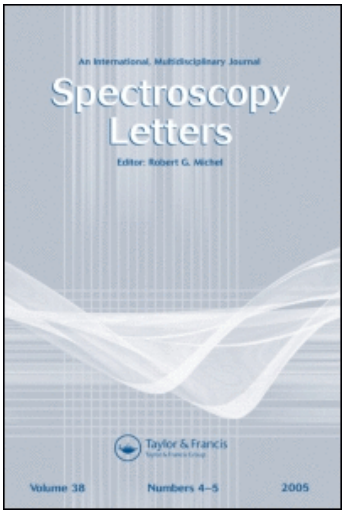

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PMR Spectrometric Analysis of Stilbestrol and Some of Its Pharmaceutical Preparations

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PMR Spectrometric Analysis of Stilbestrol and Some of its Pharmaceutical Preparations.

Key words: PMR Spectrometry, Stilbestrol PMR analysis.

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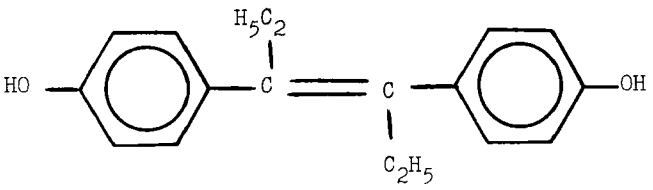
Abstract

A novel method is developed using PMR technique for quantitative determination of stilbestrol and some of its pharmaceutical preparations. The method developed is accurate, rapid, and precise. It involves comparing the integral of the nice triplet system of stilbestrol spectrum (positioned at 0.73 δ) to that of the sharp singlet signal (positioned at 6.25 δ) of maleic acid which is used as internal standard.

Introduction

Stilbestrol, 3,4-di-(4-hydroxyphenyl)hex-3-ene is a synthetic estrogen first synthesized by Dodds, et. al. in 1938[1].



The drug is official in both B.P. (1973) and U.S.P. XIX (1975). The official methods of assay of stilbestrol in both pharmacopeas are spectrophotometric ones.[2][3]

Different colorimetric methods for the assay of stilbestrol[4-14] and its dosage forms[15-20] were reported. Some biological methods for standardization of stilbestrol were also reported.[21-24]

The present investigations describe a new method for the assay of stilbestrol and of some of its dosage forms. It involves the application of PMR spectroscopy.

Experimental:

Materials

Authentic stilbestrol (B.D.H. Chemicals Ltd., Poole, England) previously assayed using the B.P. method* and stilbestrol tablets and ampoules (IBSA, institut Biochemique Societe Anonime - Lugano 3, Suisse) were used as the samples,

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* The mean percent recovery was found to be 100.2%
** A Varian T60-A NMR spectrometer was used throughout this work.

maleic acid (B.D.H. Chem. Ltd., Poole, England) as the internal standard and methanol as solvent.

Procedure:

For authentic stilbestrol

Dissolve 100 mg of stilbestrol and 50 mg of maleic acid in 2 ml of methanol, transfer 0.5 ml of the clear solution to an NMR tube. Place the tube in an NMR spectrometer,** adjusting the spin rate to eliminate spining side bands as much as possible and record the spectrum. Integrate the peaks of interest (the CH_3 - protons of stilbestrol at 0.73 δ and the CH = CH protons of maleic acid at 6.25 δ) and record the mean of the three integrations. The amount of stilbestrol may be calculated as follows :

$$\text{mg of stilbestrol} = A_1 / A_2 \times Ew_1 / Ew_2 \times W_2$$

A_1 = integral value of the CH_3-triplet of stilbestrol

A_2 = integral value of the CH = CH singlet of maleic acid

Ew_1 = Mol. wt. of stilbestrol/6.

Ew_2 = Mol. wt. of maleic acid/2.

W_2 = Wt. (mg) of maleic acid.

Samples of pure stilbestrol were analysed. Maleic acid in the same amount was added to each tube as an internal standard. The mean recovery in ten separate experiments was determined (Table I).

Table I : PMR analysis of stilbestrol and some of its pharmaceutical preparations.

	Item	Recovery %	Standard deviation
1.	Authentic Stilbestrol	100.06%	± 0.40
2.	Stilbestrol dipropionate tablets	102.1%	± 1.25
3.	Stilbestrol dipropionate ampoules.	101.6%	± 0.97

For Stilbestrol tablets

Tablets are claimed to contain stilbestrol as dipropionate salt.

A quantity of the mixed contents of 20 tablets equivalent to 75 mg of stilbestrol was hydrolysed with 20% sodium hydroxide solution in a steam bath for 20 minutes, the solution was acidified with hydrochloric acid and finally saturated with sodium carbonate. The alkaline solution was extracted three times each with 20 ml of solvent ether. The combined ethereal extracts were evaporated to dryness. To the residue, 50 mg of maleic acid in 2 ml methanol was added. In an NMR tube, pipette 0.5 ml of the clear solution, run the PMR spectrum of the solution and proceed as previously described under authentic stilbestrol. The mean recovery in ten separate experiments was determined (Table I).

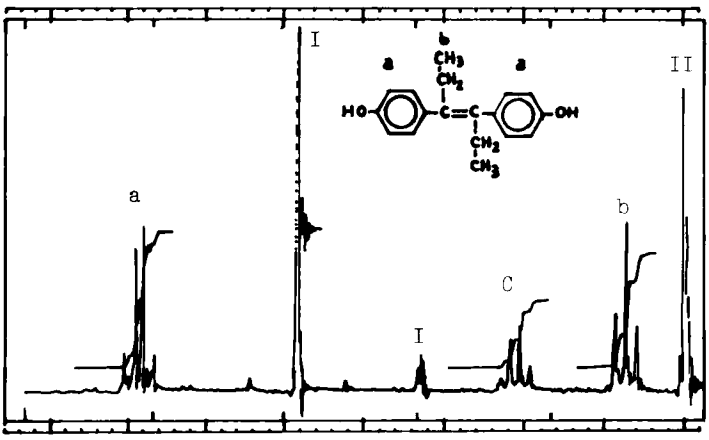

Figure 1 - NMR spectra of stilbestrol in deutrated methanol I and TMS. (tetramethylsilane II).

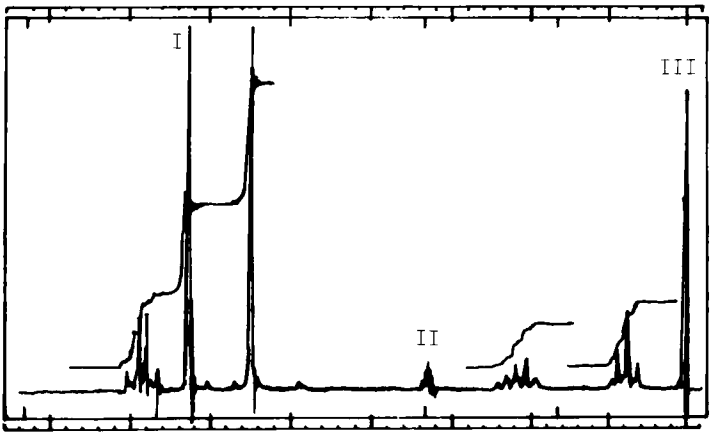

Figure 2 - NMR spectra of stilbestrol, maleic acid (I) in deutrated methanol II and TMS (tetramethylsilane) III.

For stilbestrol ampoules

The ampoules claimed to contain stilbestrol as dipropionate. The method used for the tablets assay was applied exactly for the determination of the ampoules using the mixed contents of

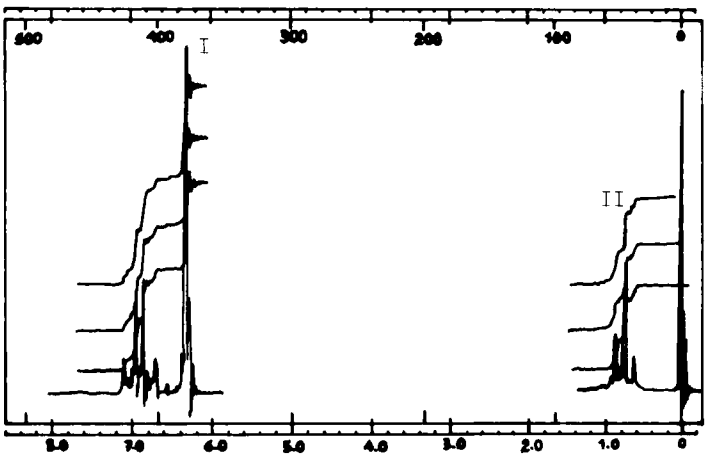

Figure 3 - signals of interest, the singlet signal of maleic acid (I) and the triplet system of stilbestrol II).

20 ampoules. The mean recovery in ten separate experiments was determined (Table I).

Results and Discussion

Quantitative determinationsof authentic stilbestrol (1) and some of its dosage forms i.e., tablets (2) and ampoules (3) was performed with accurate and precise results.

Table (I) shows the percentage recovery and standard deviation in each case.

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