–3.2 between the maprotiline related compound D and maprotiline peaks, *System suitability solution*. [Note—If necessary, adjust the pH of *Mobile phase*, in increments of 0.1 pH unit, by adding a 50% (v/v) solution of acetic acid if the *Resolution* is less than 1.8, or by adding the *Ammonia solution* if the *Resolution* is greater than 3.2.]

Tailing factor: 0.9–2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of maprotiline hydrochloride ($C_{20}H_{23}N \cdot HCl$) in the portion of Maprotiline 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 Maprotiline Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities, Procedure 1**

▲**Ammonia solution:** Prepare as directed in the *Assay*.▲ (USP 1-May-2021)

Mobile phase: Dissolve 0.6 g of ammonium acetate in 200 mL of water, and add 2 mL of ▲*Ammonia solution*▲ (USP 1-May-2021), 150 mL of 2-propanol, and 650 mL of methanol. Adjust with diluted glacial acetic acid to a pH of 8.3.

System suitability solution: 1 mg/mL of USP Maprotiline Hydrochloride RS and 0.1 mg/mL of USP Maprotiline Related Compound D RS in *Mobile phase*

Standard stock solution: 0.2 mg/mL of USP Maprotiline Hydrochloride RS in methanol

Standard solution: 0.002 mg/mL of USP Maprotiline Hydrochloride RS in *Mobile phase*, from *Standard stock solution*

Sample solution: 1 mg/mL of Maprotiline Hydrochloride in *Mobile phase*. [Note—A small quantity of methanol, NMT 10% of the final volume, can be used to aid the dissolution.]

Chromatographic system

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

Mode: LC

Detector: UV 272 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Autosampler temperature: 4°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of maprotiline

System suitability

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

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: 1.8–3.2 between the maprotiline related compound D and maprotiline peaks, *System suitability solution*. [Note—If necessary, adjust the pH of the *Mobile phase*, in increments of 0.1 pH unit, by adding a 50% (v/v) solution of acetic acid if the *Resolution* is less than 1.8, or by adding ▲*Ammonia solution*▲ (USP 1-May-2021) if the *Resolution* is greater than 3.2.]

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Maprotiline Hydrochloride taken:

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

r_U = peak area of any impurity from the *Sample solution*

r_S = peak area of maprotiline from the *Standard solution*

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

C_U = concentration of Maprotiline 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%.▲ (USP 1-May-2021)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Maprotiline acrylaldehyde analog[a]	0.3	—	0.2[b]
Maprotiline dimer[c]	0.5	1.16	0.2
Desmethylmaprotiline[d]	0.7	1.15	0.2
Maprotiline related compound D	0.9	1.0	0.2
Maprotiline	1.0	—	—
N-Methylmaprotiline[e]	1.2	1.0	0.2
Any individual unknown impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 3-(9,10-Dihydro-9,10-ethanoanthracen-9-yl)acrylaldehyde.

[b] Determined in the test for *Organic Impurities, Procedure 2*.

[c] *N*-Methyl-*N*,*N*-bis[3-(9,10-dihydro-9,10-ethanoanthracen-9-yl)propyl]amine.

[d] 3-(9,10-Dihydro-9,10-ethanoanthracen-9-yl)propan-1-amine.

[e] 3-(9,10-Dihydro-9,10-ethanoanthracen-9-yl)-*N*,*N*-dimethylpropan-1-amine.

• **Organic Impurities, Procedure 2**

Ammonium bicarbonate solution: 3.95 g/L of ammonium bicarbonate solution. Adjust with 2 M ammonium hydroxide to a pH of 8.1.

Mobile phase: Acetonitrile, methanol, tetrahydrofuran, and *Ammonium bicarbonate solution* (80: 32: 4.5: 20)

Standard stock solution: 0.2 mg/mL of USP Maprotiline Hydrochloride RS in methanol

Standard solution: 0.002 mg/mL of USP Maprotiline Hydrochloride RS in *Mobile phase* from *Standard stock solution*

Sample solution: 1.0 mg/mL of Maprotiline 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

Temperatures

Autosampler: 4°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of maprotiline

System suitability

Sample: *Standard solution*

[Note—The relative retention times for maprotiline acrylaldehyde analog and maprotiline are 0.27 and 1.0, respectively.]

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of maprotiline acrylaldehyde analog in the portion of Maprotiline Hydrochloride taken:

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

r_U = peak response of maprotiline acrylaldehyde analog from the *Sample solution*

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

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

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

F = relative response factor for maprotiline acrylaldehyde analog, 2.2

Acceptance criteria: NMT 0.2%

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 80° to constant weight.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards ⟨11⟩**

USP Maprotiline Hydrochloride RS

USP Maprotiline Related Compound D RS

3-(9,10-Dihydro-9,10-ethanoanthracen-9-yl)-*N*-methylprop-2-en-1-amine hydrochloride.

$C_{20}H_{21}N \cdot HCl$ 311.85

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

Topic/Question	Contact	Expert Committee
MAPROTILINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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