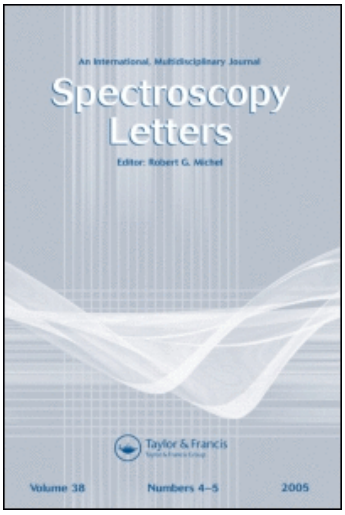


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Determination of Chlorpropamide and Its Tablets By PMR Spectrometry

Sonia Z. El-Khateeb[a]; H. N. Assaad[a]; H. N. Ellaithy[a]; A. S. Ahmad[a]
[a] Analytical Chemistry Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt

To cite this Article El-Khateeb, Sonia Z. , Assaad, H. N. , Ellaithy, H. N. and Ahmad, A. S.(1987) 'Determination of Chlorpropamide and Its Tablets By PMR Spectrometry', Spectroscopy Letters, 20: 2, 89 — 96
To link to this Article: DOI: 10.1080/00387018708081530
URL: http://dx.doi.org/10.1080/00387018708081530

SPECTROSCOPY LETTERS, 20(2), 89-96 (1987)

Determination of Chlorpropamide and Its Tablets By PMR Spectrometry

Sonia Z. El-Khateeb,* H. N. Assaad, M. M. Ellaithy and A. S. Ahmad

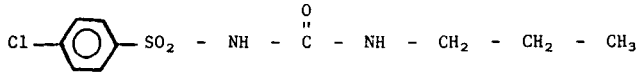
Analytical Chemistry Department, Faculty of Pharmacy, Cairo University Cairo, Egypt.

ABSTRACT:

A new method, involving the application of PMR spectrometry for the assay of chlorpropamide and its tablets, is proposed. The PMR spectrum of chlorpropamide has a well-defined triplet (around 0.8 ppm) and quartet (near 7.8 ppm), which are chosen for quantitative analysis. The method is based on comapring the integral of these signals to that of the sharp singlet of maleic acid at 6.3 ppm which is used as internal standard. The proposed method is simple and rapid, also it gives accurate and reproducible results when applied for the analysis of both authentic chlorpropamide and its tablets. In addition, the PMR spectrum obtained helps in confirming identity and purity of the drug.

INTRODUCTION:

Chlorpropamide (N-p-chlorobenzensulphonyl-N', propyl urea), an orally active hypoglycemic agent used in the management of certain types of maturity onset diabetes[1]. It has the structure shown below. It is official in both BP 1973 and BP 1980. The assay method for the pure substance involves the direct titration of the alcoholic solution with standard alkali using phenolphthalein as indicator [2]. While the assay for chlorpropamide in tablets involves the alcoholic extraction of the active constituent followed by measuring the absorbance of the acidified extract at 232 nm[3].



Several other analytical procedures for chlorpropamide have been reported,

*To whom correspondence should be address.

including titrimetric[4-9], spectrophotometric[10-13], colorimetric[14-16] and polarographic[17] methods. In addition to chromatographic procedures including paper[18], thin-layer[19-21] and gas-liquid[22,23] chromatography of chlorpropamide in both pharmaceutical products and biological fluids. Also high performance liquid chromatographic procedures have been reported[24,25]. This communication describes a new method, involving the application of PMR Spectrometry for the assay of chlorpropamide and its tablets.

EXPERIMENTAL:

A Varian T60-A NMR Spectrometer was used throughout the study. The internal standard maleic acid was purchased from British Drug Houses, while deuterated acetone (d_6) and tetramethylsilane (TMS) were purchased from Aldrich Chemical Company Inc. (U.S.A.). Authentic Chlorpropamide and Pamadin tablets were kindly supplied by El-Khaira Pharmaceutical Company, Cairo, A.R.E.

PROCEDURE:

For Authentic Chlorpropamide:

place a weighed aliquot of chlorpropamide, in the range of 15 - 40 mg, in small glass-stoppered test tube. Add 1.0 ml deuterated acetone (d_6) containing the internal standard, maleic acid; the concentraction of which is 20 mg/ml. Stopper the tube and shake till dissolves, then transfer 0.5 ml of the clear solution to an analytical NMR tube and record the PMR spectrum taking care to adjust the spin rate to eliminate side bands as much as possible. Reference all peak field positions to TMS at 0.00 ppm.

The peaks of interest are integrated three times and get the average of each. Calculate the weight of the drug from the following equation:

$$W_c = \frac{H_m \cdot M_c}{H_c \cdot M_m} \cdot \frac{I_c}{I_m} \cdot W_m$$

Where I = Integral of signal (mm).
H = Number of protons within the signals.
M = Molecular weight.
W = Weight (mg).

The subscripts "c" and "m" stand for chlorpropmaide and maleic acid respectively. The above equation could be written as:

$$W_c = \frac{2 \times 276.7}{3 \times 116.04} \cdot \frac{I_c}{I_m} \cdot 20 \quad \text{----------(1)}$$

OR

$$W_c = \frac{2 \times 276.7}{4 \times 116.04} \cdot \frac{I_c}{I_m} \cdot 20 \quad \text{----------(2)}$$

Equation (1) is applied for calculation of chlorpropamide weight using the integral ratio of methyl protons, while equation (2) is applied when the integral ratio of the aromatic protons is used.

FOR PAMADIN TABLETS:

Each tablet is labelled to contain 250 mg chlorpropmaide.

Weigh and finely powder not less than twenty tablets. Accurately, weight portions of powder equivalent to 18-35 mg active ingredient into small glass stoppered test tube. Dissolve in 1.0 ml deuterated acetone (d_6) containing maleic acid (20 mg/ml). Stopper the tube and mix well. Transfer 0.5 ml solution to NMR tube and get the spectrum as previously mentioned under authentic chlorpropamide.

RESULTS AND DISCUSSION:

The PMR spectrum of chlorpropamide in acetone (d_6), using maleic acid is shown in figure (1). All signals, measured in delta scale, are referenced to TMS whose singlet is positioned at 0.00 ppm. The spectrum is characterized by a well defined triplet near 0.8 ppm correspond to the methyl protons, in addition to two multiplets one near 1.4 ppm and the other near 3.2 ppm which correspond to the two non-equivalent methylene protons. The para-chloro substituted aromatic ring shows its characteristic pattern around 7.8 ppm. Both signals at 0.8 ppm and 7.8 ppm have been chosen for quantitative determination of chlorpropamide by comparing their integral values to that of a known concentration of the internal standard maleic acid (previously recommended)[26,27]. The downfield resonance peak at 6.3 ppm corresponds to the two equivalent methylene protons of maleic acid results in interference-free quantitative analysis. Although the two multiplets at 1.4 ppm and 3.2 ppm are not suitable for quantitative analysis; yet they help, in addition to the other analytical signals, in confirming the identity of the drug.

Table I shows the percent recoveries obtained when the proposed method is used for the assay of the authentic chlorpropamide using the integral values of both methyl and aromatic protons. The results demonstrated good precisions (average recoveries 99.99 ± 0.17% and 99.73 ± 0.33%) using aromatic and methyl protons respectively). On the other hand, when the method is used for the assay of Pamadin tablets (two different batches) it gives reasonable results as indicated in Table III (average recoveries is 99.88 ± 0.31%).

Figure (2) indicates a linear relationship between the integral ratio (I_c/I_m) in milimeters and the concentration in miligrams. From figure (2) it is clear that the slopes K_1 and K_2 of the two lines are 0.0419 and 0.0315 for the aromatic and methyl protons respectively. Both K_1 and K_2 were obtained by dividing the integral ratio values by the corresponding concentra-

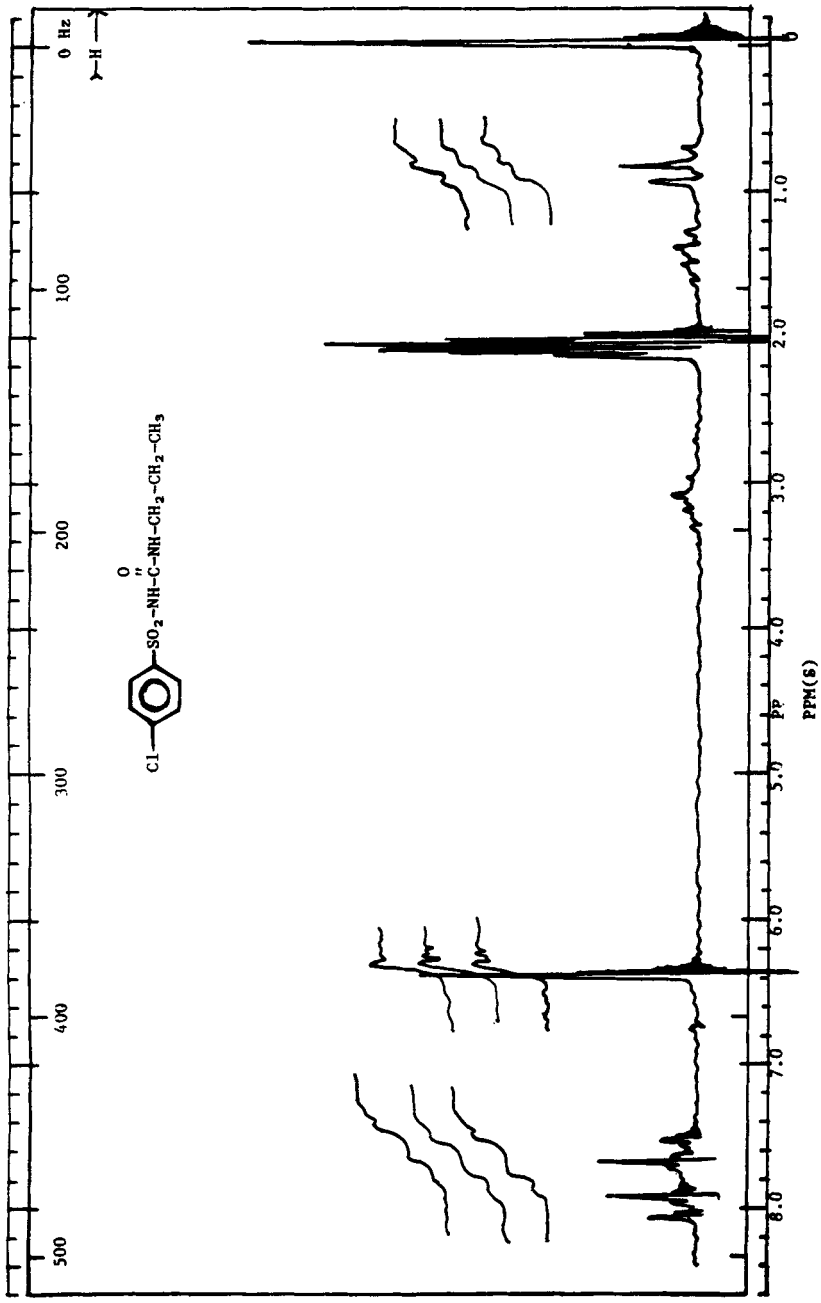


Figure (1) - PMR Spectrum of Chlorpropamide, containing maleic acid, in acetone (d_6).

Table I - The Percentage Recoveries of Authentic Chlorpropamide

Sample No.	Chlorpropamide						
	Taken (mg)	Aromatic protons			Methyl protons		
		Integral* Ratio I_c/I_m (mm)	Found (mg)	Recovery %	Integral* Ratio I_c/I_m (mm)	Found (mg)	Recovery %
1	15	0.63	15.02	100.13	0.47	14.94	99.58
2	20	0.84	20.03	100.13	0.63	20.02	100.11
3	22	0.92	21.93	99.69	0.69	21.93	99.67
4	25	1.05	25.03	100.12	9.78	24.79	99.16
5	27	1.13	26.95	99.78	0.85	27.01	100.04
6	30	1.26	30.04	100.13	0.94	29.94	99.80
7	32	1.34	31.95	99.84	1.00	31.78	99.30
8	35	1.47	35.05	100.14	1.10	34.96	99.89
9	37	1.55	36.95	99.87	1.16	36.87	99.65
10	40	1.68	40.05	100.12	1.26	40.04	100.10
Average % Recovery		99.99 ± 0.17**			99.73 ± 0.33**		

* Average of at least three measurements.

** Standard deviation.

The concentration of maleic acid in all experiments is 20 mg/ml.

tions, by using the slope values it is easy to calculate the concentration of chlorpropamide directly by dividing the obtained integral ratio by the corresponding slope value.

Table II shows the percent recoveries obtained when the slope values were used for calculation of chlorpropamide concentration in four different determinations. The percent recoveries obtained by the proposed method comply with the requirements cited by BP 1980[2,3] for chlorpropamide powder (99-101%) and for its tablets (92.5-107.5%).

The B.P. 1980 method for chlorpropamide tablets depends on the ultraviolet measurement of its methanolic extract at 232 nm ($A[1\%,1cm]=598$). While the official method of determining authentic chlorpropamide powder in B.P. 1980

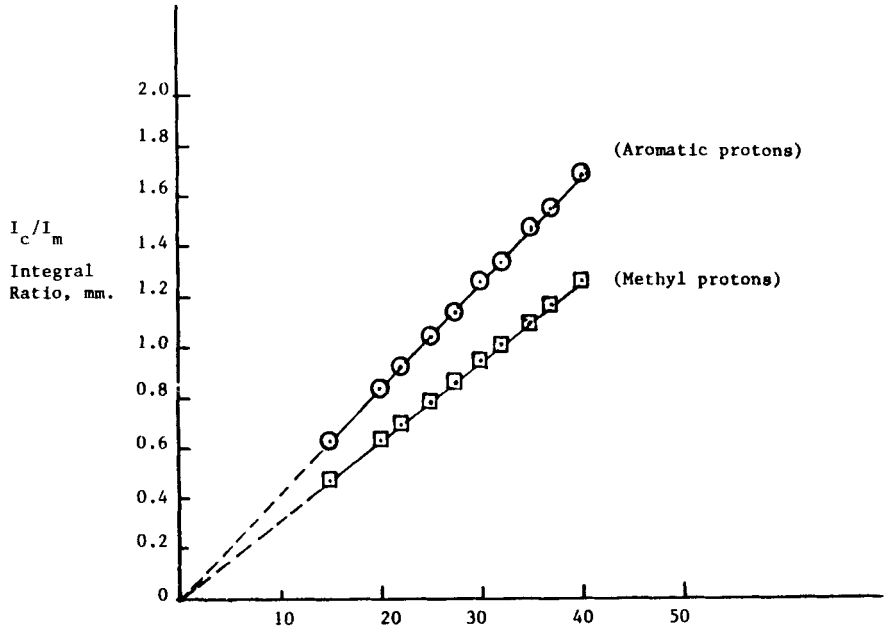


Figure (2) Calibration Graph of chlorpropamide.

depends on neutralisation reaction of the acidic proton ($-SO_2-NH-CO-$) using standard alkali sodium hydroxide, therefore, although the official method is specific for the determination of chlorpropamide tablet, yet it lacks specificity for the authentic drug. On the other hand the proposed method is specific for the drug in both authentic and pharmaceutical formulation. In addition to the specificity of the proposed procedure, there was no evidence for interference from tablet excepients when the method was applied for Pamadin tablets.

The method is simple, rapid and provides the PMR spectrum of the drug which helps in the identification and checking the purity of the drug.

REFERENCES:

1 - S. Sved, I. J. Mcgdveray and N. Beaudoin, J. Pharm. SCi., 65 (9) 1356 (1976).

2 - British pharmacopoeia 1980, London Majesty's Stationary office, Vol. I p. 107.

3 - British pharmacopoea 1980, London Majesty's Stationary office, Vol. II p. 748

Table II - The Percentage of Recoveries of Authentic Chlorpropamide Using Slope Values

Sample No.*		Chlorpropamide			
	Taken (mg)	Aromatic protons $K_1 = 0.0419$		Methyl protons $K_2 = 0.0315$	
		Found (mg)	Recovery %	Found (mg)	Recovery %
1	20	20.00	100.00	20.00	100.00
2	25	24.99	99.96	24.92	99.68
3	30	29.95	99.83	30.00	100.00
4	35	35.01	100.03	34.99	99.97
Average % Recovery		99.95 ± 0.09		99.91 ± 0.15	

* Average of at least three experiments.

4 - J. B. Dave and J. L. Patel, Indian J. pharm., 21, 226 (1959).

5 - A. Liukkonen, Farm. Aikakanslehti, 69, 139 (1960); Through chem. Abstr., 54, 15835 (1960).

6 - L. O. Gverello and J. Dobrecky, Rev. Asoc. Bioquim Argent, 33, 178 (1968); Through Anal. Abst., 18, 2748 (1970).

7 - British Pharmacopoeia 1963, London Her Majesty's Stationary Office, p. 176.

8 - British Pharmacopoeia 1973, London Her Majesty's Stationary Office, p.

9 - M. M. Amer and M. I. Walash, Bul. Fac. pharm., Cairo Univ., 12, 2 (1973).

10 - United States Pharmacopoeia 17th Rev., U.S. pharmacopeial convention, Inc., Rockville, MD, 1965, p. 130.

11 - P. Mesnard and R. Crockett, Congr. SCi., Farm., 21, Pisa, Conf. Commun., 1961, 702; Through chem. Abstr. 59, 1441 (1963).

12 - R. L. Wagner and T. J. Toolan, Ann. N. Y. Acad. SCi., 74, 449 (1959).

13 - A. A. Badr and S. E. Ibrahim, pharmazie, 37 (5), 378 (1982).

14 - K. K. Kaistha, J. pharm. SCi., 58, 235 (1969).

15 - S. B. Matin and M. Rowland, J. Pharm. pharmacol., 25, 186 (1973).

16 - F. Said, M. M. Amer and M. I. Walash, Egypt. pharm. Bull., 58, 469 (1966).

17 - A. E. Silva and M. R. Hackman, Anal. chem., 44, (7), 1145-1151 (1972).

Table III - The Percentage Recoveries of Chlorpropamide from Pamadin Tablets

Sample No.*	Integral Ratio I_c/I_m**	Chlorpropamide Claimed (mg)	Found (mg)	Recovery %
1	0.75	18	17.88	99.33
2	0.84	20	20.03	100.13
3	1.01	24	24.08	100.17
4	1.09	26	25.99	99.96
5	1.17	28	27.89	99.61
6	1.34	32	31.95	99.84
7	1.47	35	35.05	100.14

Average % Recovery = 99.88 ± 0.31***

Concentration of maleic acid in all solutions is 20 mg/ml

* Average of at least three measurements.

** Using Aromatic protons integrals.

*** Standard deviation.

18 - J. K. Chakrabarti, J. chrom., 8 (3), 414-416 (1962).
19 - S. P. Agarawal, M. I. Walash and M. I. Blake, Indian J. pharm., 35, 6 (1973).
20 - Ford, L. James, Stewart, F. Alan and R. H. Micheal, J. pharm. pharmacol., 726, 31 (1979).
21 - P. G. Takla and S. R. Joshi; J. pharm. Biomed. Anal, 1 (2), 189-193 (1983).
22 - K. Sabih and K. Sabih, J. pharm. SCi., 60, 1669 (1971).
23 - L. F. Prescott and D. R. Redman, J. pharm. pharmacol., 24, 24, 713 (1972).
24 - R. E. Hill and Grichioto, J. chromat., 145, 165 (1978).
25 - V. Gupta, Anal. Lett., 17, 2119 (1984).
26 - S. S. M. Hassan, J. of Association Official Analytical Chemists, 61, 1 (1978).
27 - S. Z. El-Khateeb, Spectroscopy Letters, 19 (3), 193-206 (1986).

Date Received: 10/01/86
Date Accepted: 11/14/86