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DETERMINATION OF ETORICOXIB IN BULK FORMULATIONS BY RP-HPLC METHOD

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ABSTRACT

For the determination of Etoricoxib in bulk formulations a rapid, selective and simple RP-HPLC method was formed and used, by optimizing stationary phase, composition of mobile phase and other parameters. Study was performed on RP- C-18 (250 x 4.6 mm), 5 µm column (Symmetry, Waters) with the mobile phase Acetonitrile: Phosphate buffer in the ratio of 70:30 v/v. At a flow rate of 1 ml/ min, the mobile phase was pumped and the detection was monitored at 220 nm. Short retention time was observed of the drug i.e**.** 9.589 min. The calibration curve was linear from 70ppm to 130 ppm and correlation coefficient of 0.998144. The intra-day precision (%RSD) was 0.99 and inter-day precision (% RSD) was in the range 0.99 to 1.21. The assay was found to be 99.28 %. The above method was successfully used for the assay of etoricoxib in bulk formulations.

KEYWORDS: Etoricoxib, RP-HPLC, Assay, Bulk formulation.

INTRODUCTION

Non-Steroidal Anti- Inflammatory drug (NSAID) Etoricoxib “Fig. 1”, is a selective cyclo-oxygenase-II (cox-II) inhibitor, which reduces production of Prostaglandins (PG’s) that ultimately eases pain and inflammation. Etoricoxib is now widely used in conditions like osteoarthritis, rheumatoid arthritis, gout, lower back pain and ankylosing spondylitis. It has proved as a good alternative in the management and treatment of pain and arthritis, as compared to other NSAIDs.[1,2,3]

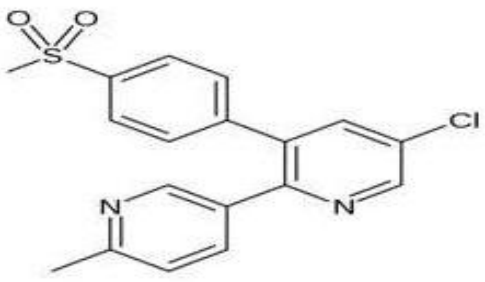

Fig. 1: Chemical structure of etoricoxib.

IUPAC name of Etoricoxib is 5-chloro-6'-methyl-3- [4- (methylsulfonyl) phenyl]-2, 3'-bipyridine. Its molecular formula is $C_{18}H_{15}ClN_2O_2S$. Review of literature shows that various analytical methods have been developed like HPLC techniques, Ultra-Violet and Visible spectrophotometric methods, HPTLC, LC/Mass spectrophotometry, etc.[5-11] for the analysis of Etoricoxib in serums,[12] plasma,[13] bulk formulations and pharmaceutical dosage forms.[14,15] So, a new column chromatographic method (RP-HPLC) should be developed for the estimation of the drug with high sensitivity and selectivity, which can prove to be very useful for the estimation of etoricoxib in various pharmaceutical formulations.

MATERIALS AND METHODS

Chemicals and Materials

All solvents (Acetonitrile, Methanol and Potassium dihydrogen phosphate) were of HPLC grade. All other materials purchased were of analytical grade E-Merck, Qualigens, and Rankem etc. The Etoricoxib working standard and sample formulations were procured as a sample from one of the reputed pharmaceutical companies of Haridwar i.e. Akums Drugs and Pharmaceuticals Ltd. Millipore water and Whatman filter paper Grade-I were used throughout the experimental work.

Chromatographic conditions

In this study shimadzu LC-2010A-HT HPLC system with 2010A auto sampler was used, stationary phase used was Waters Symmetry RP- C-18 (250 x 4.6 mm), 5 µm column. Mobile phase used was Acetonitrile: Phosphate buffer (70:30 v/v) with isocratic elution at the flow rate of 1.0 ml/ min. Ambient temperature was maintained, run time was 10 min and 20 µl was the volume of injection. Detection was done at 220 nm wavelength.

Mobile phase preparation

Phosphate Buffer - 3.4gm of monobasic potassium phosphate (KH_2PO_4) was dissolved in water to make 1000 ml of this solution with pH 4.7. Then mobile phase was made in the composition of acetonitrile: phosphate buffer (70:30 % v/v).

Standard solution preparation

Working standard solution of Etoricoxib was prepared by weighing 25 mg of drug and then it was added in 50 ml volumetric flask. 25 ml mobile phase was added and the solution was sonicated for 15 min. Later the mobile phase was added to make up the volume upto 50 ml. Then, 10 ml of the above solution was taken and diluted to 50 ml with mobile phase. 0.45µ nylon membrane filter was used to filter the final solution. Concentration of the working standard was 100 ppm.

Sample solution preparation

Sample was accurately weighed equivalent to 25 mg of Etoricoxib and it was transferred in 50 ml volumetric flask. 25 ml mobile phase was added and the solution was sonicated for 15 min. Later the mobile phase was added to make up the volume upto 50 ml. Then, 10 ml of the above solution was taken and diluted to 50 ml with mobile phase. 0.45µ nylon membrane filter was used to filter the final solution. Concentration of the sample solution was 100 ppm.

Determination of etoricoxib by assay

Standard solution, Sample solution and blank solution were taken in the same volume i.e. 20 µl and all the three were injected into the HPLC system separately. Later their chromatograms were recorded “Fig. 2” and “Fig. 3”. The results of the assay are presented in Table 1.

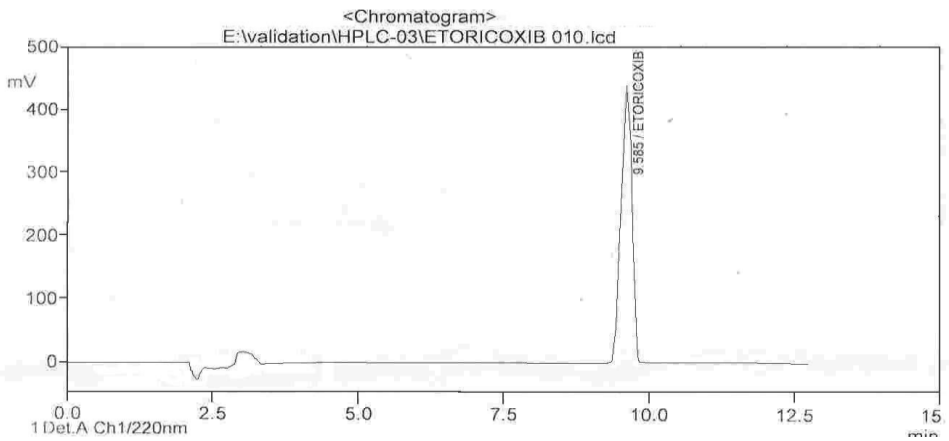

Fig. 2: Etoricoxib standard solution chromatogram.

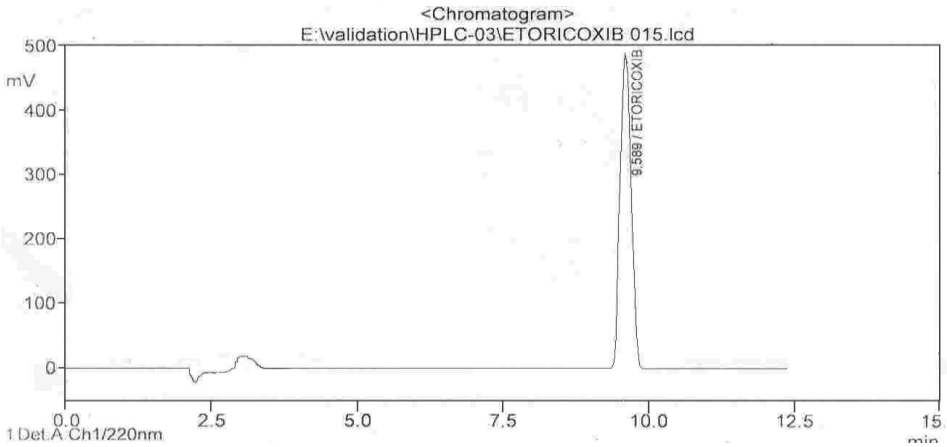

Fig. 3: Etoricoxib test solution chromatogram.

Table 1: Etoricoxib assay.

S. No.	Etoricoxib solution	Average Retention Time	Average area	Labeled amount per tablet	Amount found per tablet	Assay %
1	Standard	9.565*	5674128*	-	-	-
2	Test	9.589*	5725264**	90 mg	89.36 mg	99.28 %

** Average retention time and area of etoricoxib standard solution (5 replicate)*

*** Average retention time and area of etoricoxib test solution (duplicate)*

Calibration curve of etoricoxib

It was drawn by plotting the area of the drug i.e. Etoricoxib (Y) against concentration of etoricoxib (X). Different concentration levels of the drug were determined, like from 70ppm to 130. The coefficient of Correlation was 0.998144**.** The outcome revealed that a distinguished correlation exists between concentration of Etoricoxib and response factor within the given concentration range. The conclusions are outlined in Table 2 and the linear calibration curve is shown in "Fig. 4".

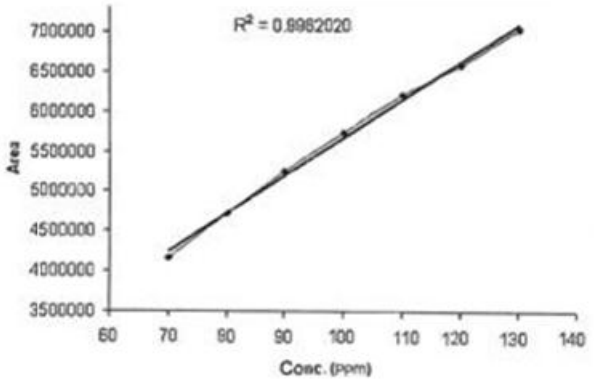

Fig. 4: Etoricoxib calibration curve.

Table 2: Linearity of etoricoxib.

S. No.	Concentration (in ppm)	Area
1	70	4366233
2	80	4925283
3	90	5451362
4	100	5944168
5	110	6409950
6	120	6786086
7	130	7237138
	Correlation coefficient	**0.998144**

Acceptance Standard: The Regression coefficient (R^2) and Correlation coefficient value should not be less than 0.997.

Recovery

The accuracy of the method was determined by recovery experiments by spiking the known concentration of the drug Etoricoxib (in raw material form, i.e. API) into the placebo at 70%, 100% and 130% of the labeled amount in triplicate. The quantity of Etoricoxib was analyzed as per the above method of the test, then % recovery was also calculated and given in Table 3.

Table 3: Recovery of etoricoxib.

S. No.	API spiked in Placebo (mg)		Recovery (mg)	% Recovery
1	70%	69.36	68.47	98.94
2	100%	99.73	97.89	100.08
3	130%	129.14	127.74	99.68

Acceptance Standard: The % Recovery at each spike level should be between 98 and 102.

Intraday and Interday precision

The precision (system and method) were exhibited by intraday variation studies. In this procedure 5 injections of the standard solution (in replicate) and 6 successive injections of the sample solution (in duplicate) were injected. Chromatograms were produced and percent assay and % RSD were computed for Etoricoxib, Table 4.

Table 4: Etoricoxib intraday precision.

S. No.	Labelled claim	Amount of Etoricoxib*	% Assay*
1	90 mg	89.35 mg	99.26
2	90 mg	89.61 mg	99.63
3	90 mg	88.86 mg	98.78
4	90 mg	90.03 mg	100.11
5	90 mg	91.08 mg	101.47
6	90 mg	88.94 mg	98.97

Mean	89.64 mg	99.70
Standard Deviation (SD)		0.99
Relative Standard Deviation (% RSD)		0.99

**Average of two scans*

Acceptance Standard: The % RSD should not be more than 2 %.

In Inter day precision two different analysts (A-1 and A-2) performed the study. 6 replicate injections of sample solutions in succession were injected by both the analysts and the chromatograms were produced. Later % RSD was determined and presented in Table 5.

Table no. 5: Etoricoxib interday precision.

S. No.	Amount of drug present*		% Assay of Etoricoxib*	
	Analyst - I	Analyst - II	Analyst - I	Analyst - II
1	89.35 mg	90.92 mg	99.26	100.86
2	89.61 mg	89.47 mg	99.63	99.38
3	88.86 mg	89.28 mg	98.78	98.16
4	90.03 mg	88.73 mg	100.11	98.62
5	91.08 mg	90.48 mg	101.47	100.59
6	88.94 mg	90.89 mg	98.97	100.92
Mean	89.64 mg	89.96 mg	99.70	99.76
Standard Deviation			0.99	1.20
% Relative Standard Deviation			0.99	1.21
Overall Mean				99.73
Overall SD				1.05
Overall % RSD				1.05

**Average of two scans*

Acceptance Standard: The % RSD should not be more than 2%.

Specificity

This HPLC method's specificity was demonstrated and noticed by absolute separation of the drug, Etoricoxib in existence of placebo tablet. In addition to this, there was zero intervention at the Etoricoxib retention time in the graphs. This reveals that the peak of analyte was refined and clear and the formulation's excipients did not hinder with the analyte.

System suitability tests

This test is performed to ensure that the method can generate results of acceptable accuracy and precision. The USP (2000) defines parameters that can be used to determine system suitability prior to analysis. The system suitability parameters like Theoretical plates, Resolution (R), Tailing factor (T), LOD (mg/ml), LOQ (mg/ml) were calculated and compared with standard values to determine whether the proposed HPLC method for the determination of Etoricoxib in bulk formulations was validated or not.

System suitability test was performed by injecting 5 replicate standard solution in different stages of the method validation.[16] The evaluation is computed in the Table 6.

Table 6: System suitability tests.

S. No.	Name of the Experiment	Theoretical Plates	Tailing Factor
1	ASSAY	11925.68	1.024
2	LINEARITY	11983.37	1.061
3	RECOVERY	12043.25	1.062
4	PRECISION		
4.1	Intraday Precision	11147.61	1.137
4.2	Interday Precision	11251.73	1.273
5	SPECIFICITY	12261.21	1.429

Acceptance Standard: Theoretical Plates should not be less than 2000 and the Tailing Factor should not be more than 2.

RESULTS AND DISCUSSION

The extraction of the sample from the stationary phase i.e. column is mainly influenced by the polar mobile phase. So, distinct mobile phases were tested but acceptable results viz. well resolved, separated and symmetrical peaks were only obtained with the composition of acetonitrile: phosphate buffer (70:30 v/v). The Retention time of the drug Etoricoxib was established at 9.589 min. It was also found that the drug follows linearity range with the concentration of 70 ppm to 130 ppm. The RSD value for all the parameters which were used in this study, viz. recovery and precision was less than 2%. This shows that method used was accurate and precise. The system suitability parameters are within the specified limits, which implies that the excipients present in the formulation did not hampered the proposed method. The method was found to be simple, precise, accurate, specific and rapid for determination of etoricoxib in bulk formulation. The mobile phase is simple to prepare and economical.

Chromatogram which reveals the separation of Etoricoxib are given in “Fig. 2” and “Fig. 3”.

CONCLUSION

The results of this study showed that the proposed RP-HPLC method for the determination of the drug Etoricoxib in bulk formulation is simple, precise, rapid, specific and accurate. Hence, it can be easily adopted for the determination of etoricoxib in routine work in various Pharmaceutical Industries and in Research Laboratories.

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