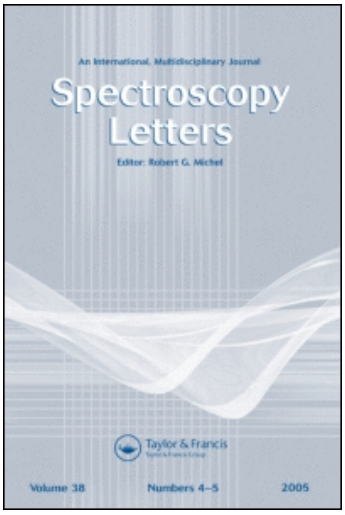

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Application of PMR Spectrometry in Quantitative analysis of Cloxacillin in some Pharmaceutical Preparations

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APPLICATION OF PMR SPECTROMETRY IN QUANTITATIVE ANALYSIS OF CLOXACILLIN IN SOME PHARMACEUTICAL PREPARATIONS

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Key Words: PMR assay, cloxacillin in pharmaceutical dosage forms, NMR assay cloxacillin sodium in pharmaceutical dosage forms, Amoxil, PMR assay in pharmaceutical dosage forms.

Abstract

A simple, accurate and specific proton magnetic resonance (PMR) procedure was developed for the assay of cloxacillin sodium and cloxacillin in combined cloxacillin-ampicillin dosage forms. The average recovery of the authentic drug and in capsules were 100.16 ± 0.53 and 100.48 ± 1.08 respectively. Reproducible results were obtained when the drug was determined in the combined cloxacillin - ampicillin capsules

Introduction

Cloxacillin (amoxil) is a semisynthetic penicillin that is highly resistant to inactivation by penicillinase. Among the other methods reported for the assay of cloxacillin and/or its sodium salt is a colorimetric procedure, which is based on the reaction with hydroxylamine and generation of a red-colored chelate with ferric salt[1]. Automatic version of this method have been used[2]. The British Pharmacopoeia 1980[3] describes another colorimetric method for the assay of cloxacillin sodium and its dosage forms using imidazole - mercury reagent and measuring the absorbance at 346 nm. A polarographic method for the assay of cloxacillin in serum has been also reported[4].

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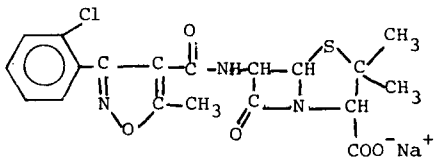
Table 1. Proton Magnetic Resonance Assignment for Cloxacillin Sodium.



Assignment	Chemical Shift (ppm) and multiplicity	
Aromatic	7.50	multiplet
6-H	5.62	doublet
5-H	5.46	doublet
3-H	4.81	singlet
5-CH_3 (isoxazole)	2.63	singlet
2-β-CH_3	1.43	singlet
2-α-CH_3	1.39	singlet

The drug was separated from several other penicillins and quantitatively determined by gas chromatographic techniques[5,6]. Several thin layer chromatographic methods have been also reported for the separation and quantitation of cloxacillin[7-10]. Other methods used for the assay of the drug are polarimetric[11], infrared spectrophotometric[12] and biological methods[13-17]. This paper describes a simple and specific method for the assay of cloxacillin and its sodium salt in different dosage forms, using the proton magnetic resonance technique.

Experimental

Materials

All spectra were recorded on a Varian T-60A, 60 MHz spectrometer using deuterium oxide and hexadeutrated dimethylsulfoxide as the solvents, maleic acid as an internal standard.

Table 2. Results of the determination of Cloxacillin Sodium in an Authentic Sample.

Sample No.	Internal standard (mg)	Cloxacillin sodium		
		added (mg)	found (mg)	% recovery (w/w)
1	50	50	50.25	100.40
2	60	60	59.95	99.92
3	75	75	74.99	99.99
4	80	80	80.90	101.13
5	110	110	110.03	100.03
6	120	120	120.75	100.63
7	90	90	89.92	99.11
8	115	115	115.05	100.04
9	150	150	150.61	100.41
10	125	125	124.98	99.98
			Average % recovery	= 100.16
			S.D.	= 0.53

Methods

For the assay of authentic cloxacillin sodium and cloxacillin sodium capsules

Weigh the specified amount of the sample into glass-stoppered weighing bottles. Add 50 mg of maleic acid and 0.6-0.8 ml of deuterium oxide to each bottle. Shake vigrously for 5 minutes and transfer the clear filtered solution to NMR tube and obtain the spectrum. Integrate, three times, the peaks of interest and determine the average integral of each peak. The amount of the drug is then calculated in the usual manner.

For the assay of cloxacillin in combined ampicillin-cloxacillin capsules

The above procedure was repeated using hexadeutrated dimethyl sulfoxide (DMSO-d_6) as solvent.

Table 3. Results of the determination of Cloxacillin Sodium in Capsules.

Sample No.	Internal standard (mg)	Cloxacillin sodium		
		Claimed (mg)	Found (mg)	% recovery (w/w)
1	50	92	93.05	101.14
2	50	89	98.52	100.58
3	50	105	104.98	99.98
4	50	102	103.21	101.19
5	50	110	110.90	100.82
6	50	90	92.31	102.57
7	50	108	106.31	98.44
8	50	105	107.18	102.08
9	50	91	93.20	102.42
10	50	88	87.03	98.90
			Average % recovery =	100.48
			S.D. =	1.08

Results and Discussion

The PMR spectrum of cloxacillin sodium in deuterium oxide shows among other peaks (Table 1), a sharp singlet at 2.63 ppm attributed to the methyl group of the isoxazole ring of cloxacillin. This is separated from other signals allowing accurate and interference free determination of the drug. Maleic acid is used as the internal standard due to the nice location of its sharp singlet in the clean area of the spectrum (6.15 ppm) and also due to its solubility in the solvents used in the assays.

Tables 2-4 show the percent recovery when the proposed method is used for the quantitation of cloxacillin and cloxacillin sodium in different dosage forms. The results were found to be in

Table 4. Results of the Determination of Cloxacillin in combined cloxacillin - ampicillin capsules.

Sample No.	Internal standard (mg)	Cloxacillin		
		Claimed (mg)	Found (mg)	% Recovery (w/w)
1	100	80	82.31	102.89
2	100	85	84.03	98.86
3	100	90	92.39	102.66
4	100	95	94.21	99.17
5	100	100	103.21	103.21
6	100	105	106.17	101.11
7	100	110	110.29	100.26
8	100	115	117.23	101.94
9	100	120	123.14	102.62
10	100	125	126.03	100.82
		Average % recovery = 100.77 S.D. = 1.30		

good agreement with those of the official method[3]. The method reported has the advantage, over other reported methods, of simple, accurate and reproducible. Moreover, the PMR spectrum of the drug helps in checking its identity and purity.

References

1. Code of Federal Regulations, Title 21, April 1973, Revision, Chapter 1, section 149j.1.

2. Lane,J.R., and Weiss, P.J., Presented at the Technicon Symposium, "Automation in Anal. Chem." New York, October 17, 1966.

3. British Pharmacopoeia, Her Majesty's Stationary Office, London, 1980, p.

4. Benner, E.J., Presented at the 10th Interscience Conference on Antimicrobial agents and Chemotherapy, Chicago, October 18-21 (1970).

5. Kawai, S., and Hashiba, S., Bunseki Kagaku, 13 (12), 1223 (1964).

6. Hisnta, C. et al., Anal. Chem. 43, 1530 (1971).

7. Wagman, G.H., and Weinstein, J.J., "Chromatography of Antibiotics", Elsevier Sci, Pub., New York, (1973), p. 140-146.

8. Schmitt, J.P., and Mathis, C., Pharma. Int. Engl. Ed., (1971), p. 522.

9. Vandamme, E.J., and Voets, J.P., J. Chromatography, 71, 141 (1972).

10. Murokawa, T., J. Antibiot. 23 (5), 250 (1970).

11. Ras mussen, C.E., and Higuchi, T.J., J. Pharm. Sci. 60 (11), 1608 (1971).

12. Colcers, et. al., J. Pharm. Belg., 24, 475 (1969).

13. Sbath, L.D., Appl. Microbiol., 15 (3), 468 (1967).

14. Saccani, F., Boll. Chem. Farm.; 106, 625 (1967).

15. Jalling, B., et al., Pharmacol. Clin. 4, 150 (1972).

16. Hooke, E.J., and Ball. G.M., J. Appl. Bacteriol. 26 (2), 216 (1966).

17. Scarlett, C.A., Agriculture (London) 73 (9) 423, (1969).

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