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SIMULTANEOUS ESTIMATION OF METAXALONE AND DICLOFENAC POTASSIUM IN COMBINED DOSAGE FORM BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY METHOD

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ABSTRACT

A simple, sensitive, rapid, and reproducible RP-HPLC chromatographic method has been developed for the estimation of diclofenac and metaxalone in pharmaceutical formulation. Chromatography was carried out on an isocratic system of JASCO with Inertsil C-18 (4.6 x 250 μm, i.d 10 μm) using a mixture of acetonitrile, methanol and water as mobile phase at flow rate of 1 mL/min and detection was done at 234 nm. The retention time for metaxalone and diclofenac potassium was found to be 3.70 min and 2.03 min, respectively. The results obtained in the proposed method are in good agreement with labeled amounts, when marketed pharmaceutical preparations were analyzed. The method was validated for parameters like accuracy, precision, ruggedness, specificity, linearity and range according to ICH guidelines. The mean recoveries from tablet formulations were between 99-101%. The detector responses were found to be linear in the concentration range of 80-120 % of the test concentration of each drug.

Keywords: RPHPLC, Diclofenac potassium, Metaxalone.

INTRODUCTION

Metaxalone, chemically 2-[(3, 4-dimethylphenoxy) methyl]-2-oxazolidinone is centrally acting muscle relaxant. Literature reported its estimation by mass[1], and by TLC[1] from commercial dosage form and in biological samples. Diclofenac potassium, potassium [0-(2,6-dichloroanilino) phenyl] acetate, is non-steroidal anti-inflammatory agent. Diclofenac is official in I.P, where as its potassium salt is official in European Pharmacopoeia. Titrimetric and other methods have been reported for its estimation by laser desorption ionization mass spectrum[2], thermal and fractional analysis[3], U.V spectrophotometry method[4-7], direct rapid and sensitive HPLC[8,9] and HPTLC technique. A

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fixed dose combination containing diclofenac potassium and metaxalone is available commercially in the market as solid dosage form and is indicated in pain-spasm-pain cycle[10]. Methods are reported for determination of diclofenac and metaxalone individually. No method is so far reported for estimation of both these drugs in combination. Hence, an attempt has been made to develop a simple, sensitive, accurate and precise analytical methods. The present communication describes RP-HPLC method for simultaneous estimation of these drugs from their combined formulation.

EXPERIMENTAL

Instrumentation

An isocratic system from JASCO with Inertsil C-18 (4.6 x 250 μm, i.d 10 μm), PU 1580 pump, UV visible (Jasco UV) detector equipped with 20 μL injecting loop was used for the study.

Chemical and reagents

Reference standard of diclofenac potassium was obtained from Sachet Labs, India and metaxalone was obtained from SUN Pharmaceuticals, India. All the reagents and chemicals were HPLC grade Merck.

Chromatographic conditions

The mobile phase consisting of methanol (HPLC grade), acetonitrile (HPLC grade) and water (HPLC grade) were filtered through 41 # Whatmann filter paper before use, degassed and were pumped from solvent reservoir in the ratio of 45 : 40 : 15 v/v into column at a flow ate of 1 mL/min. The detection was monitored at 236 nm and the run time was 3.70 min and 2.03 min for metaxalone and diclofenac potassium, respectively. The volume of injection loop was 20μL. Prior to injection of the drug solution, the column was equilibrated for at least 30 min. with the mobile phase flowing through the system. The HPLC equipment was operated at ambient temperature.

Procedure

Different pure solvents of varying polarity (viz: acetonitrile; methanol; water) were tried in different ratios in the mobile phase. During selection and optimization of mobile phase, it was found that the retention of analyte was increased with increase in aqueous phase but much excess of aqueous phase lead to base line noise and decrease in retention time, but in appropriate concentration with methanol and acetonitrile, it gave sharp and well resolved peaks. From various mobile phases tried, Acetonitrile : Methanol : Water (45 : 40 :

15 v/v) was selected, since it gave sharp, well-resolved peaks with symmetry within limits and significant reproducible retention time of diclofenac potassium and metaxalone. The stock standard solutions of metaxalone and diclofenac potassium were prepared by dissolving and sonicating (15 min.) 50 mg of each drug in 100 mL of selected mobile phase : Acetonitrile : Methanol : Water (45 : 40 : 15 v/v) separately. The aliquot portions of stock standard solution were scanned individually on the Shimadzu U.V-Visible spectrophotometer (Model UV2409) in the range 200-400 nm using mobile phase as blank. The isobestic point was considered as detecting wavelength i.e. 236 nm. Subsequent dilutions of individual standard stock solutions within the concentration range of 10-100 µg/mL and 5-50 µg/mL for diclofenac potassium and metaxalone respectively were made with the mobile phase and calibration curve was constructed by plotting concentration vs. peak area ratio. The linearity experiment was carried out in triplicate to ascertain accuracy and precision of the method.

Assay

Commercial brand of diclofenac potassium and metaxalone were chosen for testing suitability of proposed method to estimate diclofenac potassium and metaxalone simultaneously in tablet dosage form. Twenty tablets were weighed; average weight was determined and then crushed and powdered fine with through mixing. Accurately weighed tablet powder equivalent to 100 mg of metaxalone was transferred to 100 mL volumetric flask and mobile phase was added to give 1 mg/mL solution. It was shaken vigorously for 5-10 min. Later volume was made up to mark with mobile phase. The solution was passed through Whatman filter paper No. 41. Further dilutions were made to get concentration of 80 µg/mL of metaxalone and 10 µg/mL of diclofenac potassium. Equal volume (20 µL) of standard and sample solutions were injected separately after equilibrium of stationary phase. The chromatogram were recorded and the response i.e. peak area of major peaks were measured. The content of metaxalone and diclofenac was calculated by comparing a sample peak with that of standard.

Amount of drug in tablet was calculated using formula –

$$\% \text{ Label claim} = \frac{A_t}{A_s} \text{ X } \frac{D_s}{A_t} \text{ X } \frac{W_s}{W_t} \text{ X } \frac{A}{LC} \text{ X } 100 \qquad \ldots(1)$$

Where, A_t is area for sample solution, A_s is area for standard solution, D_s is dilution factor for standard solution, D_t is dilution factor for sample solution, W_s is weight for standard solution, W_t is weight of sample solution, LC is label claim and A is average weight. The results are furnished in Tables 1 and 2.

Table 1: Results and statistical data for estimation of metaxalone and diclofenac in marketed formulation

Brand name: Flexura-D (Sample) Avg. wt.: 0.585g

Sr. No.	Peak area of standard		Peak area of aample		% Drug estimation	
	Metaxalone	Diclofenac	Metaxalone	Diclofenac	Metaxalone	Diclofenac
1			775601.6	316360	101.04	99.72
2			774998.9	317361	100.96	100.40
3	774719.5	304354	776019.9	315998	101.15	99.61
4			775700.1	318071	100.91	100.29
5			775990.8	316359	101.09	99.72
				Mean	101.03	99.94
				S.D.	0.8649	0.362
				C.V.	0.8612	0.359

Table 2: Assay and recovery studies

Sr. No	Formulation	Statistical data	% Estimation and statistical data		% Recovery	
			Metaxalone	Diclofenac	Metaxalone	Diclofenac
1	Lab. mixture	Mean	100.25	101.48	--------	--------
		S.D	0.9244	0.7110	--------	--------
		C.V	0.9241	0.7108	--------	--------
2	Marketed tablet (Sample)	Mean	101.03	99.94	101.05	99.87
		S.D	0.864	0.362	0.0953	0.3650

Table 3: Summary of system suitability parameter

Sr. No.	Parameter	Metaxalone	Diclofenac
1	Peak area	774719.5	304354
2	No. of theoretical plates	13098.9	10920.25
3	Retention time	3.72	2.03
4	Asymmetry	1.12	1.16
5	Capacity factor	7.4	4.04
6	Selectivity	1.84	
7	Resolution	14.78	

Table 4: Validation study; Summary of results for ruggedness studies

Parameter	Statistical data	% Estimation by HPLC method	
		Metaxalone	Diclofenac
Interday	Mean	101.54	100.18
	S.D	0.3502	0.149
	C.V	0.3504	0.147
Intraday	Mean	101.05	100.12
	S.D	0.953	0.795
	C.V	0.949	0.792
Different Analyst	Mean	101.05	101.64
	S.D	0.8768	0.3536
	C.V	0.8765	0.3531

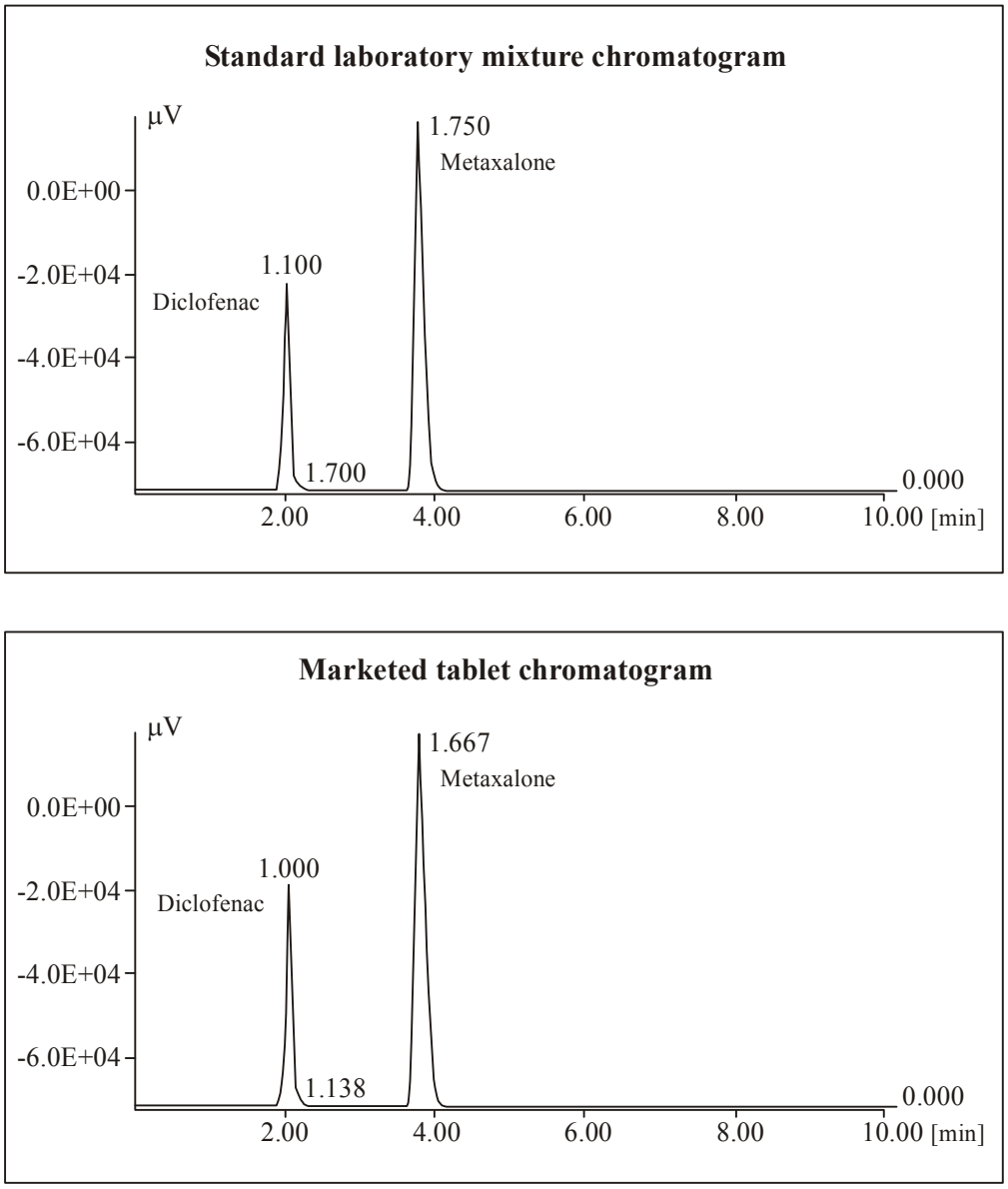

Fig. 1: Comparison of marketed tablet (Flexura-D) Chromatogram against chromatogram obtained with standard laboratory mixture

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