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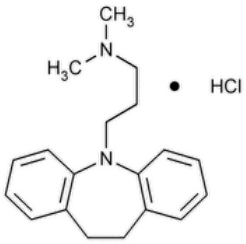
Imipramine Hydrochloride



$C_{19}H_{24}N_2 \cdot HCl$ 316.87

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

5-3-(Dimethylamino)propyl-10,11-dihydro-5*H*-dibenz[*b*,*f*]-azepine monohydrochloride CAS RN®: 113-52-0; UNII: BKE5Q1J60U.

» Imipramine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{19}H_{24}N_2 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Desipramine Hydrochloride RS
USP Imipramine Hydrochloride RS
USP Iminodibenzyl RS $C_{14}H_{13}N$ 195.28

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩, *Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) ·

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

C: Dissolve 0.10 g in 2 mL of alcohol, and add 1 mL of 2 N nitric acid and 3 drops of silver nitrate TS: a white precipitate is formed, and it dissolves on the dropwise addition of ammonium hydroxide.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Related compounds—[Note—Use low-actinic glassware throughout the following procedure.]

Mobile phase, System suitability solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay*.

Standard solution—Dissolve accurately weighed quantities of USP Imipramine Hydrochloride RS and USP Iminodibenzyl RS in acetonitrile, and dilute with a mixture of water and acetonitrile (5:3) to obtain a solution having known concentrations of about 2.5 µg of each component per mL.

Test solution—Transfer about 63 mg of Imipramine Hydrochloride, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with a mixture of water and acetonitrile (5:3), and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. The relative retention times are about 0.8 for *N*-(dimethylaminopropyl) iminostilbene and 1.0 for imipramine. Calculate the percentage of iminodibenzyl in the portion of Imipramine Hydrochloride taken by the formula:

$$5(C/W)(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Iminodibenzyl RS in the *Standard solution; W* is the weight, in mg, of Imipramine Hydrochloride taken to prepare the *Test solution;* and r_U and r_S are the iminodibenzyl peak responses obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.1% of iminodibenzyl is found. Calculate the percentage of each other impurity in the portion

of Imipramine Hydrochloride taken by the formula:

$$5(C/W)(r_i/r_S)$$

in which C is the concentration, in µg per mL, of USP Imipramine Hydrochloride RS in the *Standard solution; W* is the weight, in mg, of Imipramine Hydrochloride taken to prepare the *Test solution;* r_i is the peak response of each individual impurity, excluding iminodibenzyl, obtained from the *Test solution*, and r_S is the peak response of imipramine obtained from the *Standard solution:* not more than 0.1% of *N*-(dimethylaminopropyl)iminostilbene is found; not more than 0.2% of any other impurity is found; and the total of all impurities found is not more than 1.0%.

Assay—[NOTE—Use low-actinic glassware throughout the following procedure.]

Mobile phase—Prepare a filtered and degassed mixture of 0.06 M sodium perchlorate, acetonitrile, and triethylamine (625:375:1), and adjust with perchloric acid to a pH of 2.0. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

System suitability solution—Transfer about 15 mg of USP Imipramine Hydrochloride RS and about 15 mg of USP Desipramine Hydrochloride RS, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with a mixture of water and acetonitrile (5:3) to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Imipramine Hydrochloride RS in a mixture of water and acetonitrile (5:3) to obtain a solution having a known concentration of about 0.3 mg per mL.

Assay preparation—Transfer about 30 mg of Imipramine Hydrochloride, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with a mixture of water and acetonitrile (5:3) to volume, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 269-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The column temperature is maintained at 40°, and the flow rate is about 1.5 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between the imipramine and desipramine peaks is not less than 1.3. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0% for imipramine.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of $C_{19}H_{24}N_2 \cdot HCl$ in the portion of Imipramine Hydrochloride taken by the formula:

$$100C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Imipramine Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the imipramine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

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

Chromatographic Database Information: Chromatographic Database

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