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Estimation of Etoricoxib in Tablet Dosage form by RP- HPLC using Internal Standard with Emphasize on Specificity Parameter Method

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ABSTRACT

A simple, precise and rapid RP-HPLC method was developed for the estimation of etoricoxib in pharmaceutical dosage forms. The method was carried out on a ODS Hypersil C_{18} (250 x 4.6 mm) column using a mixture of acetonitrile: water (55:45 v/v). The detection was carried out at 269 nm using caffeine as an internal standard. The linearity was found to be 10 to 60µg/ml injection with correlation coefficient of 0.999. The percentage recovery was found to be 99.24± 1.064 to 102.66±1.22. The result of analysis of marketed formulation was found to be 99.09±0.473 to 99.55±0.493%. The method was validated and studied for the various parameters like accuracy, precision, ruggedness and specificity study . The proposed method was successfully applied for the estimation of etoricoxib in pharmaceutical dosage forms.

Key words: Etoricoxib, HPLC, Pharmaceutical dosage forms.

INTRODUCTION

Etoricoxib(ETO),5-chloro-2-(6-methyl pyridine-3-yl)-3-(4-methyl- sulfonylphenyl) pyridine , $C_{13}H_{12}N_2O_5S$ is a Non-steroidal anti-inflammatory and recommended to relieve the signs and symptoms of osteoarthritis, rheumatoid arthritis and acute pain chronic back pain, dysmenorrhoea, spondylitis and acute gouty arthritis[1]. The use of an internal standard (IS) helps to eliminate analytical errors due to dilutions. Considering the general requirements for internal standard, caffeine (IS) was chosen as an internal standard.

Literature survey has revealed various methods for estimation of Etoricoxib biological fluids. Similarly various methods[2-9] have been reported for determination of Etoricoxib in pharmaceutical formulations and from biological fluids.

The literature does not cite any method for estimation of Etoricoxib by RP-HPLC in pharmaceutical preparations using an internal standard. The intent of the present study was to develop a new RP-HPLC method for determination of Etoricoxib in pharmaceutical formulations using internal standard caffeine.

MATERIAL AND METHODS

Etoricoxib working standard was a gift sample from Sun Pharmaceutical Industries Ltd., Vapi, India, whereas caffeine was obtained from Zim Laboratories Ltd., Nagpur, India. Methanol, Acetonitrile (HPLC grade, S. D. Fine Chemicals, India) and triple distilled water were used in this investigation. Commercially available different brands of etoricoxib tablets(claimed to contain 60, 90& 120 mg of the drug) were procured from the local medical market. Quantitative HPLC was performed on a isocratic mode of High Performance Liquid Chromatography (Shimadzu HPLC Class 10A VP series) with LC-10AS pumps, a multi wavelength UV/VIS detector and Hypersil (250 mm×4.6 mm i.d., particle size 5 µ) column. The HPLC system was equipped with the software Class -10VP series version (Make: Shimadzu).

EXPERIMENTAL

The mobile phase was prepared by mixing Acetonitrile and Water in proportion (55:45 v/v). The mobile phase was filtered through a 0.4 µm membrane filter, degassed. The mobile phase was passed from the solvent reservoir to the column at a flow rate of 0.9ml/min. The run time was set at 7 min. The volume of injection loop was 20 µl. The column was equilibrated for at least 45 min with the mobile phase flowing through the HPLC systems. The drug chromatograms were recorded at 269 nm and the data were acquired, stored and analyzed with the software.

Working standard solution of etoricoxib (30 µg/ml) was prepared by suitable dilution of the stock solution (1000 µg/ml in methanol) with the mobile phase. Different concentrations ranging from 10 to 60µg/ml were prepared and taken in 10 ml volumetric flasks, caffeine solution (100 µg/ml) was prepared and 1.0 ml added to each drug solution and this mixture was diluted upto the mark with mobile phase to get desired concentration range. Each of drug solutions were injected three times into the HPLC system and the peak area and retention time was recorded (Fig. 1).

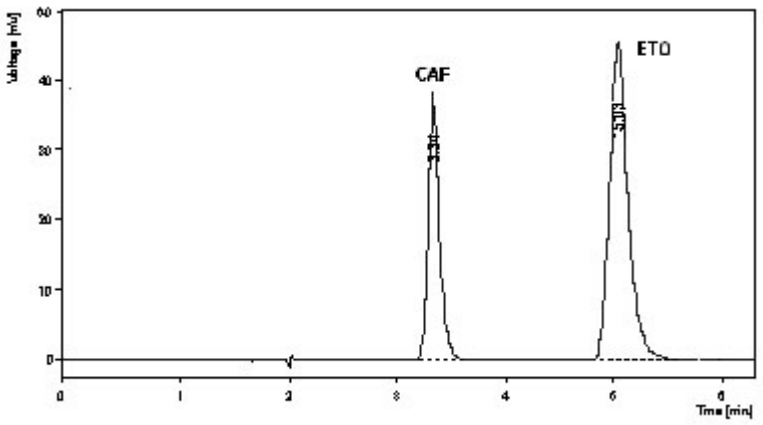

Fig. 1: Chromatograms of standard solution of etorcoxib with Internal standeard (Retention Time: Caffeine (IS)-3.34min and Etoricoxib-5.03 min)

Estimation of drug in Marketed Formulations

Twenty tablets each of the brand (with etoricoxib dose 60, 90 and 120 mg) were accurately weighed and average weight was calculated. The tablets were crushed to obtain fine powder. An accurately weighed quantity of tablet powder of each brand equivalent to about 10.0 mg of etoricoxib was transferred to a 10.0 ml volumetric flask, shaken with sufficient quantity of methanol for 15 min and the volume was made up to the mark with the same

solvent. All the solutions were filtered through Whatman filter paper No.1 and clear filtrate was transferred to 10.0 ml volumetric flasks containing 1.0 ml of solution IS of concentration (100 µg/ml) and mixed contents were diluted to mark with mobile phase. Etoricoxib tablets with varying dose 60 mg, 90 mg and 120 mg were analyzed and chromatograms were recorded(Figure-2). The obtained results are given in (Table-1a & Table1b).

Table 1(a): Summary of system suitability parameters

	Parameters	Caffeine(IS)	Etoricoxib
1.	Linearity	10 to 60 µg/ml	
2.	Slope	0.0701	
3.	Intercept	0.0231	
4.	Regression Coefficient (r^2)	0.9990	
5.	Retention Time±SD	3.33±0.0157	5.05±0.0047
6.	Resolution factor±SD	9.521±0.233	
7.	Capacity Factor±SD	2.33±0.015	4.05±0.0047
8.	Assymetry±SD	1.08±0.0219	1.15±0.0155

Table 1(b): Observations and results for estimation of etoricoxib in tablet Formulation

Brand	Labeled Claim (mg/tablet)	Amount Estimated (mg/tablet)	% Estimation*	S.D.	%RSD	S.E.
TB-1	60	59.72	99.55	0.473	0.175	0.081
TB-2	90	89.78	99.09	0.493	0.765	0.211
TB-3	120	119.56	99.61	0.174	0.475	0.077

TB-1 Retoz® Tablet (Dr. Reddy's Laboratory., Hyderabad)

TB-2 Etody® Tablet & TB-3 Etoshine® Tablet (Sarabhai Piramal Pharmaceuticals Pvt. Ltd., Vadodara)

*Mean of three observations

Method Validation

Recovery (Accuracy)

The method was validated as per ICH guidelines. The accuracy of the method was determined by recovery experiments. The recovery studies were carried out six times and the percentage recovery and standard deviation of the percentage recovery were calculated and presented in (Table – 2). From the data obtained, added recoveries of standard drugs were found to be accurate.

Linearity

The calibration curve of etoricoxib was constructed by plotting the ratio of the peak area of etoricoxib to the peak area of internal standard (Y) against concentration of etoricoxib (X). It was found to be linear with a correlation coefficient of 0.999, the representative linear regression equation being Y= 0.0701 X +0.0231. The % RSD, based on the peak area ratios for triplicate injections were found to be well below 2 %.

Precision (Ruggedness)

The performed method was validated for ruggedness through its intra-day and inter-day precision . The intra-day and inter-day (3 days, n= 3) precision were expressed as relative standard deviation was well below 2% (Table–1b & Table-3).

The HPLC method developed in the present study was used to quantitatively estimate etoricoxib in tablet dosage forms.

Specificity study

The specificity studies were carried out by attempting deliberate degradation of the tablet sample by exposure to various stress conditions. (Tablet containing 60mg etoricoxib). Accurately weighed quantities of tablet powder (specified in procedure) were taken in five different volumetric flasks and they were stored for 24 h under different conditions as follows:

a) At 50°C after addition of 1.0 ml of 0.1N NaOH (alkali)
b) At 50°C after addition of 1.0 ml of 0.1N HCl (Acid)
c) At 50°C after addition of 1.0 ml of 3% H_2O_2 (Oxide)
d) At 60°C (Heat)
e) UV light exposure for 24 h.

After 24 h the sample solutions were prepared to get the final concentration 30 µg/ml. Replicate injections of working standard solution and each of all five sample solutions were made separately under optimized chromatographic conditions and chromatograms were recorded. Peak areas of standard and sample peaks were evaluated. (Table-4)

Table 2: Results of recovery studies for estimation of etoricoxib in tablet

S. No.	Amount of std. drug recovered (mg)	Percent Recovery *etoricoxib
1.	5.143	102.66
2.	10.269	102.49
3.	15.259	101.54
4.	19.887	99.24
5.	25.394	101.38
	Mean	101.46
	± S.D.	1.22
	% R.S.D.	1.34

Table 3: Results of Ruggedness Studies: for estimation of Etoricoxib in tablet

	Intra Day	Inter Day	Different Analysts
	% of labeled claim*		
Mean	98.86	99.32	99.71
± S.D.	0.661	0.086	0.160
% R.S.D.	0.669	0.087	0.161

*Each reading is average of three observations

Table 4: Results of specificity studies for estimation of etoricoxib in tablet

S. No.	Stress conditions	%Percent oflabeled claim* Etoricoxib
1.	Acid	94.56
2.	Alkali	99.99
3.	Oxide	98.84
4.	Heat	99.94
5.	UV chamber	99.36
6.	Normal	100.06

*Each reading is a mean of three observations

DISCUSSION

Analysis of tablets containing etoricoxib was carried out by using the optimized mobile phase containing Acetonitrile: Water (55:45 v/v). UV detection was carried out at 269nm. System suitability tests were carried out using freshly prepared standard stock solution of etoricoxib with internal standard caffeine the parameters obtained with 20 ìl injection volume are summarized in Table-1a.

The low % RSD value for intraday and interday precision revealed that the proposed method is rugged. The results obtained by the proposed method were close to the label claim of both drugs. The lower values of % RSD indicate that the method is precise and accurate (Assay results Table-1). Also, when a known amount of the drug solution was added to a powdered sample of the dosage form and subjected to an estimation of the drug by the proposed method, there was a significant recovery of etoricoxib indicating that the proposed procedure for the estimation of etoricoxib in the tablet dosage forms is accurate. (Table-2).

Three different brands, TB-1, TB-2 and TB3 of tablets were taken for this study. Results of all Brands showed almost 100%. The results of specificity studies showed that Etoricoxib was stable on exposure to various stress conditions. Any by-products of synthesis due to chemical reaction under stressed condition that may be present. It had been observed that acid degradation sample shows unknown interference and there is a significant deviation in the assay results compare to the results of normal sample (Table 4). Whereas other treated sample shows results nearer to the average value.

The proposed method is simple, specific, precise and accurate for simultaneous estimation of etoricoxib in tablets. The developed method can also be applied for dissolution testing of tablet formulations.

The results of the study showed that the proposed RP-HPLC method for analysis of etoricoxib in pharmaceutical dosage forms is simple, rapid, precise and accurate. It will be useful for the determination of etoricoxib in its pharmaceutical dosage forms.

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