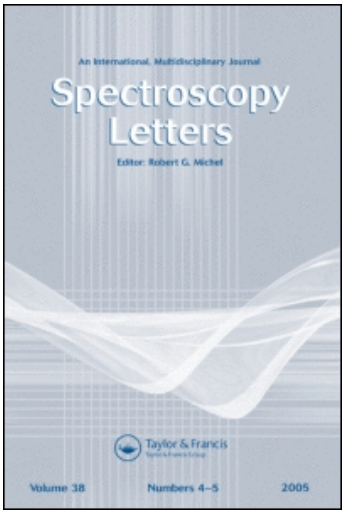

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PMR Spectrometric Analysis of Trimipramine Maleate in Pharmaceutical Preparation

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PMR SPECTROMETRIC ANALYSIS OF TRIMIPRAMINE MALEATE IN PHARMACEUTICAL PREPARATION

Key words: PMR spectrometry, Trimipramine Maleate analysis.

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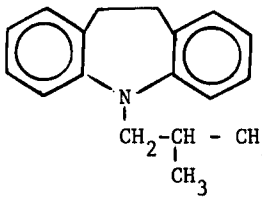
Abstract:

A new method is described for the assay of Trimipramine maleate, the hydrogen maleate of 5-(3-dimethyl amino-2-methyl-propyl)-10,11-dihydrodibenz-[b,f]- azepine and its base using pmr technique. The method employed is precise, accurate, rapid and helpful in qualitative identification and purity of the drug.

Introduction

Trimipramine maleate, the hydrogen maleate of 5-(3-dimethyl-amino-2-methylpropyl)-10-11-dihydrodibenz-[b,f]-azepine is a tricyclic antidepressant[1].



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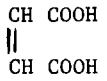

A compound first prepared by Societe des usins chimiques, in 1959[2].

The drug is official in B.P.[3] (1973), the pharmacopea describes a non-aqueous titration method for the assay of the authentic drug using 0.1 N perchloric acid in dioxan and an ultraviolet spectrophotometric method for the assay of trimipramine tablets.

Some of the methods reported in the literature were directed toward the determination of trimipramine and its maleate salt in connection with other tricyclic antidepressant, Danhier[4] described more than one method for the assay of the drug; an ultraviolet procedure using the solution of the drug in 0.01 N hydrochloric acid, a gravimetric determination with silicotungestic acid and a colorimetric analysis with Reineck salt and picric acid.

Experimental

A varian T60 A NMR spectrometer was used throughout this study.

Materials and methods

Trimipramine Capsules (Surmontil^{R}), (May & Baker Ltd., Dagenham, England) was used as the sample, hexamethylenetetramine (E. Merck AG

Darmstadt, Germany), internal standard, and deutrated chloroform as solvent.

Methods

For trimipramine base

Dissolve a quantity of the mixed content of 20 capsules equivalent to 72 mg of trimipramine and 50 mg of hexamethylenetetramine in 2 ml of deuterated chloroform, transfer 0.4 ml of the clear solution to a NMR tube. Place the tube in the NMR spectrometer, adjusting the spin rate to eliminate the spining side bands as much as possible, and record the spectrum. Integrate the peaks of interest (the aromatic protons of the dihydrodibenzazepine ring at 7.18 δ and the well-defined singlet of the CH_2- protons of the hexamethylenetetramine at 4.7 δ and record the mean of the three integrations, the amount of trimipramine may be calculated as follows:

$$\text{mg of trimipramine} = \frac{A_1}{A_2} \times \frac{EW_1}{EW_2} \times W_2$$

A_1 = integral value of the aromatic protons of trimipramine.

A_2 = integral value of the CH_2- protons of hexamethylentetramine.

EW_1 = mol. wt. of trimipramine /8.

EW_2 = mol. wt. of hexamethylenetetramine /12.

W_2 = wt (mg) of hexamethylenetetramine

For trimipramine maleate

Using the same spectra described above, integrate the peaks of -CH = CH-protons of maleic acid which is added to the integration of the aromatic protons of trimipramine.

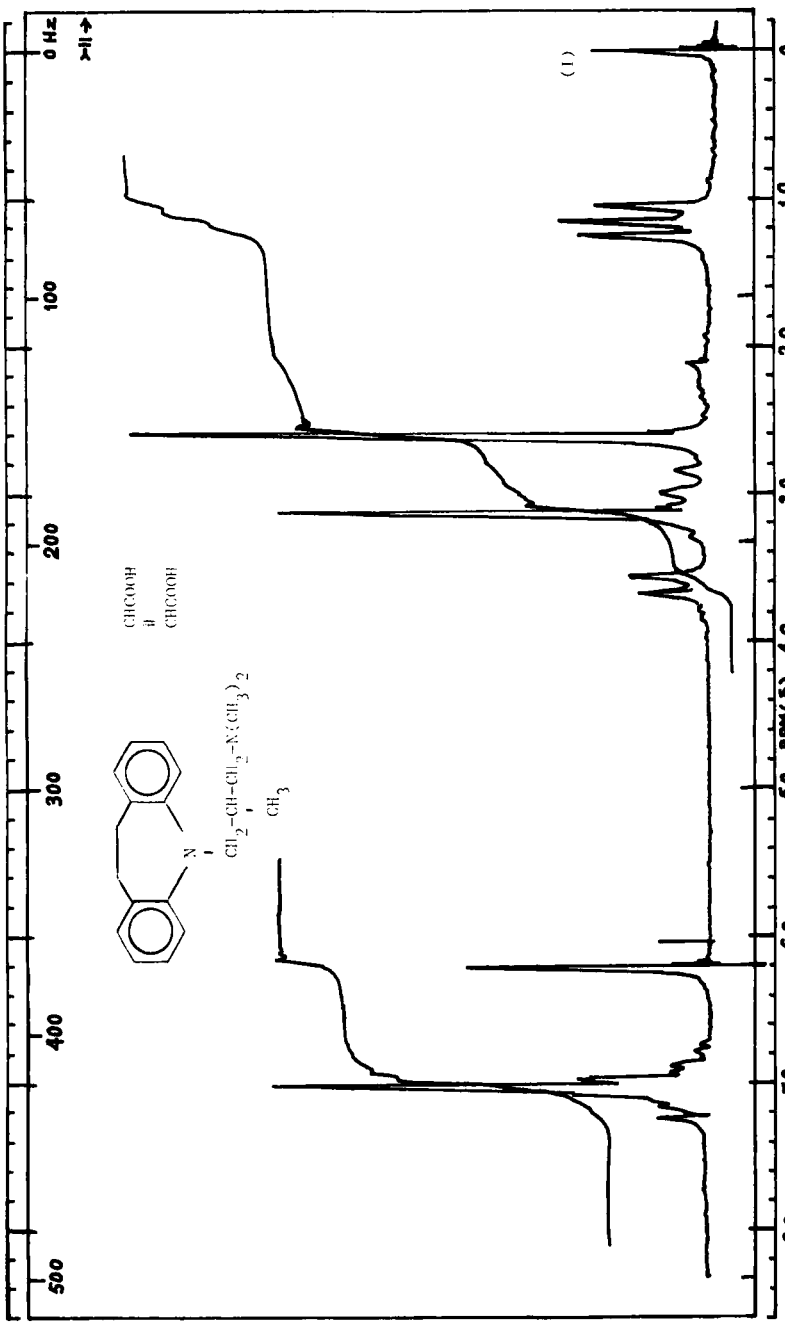

Figure 1. NMR spectra of trimipramine maleate in deutrated chloroform and TMS (tetramethylsilane) (I).

TABLE - 1 Analysis of Trimipramine base by NMR.

Sample No.	Internal standard added (mg)	Trimipramine added (mg)	Found	Recovery %
1.	50	72	70.22	97.53
2.	50	72	75.10	104.30
3.	50	72	71.90	99.86
4.	50	72	69.21	96.12
5.	50	72	73.25	101.74
6.	50	72	70.98	98.58
7.	50	72	74.92	104.06
8.	50	72	68.83	95.60
9.	50	72	69.75	96.88
10.	50	72	71.32	99.06
			Average % recovery =	99.373
			S.D. =	3.20

The amount of trimipramine maleate may be calculated as follows:

$$\text{mg of trimipramine maleate} = \frac{A_1}{A_2} \times \frac{EW_1}{EW_2} \times W_2$$

A_1 = integral value of the aromatic protons of trimipramine plus that of -CH=CH-protons of maleic acid.

A_2 = integral value of the CH_2-protons of hexamethylenetetramine.

AEW_1 = mol. wt. of trimipramine maleate/10.

TABLE - 2 Analysis of Trimipramine maleate by NMR.

Sample	Internal standard added (mg)	Trimipramine added (mg)	Found	Recovery %
1.	50	100	98.21	98.21
2.	50	100	95.90	95.90
3.	50	100	96.27	96.27
4.	50	100	107.27	102.22
5.	50	100	103.59	103.59
6.	50	100	102.53	102.53
7.	50	100	97.91	97.91
8.	50	100	98.22	98.22
9.	50	100	100.72	100.72
10.	50	100	101.85	101.85
			Average % recovery =	97.742
			S.D. =	2.93

EW_2 = mol. wt. of hexamethylenetetramine/12.

W_2 = wt. (mg) of hexamethylenetetramine.

Results and Discussion

Hexamethylenetetramine was the most satisfactory internal standard due to its nice location in the clean area of trimipramine spectrum and its solubility in the solvent used in the assay.

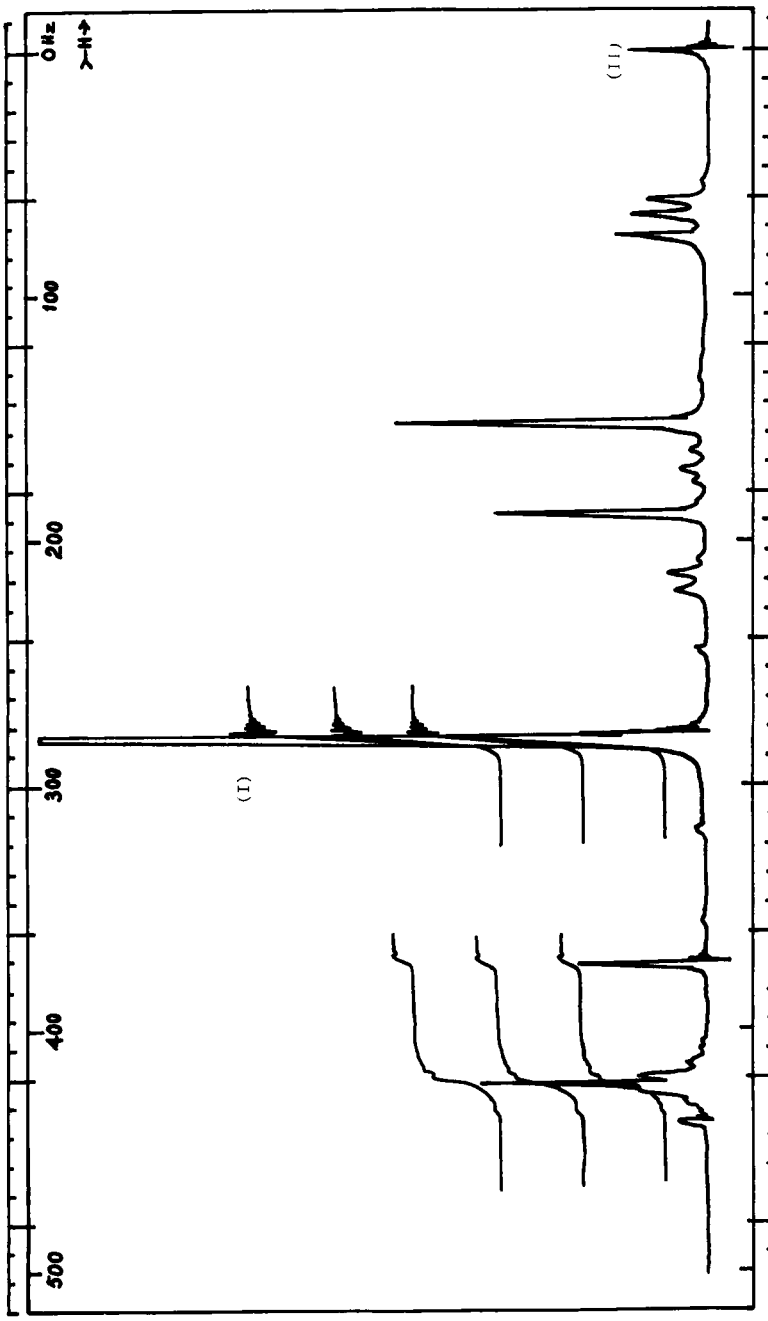

Figure 2. NMR spectra of trimipramine maleate in deutrated chloroform, hexamethylenctetramine (I) and TMS (tetramethylsilane) (II).

Table 1 shows the percent recoveries obtained when the proposed method was used for the assay of trimipramine, the results demonstrated good precision (average recovery 99.373% s.d. = 3.20). When the proposed method was used for the assay of the trimipramine maleate gave reasonable results as indicated in table 2 (average recovery = 99.742%, s.d. = 2.92).

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