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Desipramine Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-desipramine-hcl-tabs-20211231.

DEFINITION

Desipramine Hydrochloride Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$).

IDENTIFICATION

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

ASSAY

- **Procedure**

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

Mobile phase: Acetonitrile, methanol, and *Buffer* (30:20:50)

Diluent: 0.1 N 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: 0.02 mg/mL of USP Desipramine Hydrochloride RS in *Diluent*. Sonication may be used to promote dissolution.

Sample stock solution: Nominally 1–1.5 mg/mL of desipramine hydrochloride from Tablets prepared as follows. Transfer NLT 20 Tablets into a suitable volumetric flask. Add 50% of the final flask volume of *Diluent*. Sonicate the flask for NLT 15 min. Shake the flask for NLT 15 min. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.02 mg/mL of desipramine hydrochloride prepared as follows. Transfer a suitable volume of *Sample stock solution* to an appropriate volumetric flask. Add 50% of the final flask volume of *Diluent*. Shake the flask for NLT 5 min and dilute with *Diluent* to volume. Pass through a suitable filter and discard the first 5 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 250 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Flow rate: 1.5–2.0 mL/min

Injection volume: 25 µL

Run time: NLT 1.2 times the retention time of the imipramine peak

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 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response 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 = nominal concentration of desipramine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-Jan-2022)

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Standard solution: USP Desipramine Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. If necessary, dilute with *Medium* to a concentration that is similar to that of the *Standard solution.*

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at 251 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*, if needed

V = volume of *Medium,* 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (*Q*) of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 2: 50 rpm

Time

For Tablets labeled to contain 10, 25, 50, or 75 mg: 15 min

For Tablets labeled to contain 100 or 150 mg: 30 min

Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 1 L of water and sonicate to dissolve. Add 8.0 mL of triethylamine. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (65:35)

Standard stock solution: 0.555 mg/mL of USP Desipramine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Desipramine Hydrochloride RS to an appropriate volumetric flask. Add 10% of the flask volume of methanol and sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: (*L*/900) mg/mL of USP Desipramine Hydrochloride RS from *Standard stock solution*, in *Medium*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 251 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of desipramine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) dissolved:

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

r_U = peak response of desipramine 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)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of desipramine hydrochloride ($C_{18}H_{22}N_2 \cdot HCl$) is dissolved. ▲ (RB 1-Jan-2022)

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

IMPURITIES

• **Organic Impurities**

Buffer: 5.2 g/L of dibasic potassium phosphate in water. To each L of solution, add 1 mL of triethylamine 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. Add 50% of the final flask volume of *Solution B*. Sonicate for NLT 2 min. 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: Nominally 0.5 mg/mL of desipramine hydrochloride from Tablets prepared as follows. Finely powder NLT 20 Tablets. Transfer a suitable portion of this powder, equivalent to 50 mg of desipramine hydrochloride, to a 100-mL volumetric flask with the aid of *Solution B*. Add *Solution B* to about 50% of the flask volume, and sonicate the flask with occasional shaking for NLT 10 min. Allow the solution to equilibrate to room temperature. Dilute with *Solution B* to volume. Pass through a suitable filter, and discard NLT the first 2 mL of filtrate.

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*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak response of each degradation product 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 = nominal 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	0.2
Iminodibenzyl	2.1	0.55	0.5
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	2.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** When more than one *Dissolution Test* is given, the labeling states the test used only if *Test 1* is not used.▲ (RB 1-Jan-2022)

• **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 TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

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