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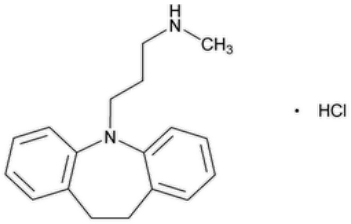
Desipramine Hydrochloride



$C_{18}H_{22}N_2 \cdot HCl$ 302.84

5*H*-Dibenz[*b*,*f*]azepine-5-propanamine, 10,11-dihydro-*N*-methyl-, monohydrochloride;

10,11-Dihydro-5-[3-(methylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine monohydrochloride CAS RN®: 58-28-6; UNII: 1Y58DO4MY1.

DEFINITION

Desipramine Hydrochloride contains NLT 98.0% and NMT 102.0% of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$).

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197M**▲ (CN 1-May-2020)
- **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, *Chloride* ⟨191⟩

Sample solution: 50 mg/mL of Desipramine Hydrochloride in alcohol

Acceptance criteria: Meets the requirements

ASSAY

- **Procedure**

Buffer: 3.4 g/L of sodium acetate trihydrate in water adjusted with glacial acetic acid to a pH of 5.0

Mobile phase: Acetonitrile, methanol, and *Buffer* (35:20:45)

Diluent: 0.1 M hydrochloric acid

System suitability solution: 0.02 mg/mL each of USP Desipramine Hydrochloride RS and USP Imipramine Hydrochloride RS in *Diluent*. Sonication may be used to promote dissolution.

Standard solution: 0.1 mg/mL of USP Desipramine Hydrochloride RS in *Diluent*. Sonication may be used to promote dissolution.

Sample solution: 0.1 mg/mL of Desipramine Hydrochloride in *Diluent*. Sonication may be used to promote dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 25-cm; 5-µm packing L10

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

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

[Note—The relative retention times for desipramine and imipramine are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between desipramine and imipramine, *System suitability solution*

Tailing factor: NMT 2, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) in the portion of Desipramine 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 Desipramine Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

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

Buffer: 5.2 g/L of dibasic potassium phosphate in water. Add 1 mL of triethylamine per L, and adjust with phosphoric acid to a pH of 6.4.

Solution A: Acetonitrile and methanol (55:45)

Solution B: *Solution A* and *Buffer* (25:75)

Solution C: *Solution A* and *Buffer* (62.5:37.5)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	85	15
35	0	100
50	0	100
50.1	85	15
60	85	15

Standard stock solution: 0.25 mg/mL of USP Desipramine Hydrochloride RS prepared as follows. Transfer a suitable quantity of USP Desipramine Hydrochloride RS to an appropriate volumetric flask, and add 50% of the final flask volume of *Solution B*. Sonicate for NLT 2 min, and allow the solution to equilibrate to room temperature. Dilute with *Solution B* to volume.

Standard solution: 0.005 mg/mL of USP Desipramine Hydrochloride RS from *Standard stock solution* in *Solution B*

System suitability solution: 0.01 mg/mL each of USP Imipramine Hydrochloride RS and USP Iminodibenzyl RS in *Standard stock solution*

Sensitivity solution: 0.3 µg/mL of USP Desipramine Hydrochloride RS from *Standard solution* in *Solution B*. Use within 24 h.

Sample solution: 0.5 mg/mL of Desipramine Hydrochloride prepared as follows. Transfer a suitable quantity of Desipramine Hydrochloride to an appropriate volumetric flask, and add 50% of the final flask volume of *Solution B*. Sonicate for NLT 2 min, and allow the solution to equilibrate to room temperature. Dilute with *Solution B* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 4-µm or 5-µm packing L1

Column temperature: 60°

Flow rate: 1.4 mL/min

Injection volume: 40 µL

System suitability

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

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

Suitability requirements

Resolution: NLT 2.0 between imipramine and iminodibenzyl, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desipramine	1.0	—	—
Imipramine	1.6	1.0	0.15
Iminodibenzyl	2.1	0.55	0.1
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

SPECIFIC TESTS

• **LOSS ON DRYING ⟨731⟩**

Analysis: Dry under vacuum at 105° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers. Protect from light.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Desipramine Hydrochloride RS

USP Iminodibenzyl RS

10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepine.

$C_{14}H_{13}N$ 195.28

USP Imipramine Hydrochloride RS

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

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

Chromatographic Database Information: Chromatographic Database

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