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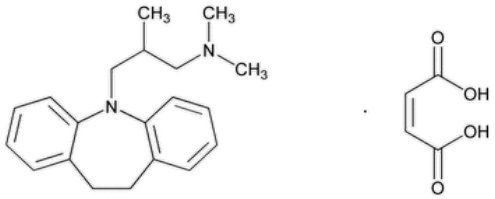
Trimipramine Maleate



$C_{20}H_{26}N_2 \cdot C_4H_4O_4$ 410.51

5*H*-Dibenz[*b,f*]azepine-5-propanamine, 10,11-dihydro-*N,N,β*-trimethyl-, *(Z)*-2-butenedioate (1:1).

5-[3-(Dimethylamino)-2-methylpropyl]-10,11-dihydro-5*H*-dibenz[*b,f*]azepine maleate (1:1) CAS RN®: 521-78-8; UNII: 269K6498LD.

» Trimipramine Maleate contains not less than 98.0 percent and not more than 102.0 percent of $C_{20}H_{26}N_2 \cdot C_4H_4O_4$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers, and store at room temperature.

Change to read:

USP Reference standards ⟨11⟩—

USP Iminodibenzyl RS $C_{14}H_{13}N$ 195.28
USP Imipramine Hydrochloride RS
USP Trimipramine Maleate RS
USP Trimipramine Related Compound A RS

▲3-(5*H*-Dibenzo[*b,f*]azepin-5-yl)-*N,N*,2-trimethylpropan-1-amine.▲ (CN 1-Aug-2024)

$C_{20}H_{24}N_2$ ▲292.43▲ (CN 1-Aug-2024)

Identification—

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

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*.

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

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

Change to read:

Related compounds—

Mobile phase and *Standard stock preparation*—Prepare as directed in the *Assay*.

Impurity stock solution—Dissolve accurately weighed quantities of USP Imipramine Hydrochloride RS and USP Iminodibenzyl RS in a suitable volume of *Mobile phase* to obtain a solution having a known concentration of about 50 µg per mL of iminodibenzyl and 56.5 µg per mL of imipramine hydrochloride.

Trimipramine related compound A solution—Dissolve a suitable quantity of USP Trimipramine Related Compound A RS in *Mobile phase* to obtain a solution having a concentration of about 50 µg per mL.

Trimipramine stock solution—Quantitatively dilute the *Standard stock preparation* with *Mobile phase* to obtain a solution having a known concentration of about 70 µg per mL of trimipramine maleate.

System suitability solution—Transfer about 7 mg of USP Trimipramine Maleate RS to a 10-mL volumetric flask, dissolve in a small amount of *Mobile phase,* add 0.1 mL each of the *Impurity stock solution* and the *Trimipramine related compound A solution,* and dilute with *Mobile phase* to volume.

Standard solution—Transfer 5.0 mL each of the *Impurity stock solution* and the *Trimipramine stock solution* with *Mobile phase* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume. Dilute the resulting solution quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a final solution having a known concentration of about 0.5 µg per mL each of iminodibenzyl, imipramine (free base), and trimipramine (free base). [Note—This solution is stable for one day at room temperature. The concentration of imipramine (free base), in µg

per mL, can be calculated using the molecular weights of imipramine (282.41) and imipramine hydrochloride (318.88). The concentration of trimipramine (free base), in µg per mL, can be calculated using the molecular weights of trimipramine (294.43) and trimipramine maleate (410.51).]

Test solution—Use the *Assay stock preparation*.

Chromatographic system—Prepare as directed in the *Assay*. Chromatograph about 10 µL of the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between imipramine and trimipramine related compound A is not less than 1.5. [NOTE—For identification purposes, the approximate relative retention times of the specified impurities are given in Table 1.]

Procedure—Separately inject about 10 µL of the *Standard solution* and the *Test solution* into the chromatograph, and record the chromatogram for three times the retention time for trimipramine. Identify the components based on their relative retention times in Table 1. Measure the peak areas of all the peaks in the *Test solution*. Calculate the percentage of imipramine and iminodibenzyl in the portion of Trimipramine Maleate taken by the formula:

$$100(C_S/C_T)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of any given impurity (free base) in the *Standard solution;* C_T is the concentration of Trimipramine Maleate, in mg per mL, in the *Test solution;* r_U is the individual peak response of the given impurity obtained from the *Test solution;* and r_S is the corresponding response for the same impurity obtained from the *Standard solution*. Calculate the percentage of trimipramine related compound A in the portion of Trimipramine Maleate taken by the formula:

$$100(1/3.6)(C_S/C_T)(r_U/r_S)$$

in which 3.6 is the relative response factor for trimipramine related compound A; C_S is the concentration, in mg per mL, of trimipramine (free base) in the *Standard solution;* C_T is the concentration of Trimipramine Maleate, in mg per mL, in the *Test solution;* r_U is the peak response for trimipramine related compound A obtained from the *Test solution;* and r_S is the peak response of trimipramine obtained from the *Standard solution*. Calculate the percentage of each unknown impurity in the portion of Trimipramine Maleate taken by the formula:

$$100(C_S/C_T)(r_i/r_S)$$

in which C_S is the concentration, in mg per mL, of trimipramine (free base) in the *Standard solution;* C_T is the concentration of Trimipramine Maleate, in mg per mL, in the *Test solution;* r_i is the individual peak response of the given impurity obtained from the *Test solution;* and r_S is the response for trimipramine obtained from the *Standard solution:* the limits of the related compounds are given in Table 1. [NOTE—Disregard any peak due to the maleate counterion eluting at a relative retention time of about 0.13.]

Table 1

Peak Identification	Approximate Relative Retention Time (RRT)	Limit % (w/w)
Trimipramine *N*-oxide[1]	0.32	NMT 0.15
Iminodibenzyl[2]	0.49	NMT 0.20
Desmethyltrimipramine[3]	0.68	NMT 0.15
Imipramine[4]	0.72	NMT 0.20
Trimipramine related compound A[5]	0.80	NMT 0.10
Trimipramine diamine[6]	2.39	NMT 0.30
Any other individual impurity	—	NMT 0.10
Total impurites	—	NMT 1.0

1 ▲3-(10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-*N*,*N*,2-trimethylpropan-1-amine *N*-oxide.▲ (CN 1-Aug-2024)

2 ▲10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepine.▲ (CN 1-Aug-2024)

3 ▲3-(10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-*N*,2-dimethylpropan-1-amine.▲ (CN 1-Aug-2024)

4 ▲3-(10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-*N*, *N*-dimethylpropan-1-amine.▲ (CN 1-Aug-2024)

5 ▲3-(5*H*-Dibenzo[*b*,*f*]azepin-5-yl)-*N*,*N*,2-trimethylpropan-1-amine.▲ (CN 1-Aug-2024)

6 ▲N^1-[3-(10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepin-5-yl)-2-methylpropyl]-N^1,N^3,N^3,2-tetramethylpropane-1,3-diamine.▲ (CN 1-Aug-2024)

Assay—

Buffer solution—Dissolve about 1.4 g of anhydrous dibasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 7.7.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, methanol, and *Buffer solution* (18:12:10). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard stock preparation—Dissolve an accurately weighed quantity of USP Trimipramine Maleate RS in a suitable volume of *Mobile phase* to obtain a solution having a known concentration of about 0.7 mg per mL.

Standard preparation—Transfer 3 mL of the *Standard stock preparation* to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume to obtain a final solution having a known concentration of about 0.21 mg per mL of trimipramine maleate.

Assay stock preparation—Dissolve an accurately weighed quantity of Trimipramine Maleate in a suitable volume of *Mobile phase* to obtain a solution having a known concentration of about 0.7 mg per mL.

Assay preparation—Transfer 3 mL of the *Assay stock preparation* to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume to obtain a final solution having a known concentration of about 0.21 mg per mL of trimipramine maleate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1.0 mL per minute. The column temperature is maintained at 30°. Chromatograph about 20 µL of the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor for the trimipramine maleate peak is not more than 2.0; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms for up to 1.5 times the retention time of trimipramine maleate, and measure the responses for the trimipramine maleate peak. Calculate the percentage of $C_{20}H_{26}N_2 \cdot C_4H_4O_4$, in the portion of Trimipramine Maleate taken by the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of USP Trimipramine Maleate RS in the *Standard preparation;* C_U is the concentration, in mg per mL, of Trimipramine Maleate in the *Assay preparation;* and r_U and r_S are the trimipramine 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
TRIMIPRAMINE MALEATE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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