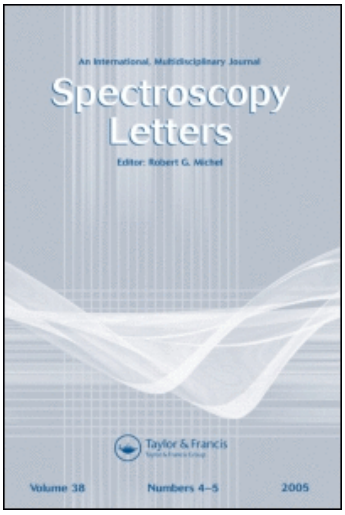

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NMR SPECTROMETRIC ANALYSIS OF ANTAZOLINE*

Key Words: Antazoline pmr analysis; pmr analysis, antazoline.

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ABSTRACT

An analytical method is described for the analysis of antazoline [2-(N-benzylanilinomethyl) imidazoline] using pmr. The procedure provides good quantitative results together with a very specific mean for identification of antazoline.

INTRODUCTION

Antazoline-[2-(N-benzylanilinomethyl) imidazoline] is a commonly used antihistaminic antiallergic agent.

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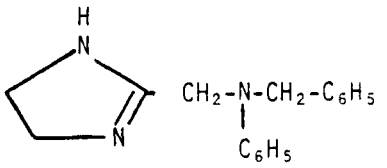

Antazoline is assayed in B.P. (1975) by nonaqueous titration using 0.1 N perchloric acid and crystal violet as indicator.[1] However, the procedure is time consuming and not very specific. In search for a more specific and quantitative assay, the NMR is applied as a tool.

This paper describes a method using NMR spectroscopy to determine antazoline in tablet formulations. Good quantitative results can be obtained together with a positive identification of the active component in terms of the NMR spectrum. The procedure proposed here provides a specific measurement technique which avoids difficulties such as exist in the titration procedure.

MATERIALS AND METHODS

Materials

Standard, antazoline HCl (Ciba-Geigy Ltd., Basle, Switzerland); antazoline tablets were used as the samples; internal standard, hexamethylcyclotrisilozane (K & K Laboratories, Viewplains, NY); carbon tetrachloride (spectroanalyzed grade).

Method

The moisture was removed from the tablets by placing them in a dessicator (over NaOH). Take three tablets and place then in a 10 ml stoppered flask. Add 5 ml of water and 500 mg sodium bicarbonate, disintegrate the tablets, and mix well. Add 5 ml of carbon tetrachloride which contains the internal standard so that the final concentration of antazoline will be about 50 mg/ml and the internal standard is about 10 mg/ml of carbon tetrachloride. Stopper the flask and place it in a shaker for 10 minutes to affect extraction and solution. Filter, using cotton pledget, then transfer 0.4 ml of the clear solution to an NMR tube. Place tube in an NMR spectrometer,[a] adjusting the spin rate to eliminate spinning side bands as much as possible, and obtain the spectrum. Integrate the peaks of interest ($-CH_2-CH_2$ of the imidazoline ring system appearing as a singlet at 3.33δ) at least three times and average the results. The amount of antazoline may be calculated as follows:

$$\text{MG of antazoline} = \frac{A_T}{A_S} \times \frac{EW_T}{EW_S} \times \text{MG of hexamethylcyclotrisiloxane.}$$

where,

[a]A Varian T-60A NMR spectrometer was used.

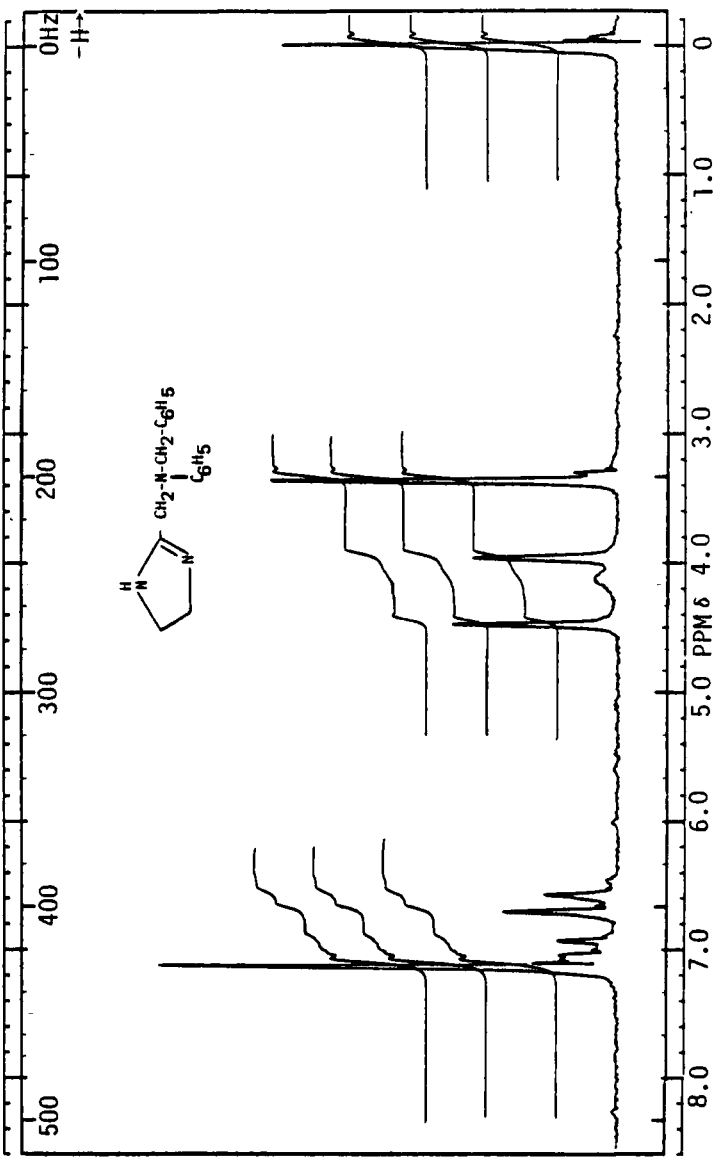

Figure 1. NMR Spectrometric Analysis of Antazoline.

A_T = integral value of the signal representing antazoline.

A_S = integral value of the signal representing the internal standard.

EW_T = molecular weight of antazoline/4 = 66.32.

EW_S = molecular weight of hexamethylcyclotrisiloxane/18 = 12.35.

RESULTS AND DISCUSSION

The choice of a suitable solvent or solvent system and internal standard should be considered carefully, especially when applied to analytical purposes using NMR. Antazoline is soluble in carbon tetrachloride (an ideal NMR solvent, cheap and introduce no interference in NMR scale). The internal standard hexamethylcyclotrisiloxane used in this study has been previously recommended.[2,3,4]

The internal standard shows a signal in the extreme upfield position at 0.00δ. The NMR spectrum of antazoline shows among other peaks a singlet at 3.33δ ($-CH_2CH_2-$bridge of imidazoline ring). This peak is ideal for precise integration, thus was chosen for establishing the method. The integrals of the singlets at 3.33δ and 0.00δ are indicators of the concentration of both antazoline and hexamethylcyclotrisiloxane.

Accordingly, a series of standard solutions were prepared and assayed (Table 1). The results demonstrated good precision and the method has been used for the assay of commercial tablets

TABLE 1

Analysis of Antazoline Standards, by NMR.

Sample No.	Internal Standard Added MG	Antazoline HCl Added MG	Found	Recovery %
1	10.06	300	298.91	99.63
2	10.06	299	302	101
3	10.06	300	283.71	94.57
4	10.06	300	307.35	102.45
5	10.06	299	294.21	98.4
6	10.06	301	288.93	95.99
7	10.06	301	289.95	96.33
8	10.06	300	290.28	96.76
9	9.98	301	287.46	95.82
10	9.98	301	287.46	95.82

Average: 98.07 ± 3.1

(Table 2). The method proved to be rapid, accurate and there was no evidence of interference from excipients present. In addition to quantitative purposes, the method is attractive since it also uses an inexpensive solvent. Measurements shown in Table 1 and 2

TABLE 2

Assay of Antazoline Tablets[b] by NMR.

Sample No.	Internal Standard Added MG	Antazoline Base declared in 3 tablets	Found (as base)	Recoveries %
1	10.00	263.83	258.55	98.00
2	10.00	263.83	258.55	98.00
3	10.00	263.83	258.55	98.00
4	10.00	263.83	251.47	95.32
5	10.00	263.83	268.62	101.82
6	10.00	263.83	274.26	103.95
7	10.00	263.83	265.82	100.75
8	10.00	263.83	265.82	100.75
9	9.98	263.83	268.62	101.82
			Average:	99.82 ± 2.67

[b]The declared amount of antazoline HCl is 100 mg/tablet which is equivalent to 87.94 mg of antazoline base.

are within B.P. (1975) monograph limits of 99-101% and 92.5-107.5% for antazoline and antazoline tablets respectively.

In summary, the method provides good quantitative results together with a very specific mean for identification of antazoline. It can be recommended as a stability indicating assay.

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