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Research Article

Simultaneous Estimation of Diclofenac Sodium and Rabeprazole by High Performance Liqiud Chromatographic Method in Combined Dosage Forms

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ABSTRACT
A simple, accurate and reproducible HPLC method have been developed for simultaneous estimation of Diclofenac sodium and rabeprazole from their tablets formulations. A phenomenex C_{18} (Luna) column of length 250×7.5 mm with particle size of the stationary phase 5 µm and S mobile phase potassium dihydrogen phosphate buffer (pH adjusted to 7.5 with 1 M sodium hydroxide) and acetonitrile in the ratio 60: 40 were used in this study. Retention time was found to be 9.20 min and 6.40 min for Rabeprazole and diclofenac sodium respectively. While that for internal standard as domperidone was 11.87 min at a flow rate of 2ml / min. Linearity was found in the concentration range of 10-50 µg /ml for both the drugs in this method. The results of analysis have been validated statistically and also by recovery studies.
Keywords: Diclofenac sodium, Rabeprazole, HPLC.

INTRODUCTION

Diclofenac Sodium is chemically Sodium salt of 2-[{2, 6-dichlorophenyl} amino] benzene acetic acid. [1] It is having anti-inflammatory and analgesic properties. [2] Rabeprazole is 2 -[{{4-{3-methoxy–propoxy}-3-methyl-2-pyridinyl} methyl} sulfinyl]-1H–benzimidazole.It is used in the management of acid related disorders. [3].Estimation of these drugs was carried out individually and with other drugs by HPLC [4-5], spectrophotometrically [6-9], HPTLC [10-11], supercritical fluid chromatography [12-13] but no HPLC method have been developed for this combination. In the present study a HPLC method was developed.

MATERIALS AND METHODS

Instruments

A high performance liquid chromatograph {Shimadzu HPLC class VP series)with two LC-10 ADVP double reciprocating plunger pump**,** LC-10 ADVP UV -visible 1700
spectrophotometer was used. The chemicals used were of HPLC grade.

Reagents and Solutions

Diclofenac sodium and Rabeprazole procured from Nicholas Piramal industries Ltd., Nicholas Piramal tower Mumbai, methanol of AR grade was used in the study. Mobile phase taken as potassium dihydrogen phosphate buffer (pH adjusted to 7.5 with 1 M sodium hydroxide) and acetonitrile in the ratio 60: 40. Commercially available two marketed tablet brands containing a combination of Diclofenac sodium and Rabeprazole were procured from local market.

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High performance liquid chromatography

Column was saturated with the mobile phase (mixture of 60 parts of potassium dihydrogen phosphate buffer {adjusted to pH 7.5 with 1M sodium hydroxide} and 40 parts of acetonitrile, adjusted to pH 7.5 with 1M sodium hydroxide) for about an hour at a flow rate of 2.0 ml/min, monitoring the eluent at 280.0 nm so as to obtain a steady base line. After the chromatographic conditions were set and the instrument was stabilized to obtain a steady baseline, 20 micro liter standard drug solution of diclofenac sodium (50 µg/ml) and rabeprazole (50 µg/ml) with internal standard domperidone (10 µg/ml) made in mobile phase were loaded into the injection port of the instrument and injected after filtration through a 0.2 micron membrane filter. The injection was repeated three times. The mean retention time for diclofenac sodium was found to be 9.20 min and for rabeprazole 6.40 min. Standard stock solution of pure drugs was made separately in mobile phase containing 100 µg/ml of diclofenac sodium, 100 µg/ml of rabeprazole and filtered through a 0.2 micron membrane filter. In a 10 ml volumetric flask, 3 ml standard stock solution of diclofenac sodium, 3 ml standard stock solution of rabeprazole and 1ml of domperidone was taken and volume made to the mark with mobile phase. This mixed standard solution was loaded in the injector port of the instrument. The solution was injected and a chromatogram was recorded. This was done to check the resolution of two drugs and domperidone. Both the drugs were found to be perfectly resolved.

Plotting of calibration curves

In a series of 10 ml volumetric flask several dilutions of diclofenac sodium (10-50 µg/ml), rabeprazole (10-50 µg/ml) and 10 µg/ml of domperidone were prepared in the mobile phase. Each solution was injected and a chromatogram was

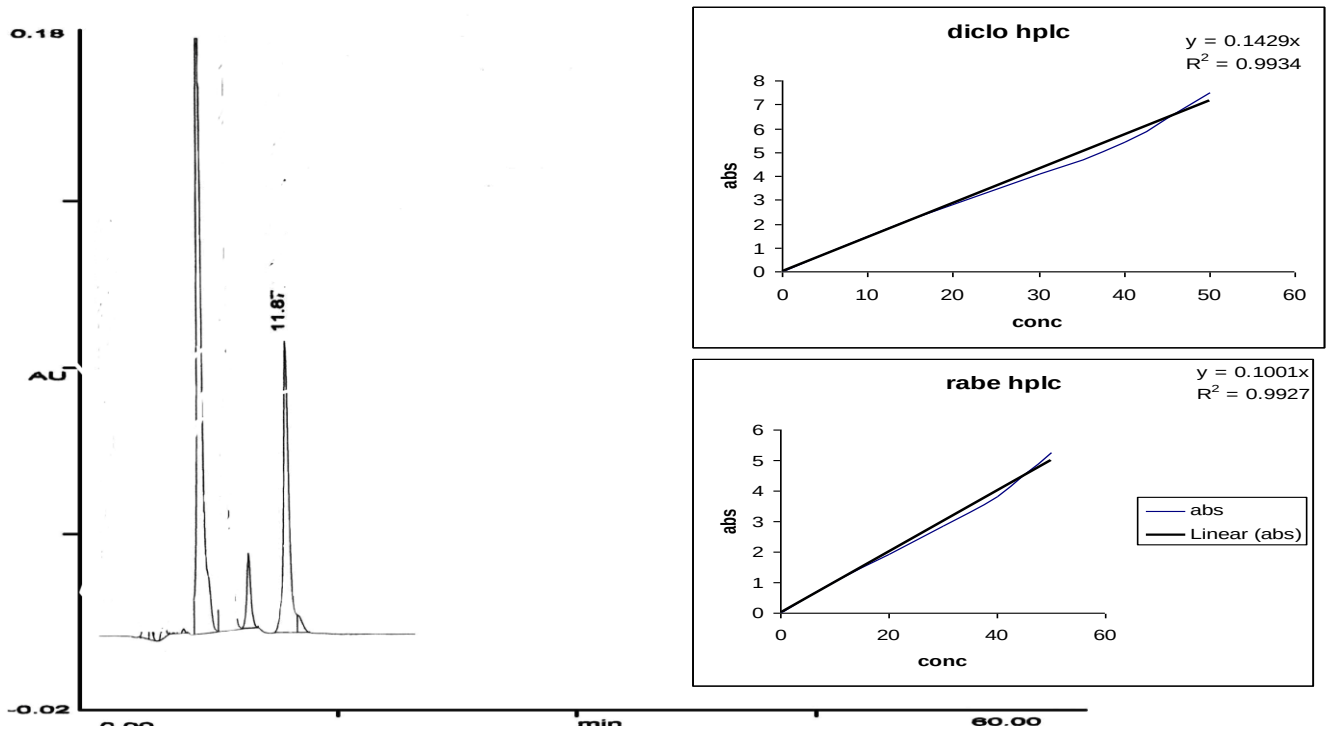

Fig. 1: Chromatogram of rabeprazole and diclofenac sodium with internal standard domperidone

Table 1: Analysis of marketed formulations

Formulation	Label Claim (mg)		%Label Claim Estimated*		S.D.		R.S.D.		C.O.V.	
	D	R	D	R	D	R	D	R	D	R
A	100	20	98.85	100.54	0.1461	0.7514	0.00148	0.00761	0.1481	0.7612
B	100	20	100.97	99.78	0.3297	0.5932	0.00324	0.00587	0.3248	0.5873

* Each value is an average of five determinations R.S.D= Relative Standard Deviation
C. O. V= Coefficient of variance R = Rabeprazole D= Diclofenac Sodium S.D = Standard Deviation

recorded. The peak area of diclofenac sodium and rabeprazole were calculated and respective calibration curves were plotted against ratio of area under curve and concentration of drug. The linearity was observed in the concentration range of 10-50 µg/ml for both the drug.

Analysis of formulations

Twenty tablets of the formulation were weighed and the average weight per tablet was calculated. Tablets were crushed and ground to a fine powder. Powder equivalent to 10 mg of diclofenac sodium was accurately weighted and transferred to a 100 ml volumetric flask containing about 75 ml mobile phase to this 1mg of domperidone was added. The powder mixture was dissolved in the mobile phase with aid of ultrasonication. The solution was filtered through Whatman filter paper no.41 into another 100 ml volumetric flask. Washed the filter paper with mobile phase and added washings to the filtrate. Volume of filtrate was made up to the mark with the mobile phase. To another 10 ml volumetric flask 3.0 ml of this solution was transferred and the volume was made up to the mark with the mobile phase. This solution was filtered through a 0.2 micron membrane filter.

After setting the chromatographic conditions and stabilizing the instrument to obtain a steady baseline, the tablet sample solution was loaded in the 20 µl sample loop of the injection port. The solution was injected and a chromatogram was recorded. The injections were repeated five times and the peak areas were recorded. A representative chromatogram has been given as Fig. 1. The peak areas of each of the drug were recorded and amount of each drug present per tablet was estimated from the respective calibration curves. The results of analysis are presented in Table 1.

Recovery studies

Recovery studies for both the marketed formulations were carried out by addition of known quantity of standard drug solution to pre analyzed tabled sample solution at three different concentration levels. The concentration of drug in final dilution was determined after addition of known concentration of pure drug and determined the percentage recovery after deduction of concentration of drug in original tablet sample. Results of recovery are reported in Table 2.

Table 2: Recovery studies

Formulations	Amount Added (µg/ml)		Amount Recovered(µg/ml)		% Recovered	
	D	R	D	R	D	R
A	2	2	1.96	2.01	98.00	100.55
	4	4	4.05	4.11	101.25	101.75
	6	6	6.01	5.93	100.16	98.83
B	2	2	1.98	2.04	99.00	102.00
	4	4	3.97	4.07	99.25	101.75
	6	6	6.05	5.89	100.83	98.16

RESULT AND DISCUSSION

The results of analysis of two drugs from of tablet formulations using this developed method were found close to 100%. Values of standard deviation were satisfactorily low indicating accuracy and reproducibility of the methods. Recovery studies were satisfactory which shows that there is no interference of excipients. The developed method was found to be simple, rapid accurate and can be used for routine analysis of two drugs from combined tablet formulations.

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