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Imipramine Hydrochloride Tablets

DEFINITION
Imipramine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$).

IDENTIFICATION

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

Sample: Powder a suitable number of Tablets, equivalent to 100 mg of imipramine hydrochloride, and macerate the powder with 10 mL of chloroform. Filter the chloroform extract through paper into a wide-mouth test tube, and evaporate the filtrate to 3 mL. Carefully add ether until the liquid becomes turbid, heat on a steam bath to produce a clear solution, cool, and allow to stand. The precipitate that is formed may be recrystallized from acetone. Filter the crystalline precipitate, wash with ether, and dry under vacuum at 105° for 30 min. Use the precipitate.

Acceptance criteria: Meet the requirements

• **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: 0.02 M ammonium bicarbonate in water. Adjust with 28%–30% ammonia solution to a pH of 8.0.

Solution B: Acetonitrile and methanol (70:30)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
1.0	90	10
5.0	60	40
7.0	60	40
10.0	48	52
13.0	48	52
14.0	20	80
16.0	20	80
16.1	90	10
18.0	90	10

Diluent: Acetonitrile and water (40:60)

Standard solution: 0.25 mg/mL of USP Imipramine Hydrochloride RS in *Diluent*

Sample stock solution: Nominally 1.0 mg/mL of imipramine hydrochloride from Tablets prepared as follows. Powder NLT 10 Tablets and transfer a sufficient portion of powder to a volumetric flask. Add 75% of the final flask volume of *Diluent*. Sonicate as needed to aid in dissolution. Allow to cool to room temperature, then dilute with *Diluent* to volume. Centrifuge and use the supernatant. [NOTE—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]

Sample solution: Nominally 0.25 mg/mL of imipramine hydrochloride from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 2.1-mm × 10-cm, 1.7-µm packing L7

Column temperature: 35°

Flow rate: 0.4 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) 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 Imipramine Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• **DISSOLUTION ⟨711⟩**

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Mode: UV-Vis

Analytical wavelength: UV 250 nm

Standard solution: USP Imipramine Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium* to a suitable concentration.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) 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 Imipramine 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 imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

Diluent: Hydrochloric acid and water (1:100)

Standard solution: 0.025 mg/mL of USP Imipramine Hydrochloride RS in *Diluent*

Sample stock solution: Transfer 1 finely powdered Tablet to a 100-mL volumetric flask with the aid of 70 mL of *Diluent* and shake by mechanical means for 30 min. Dilute with *Diluent* to volume, and filter, if necessary, discarding the first 20 mL of the filtrate.

Sample solution: Nominally 0.025 mg/mL of imipramine hydrochloride from *Sample stock solution* in *Diluent*

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: UV 250 nm

Cell: 1 cm

Blank: *Diluent*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) in the Tablet taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

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

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

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

Standard solution: 0.002 mg/mL each of USP Imipramine Hydrochloride RS, USP Depramine RS, USP Desipramine Hydrochloride RS, and USP Iminodibenzyl RS in *Diluent*. Sonicate if necessary to aid dissolution.

Sample solution: Nominally 1.0 mg/mL of imipramine hydrochloride from Tablets prepared as follows. Powder NLT 10 Tablets and transfer a portion to a volumetric flask. Add about 75% of the final flask volume of *Diluent*. Sonicate as necessary to aid dissolution. Allow to cool to room temperature, then dilute with *Diluent* to volume. Centrifuge and use the supernatant. [Note—The use of a centrifuge speed of 3000 rpm for 10 min may be suitable.]

System suitability

Sample: *Standard solution*

[Note—The relative retention times for desipramine, depramine, imipramine, and iminodibenzyl are 0.82, 0.84, 1.0, and 1.18, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the depramine and desipramine peaks

Relative standard deviation: NMT 2.5% each for desipramine, imipramine, and iminodibenzyl

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desipramine and iminodibenzyl in the portion of Tablets taken:

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

r_U = peak response of desipramine or iminodibenzyl from the *Sample solution*

r_S = peak response of USP Desipramine Hydrochloride RS or USP Iminodibenzyl RS from the *Standard solution*

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

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

Calculate the percentage of each 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 imipramine from the *Standard solution*

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

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

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

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Desipramine	0.82	0.2
Imipramine	1.0	—
Iminodibenzyl	1.18	0.5
Any individual unspecified degradation product	—	0.2
Total degradation products	—	1.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Depramine RS

3-(5*H*-Dibenzo[*b*,*f*]azepin-5-yl)-*N*,*N*-dimethylpropan-1-amine hydrochloride.

$C_{19}H_{22}N_2 \cdot HCl$ 314.85

USP Desipramine Hydrochloride RS

10,11-Dihydro-5*H*-[3-(methylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine monohydrochloride.

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

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
IMIPRAMINE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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