DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 18(3), 369-374 (1992)

RAPID LIQUID CHROMATOGRAPHIC DETERMINATION OF PARACETAMOL AND DICLOFENAC SODIUM FROM A COMBINED PHARMACEUTICAL DOSAGE

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ABSTRACT

A simple, rapid reversed-phase HPLC method for the estimation of paracetamol and diclofenac sodium simultaneously in a combined dosage was developed. A -CN bonded phase column was used with a mobile phase methanol-potassium dihydrogen phosphate (0.05M),(45:55) pH 3.5 adjusted with phosphoric acid at flow rate of 1.0 ml/min. For accurate quantitation, diltiazem hydrochloride was used as an internal standard at 270 nm.

INTRODUCTION

Many methods are available for the determination of analgesic antipyretic agent paracetamol(acetaminophen)(1,2) from pharmaceutical dosage. Diclofenac sodium, an important non-steroidal anti-inflammatory agent have been used in the treatment

of chronic rheumatoid arthritis and spondylitis. No official method is prescribed for this drug in the U.S. or British pharmacopoeia. Methods comprising spectrophotometric (3-8), proton magnetic resonance (9), TLC (10,11), GC (12) and HPLC (13) from pharmaceutical dosages have already been reported. The present report describes a complete separation method of paracetamol and diclofenac sodium from a combined pharmaceutical preparation commonly marketed in India.

METHODS AND APPARATUS

Analytical reagent grade potassium dihydrogen phosphate, orthophosphoric acid (85%), HPLC grade methanol, distilled deionised water were used to prepare mobile phase. Standard solutions of paracetamol, 0.05 mg/ml, diclofenac sodium, 0.01 mg/ml and diltiazem hydrochloride, 0.04 mg/ml were separately prepared in methanol. Four commercially available brand of tablets containing paracetamol 325 mg, diclofenac sodium 50 mg or paracetamol 500 mg, diclofenac sodium 50 mg according to the label were used and designated as A,B,C and D. The sample was prepared by crushing the tablets into powder and weighing powder equivalent to 250 mg of paracetamol accurately in a 50 ml volumetric flask. The resulting solution was then filtered through a 0.45 micron filter and 10 ml of the filtrate was diluted to

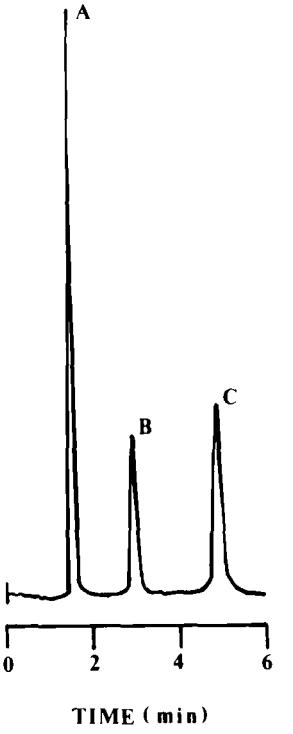

FIGURE 1

A chromatogram of the standards representing 50 µg/ml Paracetamol (A), 40 µg/ml Diltiazem hydrochloride (B) and 10 µg/ml Diclofenac sodium (C).

50 ml with the mobile phase. Further dilution was made to 50 ml with 5 ml of this solution and 5 ml internal standard(0.4 mg/ml) with the mobile phase.

A liquid chromatographic system (BRUKER Instruments, Bremen, F.R.G.) consisting of LC-21A pump, LC-313 UV-

TABLE I

ASSAY DATA FOR MARKETED BRANDS OF TABLETS

Brand	Compound	Amount labelled (mg)	Amount found (mg)	% Recovery (Mean ± S.D.)	Coefficient of Variation (%)	Standard Error of Estimation (%)
A	Paracetamol	325	321	98.76 ± 1.638	1.63	0.945
	Diclofenac sodium	50	51	102.00 ± 1.389	1.39	0.802
B	Paracetamol	325	312.05	96.01 ± 0.311	0.32	0.220
	Diclofenac sodium	50	49.92	99.84 ± 1.401	1.40	1.045
C	Paracetamol	500	490.0	98.00 ± 1.411	1.42	0.100
	Diclofenac sodium	50	51.20	102.4 ± 0.495	0.49	0.350
D	Paracetamol	500	497.08	99.42 ± 1.011	1.02	0.715
	Diclofenac sodium	50	53.86	107.72 ± 0.919	0.92	0.650

visible detector and a 7125 Rheodyne injector fitted with a 20 µl loop. The column used was NOVAPAK -CN, 150 mm X 3.9 mm, 5 µm from Water s. Data acquisition was with an integrator ORACLE-2 (INDTECH Systems, Andheri, Bombay, India).

RESULTS AND DISCUSSION

Figure 1 represents a chromatogram of standards for the separation of the drugs of interest. Quantitation was accomplished using an internal standard method expressed in terms of a plot of peak area ratio (peak area of the component / peak area of internal standard) versus concentration of the drugs in the range 8 to 80 µg/ml. The response of the detector was found to be linear with regression equations y = 48.299 x + 9.53E-07 (r=0.9999) and y = 80.099 + 5.99E-02 (r=0.9997) for paracetamol and diclofenac sodium respectively.

The present method was also applied to commercial brands of tablets, results of which are presented in Table 1. An excellent precision was achieved by this analytical procedure. The data clearly shows easy adaptability and suitability of the method for combined pharmaceutical dosage of paracetamol and diclofenac sodium.

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