DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF ETORICOXIB IN BULK AND TABLET FORMULATION

S.R. Shahi*, G.R. Agrawal, P.B. Rathi, N.V. Shinde, V.G. Somani ,.S.B. Mahamuni and A.N. Padalkar

* Government College of Pharmacy, Vedant Road, Aurangabad, M.S.-431005.
E-mail: sadhanashahi@yahoo.com

ABSTRACT

All immediate release tablets are subjected to dissolution studies in 0.1 N HCl as recommended by SUPAC-IR guidelines or in specified dissolution medium as per their official monograph. The present UV spectrophotometric method is simple, accurate, specific and highly sensitive, developed in 0.1 N HCL and very useful for analysis of immediate release tablets. The method is validated for the determination of Etoricoxib in bulk and tablet dosage form. Etoricoxib is the newest addition to the group of Non-Steroidal Anti-Inflammatory Drugs - highly selective COX-2 inhibitor. The standard solution of etoricoxib in 0.1N HCl showed maximum absorption at 233 nm. Beer-Lambert's law obeyed in the concentration range of 2-24 µg/ml, with regression, slope and intercept 0.9996, 0.072 and 0.089 respectively. The percentage recovery is 99.965 which reflect that the method is free from interference of the impurities and other additives during the estimation of drug in formulation. The proposed method can be successfully used for analysis of etoricoxib in marketed preparations. The results of analysis have been validated statistically and by recovery studies.

Keywords: *Etoricoxib, UV determination, Tablet dosage form, SUPAC guidelines.*

INTRODUCTION

Etoricoxib (5-chloro-2-[6-methyl pyridin-3-yl]-3-[4-methylsulfonylphenyl] pyridine) is a novel, selective second generation cyclo-oxygenase-2 inhibitor administered orally as an analgesic and anti-inflammatory drug that is used for the treatment of osteoarthritis, rheumatoid arthritis and gouty arthritis.[1, 2] It is an off-white crystalline powder, relatively insoluble in water, and freely soluble in alkaline aqueous solutions[3]. Etoricoxib is available in tablet dosage forms (60, 90, 120 mg) [4] and is not official in any pharmacopoeia. The chemical structure of etoricoxib[3] is shown in Figure 1.
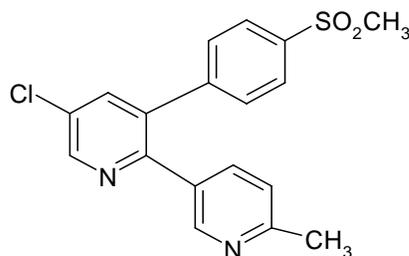
Fig 1: Chemical Structure of Etoricoxib

Literature survey revealed the availability of method of estimation of etoricoxib by HPLC in plain solution and biological fluids either alone or mixture along with its metabolic products.[5]

According to SUPAC-IR guidelines, all Immediate Release (IR) tablets especially Oro-dispersible tablets should be subjected to *in vitro* dissolution studies in 0.1N HCl or other as recommended by official monograph of drug candidate.[6] The aim of present investigation is to develop simple, rapid and cost effective analytical method for bulk drug and tablet dosage forms and its validation.

EXPERIMENTAL

Instruments
A Shimadzu UV-Visible Spectrophotometer (UV-1700) with a matched pair of 10 mm quartz cells were used for experimental purpose.

Materials
Etoricoxib was procured as gift sample from Torrent Research Center, Ahmedabad. The obtained etoricoxib was recrystallized in methanol for experimental purpose. Freshly prepared 0.1N HCl, methanol and all other chemicals and reagents were of analytical grade. The commercially available two marketed tablet brands containing Etoricoxib, 60 mg in each tablet have been used for estimation.

Preparation of Standard Stock Solution
The standard stock solution was prepared by dissolving etoricoxib in 0.1N HCl to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with 0.1N HCl separately to prepare series of concentrations from 2-24 µg/ml. The λ_{max} was found by UV spectrum of etoricoxib in 0.1NHCl, in the range of 200-400 nm and it was found to be 233 nm. Absorbance was measured at 233 nm against 0.1N HCl as blank. The calibration curve was prepared by plotting absorbance versus concentration of Etoricoxib.

Application of the Proposed Procedure for the Determination in Tablets
The proposed procedure was adopted for determination of Etoricoxib in tablets in following manner.[7] The marketed tablet formulations of etoricoxib were used for the purpose of analysis. Twenty tablets were weighed and average weight was calculated, crushed to fine powder. The powder equivalent to 60 mg of Etoricoxib was transferred in 100 ml volumetric flask and dissolved in 0.1NHCl by intermittent shaking. The volume was made up to mark to get final concentration of 600 µg/ml. The solution was then filtered through Whatmann filter paper (no.41). This solution was used as stock solution.
The working solution of drug (6 µg/ml) was prepared from standard stock solution in 0.1NHCl. The absorbance of working solution was measured and amount of Etoricoxib was calculated from the calibration curve. The readings were taken in triplicate and same procedure was repeated with another marketed tablet formulation.
All the marketed tablet formulations contain excipients which are added along with active pharmaceutical ingredient. These substances may cause some interference during estimation of active pharmaceutical ingredient. Recovery study was carried out on marketed tablet formulations and the results obtained showed that, there was no interference from excipients. From the results of recovery study it can be claimed that, the method can be used for estimation of etoricoxib in tablet dosage forms. The results obtained are shown in Table 3.

RESULTS AND DISCUSSION

Statistical evaluation of analysis and recovery study was carried out. The data obtained from the proposed method showed accuracy of method. The values of standard deviation and coefficient of variation were satisfactorily low. The percentage recovery of 99% to 101% was indicative of accuracy of method.

Validation of Method

The method was validated with respect to linearity and range, accuracy and precision, limit of detection (LOD), limit of quantitation (LOQ), selectivity and robustness.[8, 9]

Linearity and Range

The prepared aliquots (2-24 µg/ml) were scanned for absorbance at λ_{max} value 233 nm. The absorbance range was found to be 0.255-1.820. These solutions obeyed Beer-Lambert's law in above concentration range with regression of 0.9996.

Accuracy and Precision

Accuracy and precision were investigated by analyzing three concentrations of Etoricoxib (i.e. 80, 100 and 120% of 60 mg Etoricoxib tablet) in three independent replicates on the same day (Intra-day accuracy and precision) and on three consecutive days (Inter-day accuracy and precision). The data evaluated was summarized in Table 2.

Intra-day and Inter-day relative standard deviation (RSD) values and also the low RSD values obtained from the analysis of the pharmaceutical formulations (Table 3) indicated good intermediate precision of method.

To validate prediction ability of suggested method, different concentrations of etoricoxib samples were prepared and analyzed. The results were satisfactory. Using standard addition technique, the method was further validated. The standard addition technique was carried out by adding excipients (lactose, starch, magnesium stearate, mannitol etc.), with the addition of etoricoxib at 50% (30 µg/ml), 100% (60 µg/ml) and 150% (90 µg/ml), respectively in sample solution. The percent recoveries of the three concentrations were found to be close to 100%, indicative of high accuracy. The high percent recoveries indicate no interference from ingredients and excipients that might be present in different formulations. [7]

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOD (k=3.3) and LOQ (k=10) of the method was established according to ICH definitions (*C1=kS$_0$/S, where C1 is LOD or LOQ, S$_0$ is the mean standard deviation of blank determination, S is the slope of standard curve and k is the constant related to confidence interval*). LOD and LOQ of method reported in Table 1.

Robustness

Repeatability is based on the results of the method operating over short time interval under same conditions. The low RSD values of intra-day precision (Table 2), recovery (Table 2), and pharmaceutical preparations (Table 3) showed high repeatability. Making deliberate small changes in concentration of solvents used tested the robustness of method (Table 1).

The proposed UV method is simple, accurate, precise, specific and highly sensitive; developed and validated for the determination of Etoricoxib in bulk and tablet dosage form. The method is economical rapid and do not require any sophisticated apparatus in contrast to chromatographic

methods. Hence, the proposed method can be successfully used for routine quality control analysis of drug in marketed preparations.

Table 1: Data for Calibration Curve of Etoricoxib
LOD: Limit of Detection; LOQ: Limit of Quantitation

| Sr. No.	Parameters	In 0.1NHCl
1.	Absorbance maximum (λ_{max}) in nm	233
2.	Beer's law limit (μg/ml)	2-24
3.	Molar Absorptivity (L/mol/cm)	0.2113
4.	Slope	0.072
5.	Intercept	0.089
6.	Correlation coefficient	0.9996
7.	LOD (μg/ml)	0.9075
8.	LOQ (μg/ml)	2.75

Table 2: Results of recovery and precision

Sr. No.	Amount of Drug (mg)	Amount Found (mg)	% Recovery	Precision (Intra day)*	Precision (Inter-day)*
1.	8	7.96	99.5	0.119	0.090
2.	10.2	10.30	100.98	0.069	0.070
3.	12	11.93	99.41	0.151	0.151

* Percentage RSD of three samples

Table 3: Results of the Marketed Etoricoxib Tablets
* Average of three determinations, S.D.; Standard Deviation

Formulation	Amount of Drug Taken From Tablet (mg)	Amount of Drug Found In Tablet (mg)	% Labeled Claim*
Tablet 1	60	59.5	99.16±0.38
Tablet 2	60	59.4	99.00±0.36
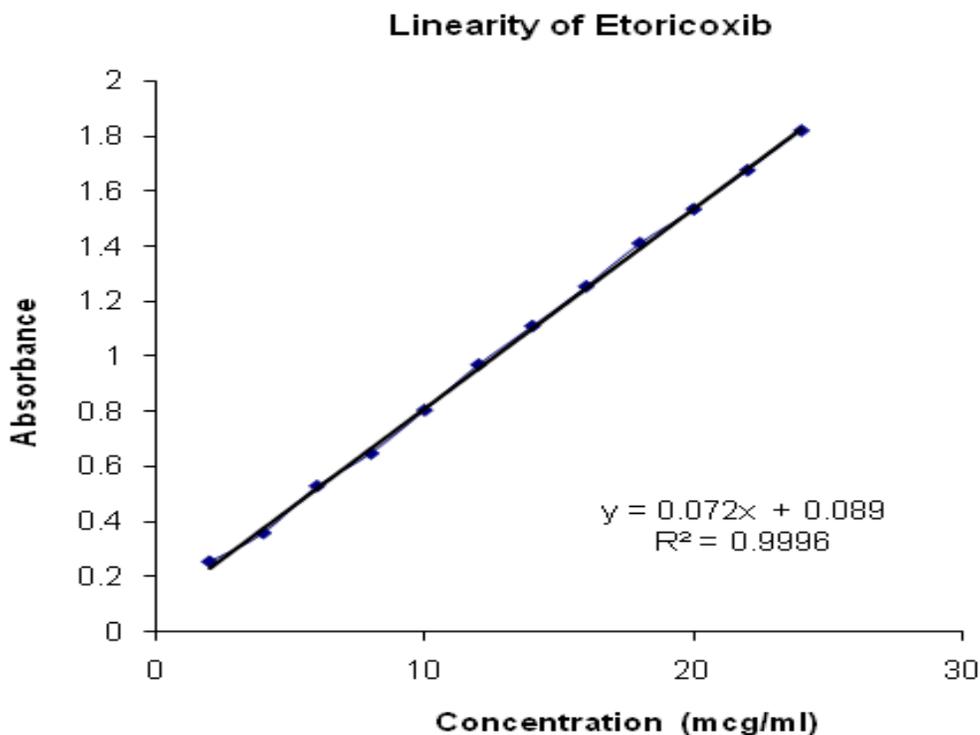
Fig 2: Calibration Curve of Etoricoxib in 0.1N HCl

REFERENCES

1. N.G.B. Agrawal and A. G. Porras, *J Clin Pharmacol.*, **41**, 1106-1110 (2001).
2. A. D. Rodrigues, R. A. Halpin, L. A. Geer, *et al. Drug Metab Dispos.*,**31**, 224-232(2003).
3. B. Chauhan, S. Shimpi, A. Paradkar, *et al. AAPS PharmSciTech*, **6 (3)**, E402-E412 (2005).
4. P. Leclercq, M.G. Malaise, *Rev. Med. Liege.,* **59**, 345, (2004).
5. N.V.S. Ramkrishna, K.N. Vishwottam, S. Wishu, *et al. J.Chromatography B,* **816**, 215-221 (2005).
6. Fda.gov. http//fda.gov/SUPAC-IR.
7. R. B. Saudagar, S. Saraf, S. Saraf, *et.al. Indian J. Pharm. Educ. Res,* **41(1)**, 24-27 (2007).
8. United States Pharmacopoeia – National Formulary, 28th edition, p.2748-2751(2005).
9. ICH-Q2R1 Validation of Analytical Procedures: Methodology International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Geneva, Switzerland (1996).