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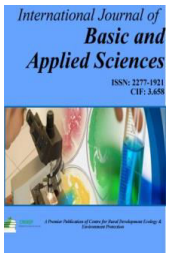
International Journal of Basic and Applied Sciences
(ISSN: 2277-1921) (Scientific Journal Impact Factor: 6.188)

UGC Approved-A Peer Reviewed Quarterly Journal



Research Paper

Development and Validation of Method for Estimation of Etoricoxib in Marketed Formulation

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ARTICLE DETAILS

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Key words:
Etoricoxib; UV spectrophotometry; Analytical techniques.

ABSTRACT

Etoricoxib, a chemical called 5-chloro-6'-methyl-3-(4-(methylsulfonyl) phenyl)-2, 3'-bipyridine, inhibits COX-2 in a dose-dependent manner, providing anti-inflammatory and analgesic benefits. It is available in tablet dosage forms and is used to alleviate symptoms of osteoarthritis, rheumatoid arthritis, primary dysmenorrhea, postoperative dental pain, acute gouty arthritis, migraines, cancer, and its prevention and treatment. Analytical techniques for Etoricoxib include visible, ultraviolet, and high-performance liquid chromatography. The primary goal of this work is to determine its concentration in bulk medicine and tablet dosage form using HPLC technique. A method has been developed for estimating Etoricoxib in both pure drug and formulation. The UV spectrum of Etoricoxib was scanned to obtain the maximum wavelength at 234 nm. The method was validated according to ICH guidelines and showed good reproducibility with a % RSD below 1.0%. The method is simple, economical, accurate, and reproducible, and can be used for routine analysis of Etoricoxib in oral dosage formulations. The method follows ICH guidelines and is applicable for determining Etoricoxib in pharmaceutical dosage formulations.

1. Introduction

High performance liquid chromatography is most accurate methods widely used for the qualitative and quantitative analysis of drug product. Analytical method development and validation play important roles in the Drug discovery, Drug development and Manufacture of pharmaceuticals. It involves detection of the purity and toxicity of a drug substance (1-4). A number of chromatographic parameters have been evaluated in order to optimize the methods in the analysis of method development in HPLC. An appropr- iate mobile phase, column, column temperature, wavelength and gradient are developed. Force degradation studies are helpful in development and validation of stability-indicating studies, determination of degradation pathways of drug substances and drug & products (5-7). Validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose. The parameters described here are according to ICH guidelines and include accuracy, precision, specificity, limit of detection, limit of quantisation, linearity, range, ruggedness and robustness. The objective of this paper is to review the method development, optimize method parameters and validation of method for drug product from developmental stage of formulation to commercial batch of product (8-10).

A powerful COX-2 inhibitor, etoricoxib is a non-steroidal anti-inflammatory medicine (11–15). Etoricoxib, a chemical name for 5-chloro-6'-methyl-3-(4-(methylsulfonyl) phenyl)-2, 3'-bipyridine, inhibits COX-2 in a dose-dependent manner but has no effect on COX-1 (Figure 1). There are anti-inflammatory and analgesic benefits provided by inhibiting COX-2 (16, 17). The powder has a crystalline structure and is off-white in colour. It is insoluble in water but dissolves completely in an acidic water solution (18). Etoricoxib is available in tablet dosage forms (60, 90, 120 mg) and is not official in any pharmacopoeia. Among its many indications, it is used to alleviate the symptoms of osteoarthritis (19-20), rheumatoid arthritis (21), primary dysmenorrhea, postoperative dental pain, acute gouty arthritis, migraines, cancer, and its prevention and treatment. There were a number of published analytical techniques for Etoricoxib, including visible, ultraviolet, high-performance liquid chromatography, and others (22-25). Finding an easy and reliable way to determine

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Received: 18-May-2025; Sent for Review on: 22-May-2025; Draft sent to Author for corrections: 28-May-2025; Accepted on: 12-June-2025; Online Available from 16-June-2025
DOI: 10.13140/RG.2.2.14324.87683
IJBAS-9991/

the concentration of etoricoxib in both bulk medicine and tablet dosage form using the HPLC technique is the primary goal of this work (26-28).

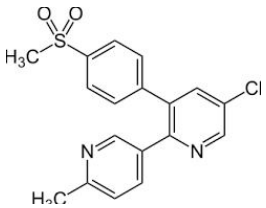

Fig 1: Etoricoxib

2. Materials and Methods

2.1 Chemicals and Materials

All solvents were of HPLC grade. Etoricoxib was received from Swapnaroop Drugs Pvt. Ltd. All analytical grade chemicals and solvents were supplied by Finar and Molychem, India. HPLC grade water was used to prepare all solutions. Freshly prepared solutions were always employed. Etoricoxib tablets were purchased from local market.

2.2 Instrumentation

The UV-Visible Spectrophotometer (Lab India) with data processing system was used. The sample solution was recorded in 1cm quartz cells against solvent mixture as blank over the range of 200-400 nm. An analytical balance was used for weighing the sample. An ultra sonicator bath was used for sonicating the tablet solution.

2.3 Procedure for Dosage Form to Determine Assay

10 ten pills were pulverised for the purpose of analysing market formulations. After measuring out 10 milligrammes of Etoricoxib tablet powder, a little amount of diluent was added to a 10 millilitre volumetric flask. The final volume was then brought up to 10 millilitres using the same. Let it sonicate for ten minutes. The final solution was filtered using a 0.22 µ syring filter. Diluting 0.1 ml of the solution with the solvent combination yielded 10 ml. Then the spectra of the solution were examined using UV/visible spectrophotometer (Lab India) against solvent mixture as a blank in 200-400 nm range (29-33).

2.4 Validation of the method

Adjusting several UFLC settings (FDA, 1995, 1997, 2000, 1994, 1987; USP, 2000) confirmed the reliability of the UFLC approach (34). Calibration plot least-squares linear regression analysis verified the UFLC method's linearity (35), the limits of detection and quantification for the medicines mentioned were determined to be three and five epochs, respectively, above and below the baseline noise, The process adhered to the guidelines established by the United States Pharmacopoeia (USP, 2000) (36), specificity (37), precision (38) accuracy (39), robustness (40) and ruggedness (41) were determined.

3. Results and Discussion

3.1 Linearity

The linearity of a test procedure is its ability to obtain results proportional to the concentration of analyte in the sample (Figure 2). This study investigated the relationship between concentration and absorbance using a standard stock solution. The solution was diluted to obtain working solutions of different concentrations and scanned using a UV-Vis spectrophotometer. The calibration curve was plotted to determine the equation of straight line, slope, intercept, and regression coefficient. The results confirmed the linear relationship between concentration and absorbance, indicating that the linearity experiment was successful for Etoricoxib within a range of 2 to 20µg/ml. The limit of detection (LOD) and limit of quantitation (LOQ) of Etoricoxib were estimated to be 0.91 µg/ml and 2.76 µg/ml, respectively. The method was found to be susceptible to quantify and detect the drug. The solutions preparation for linearity included different concentrations of stock solution, solvent mixtures, and dilutions. The results indicated that the method was susceptible to quantify and detect the drug.

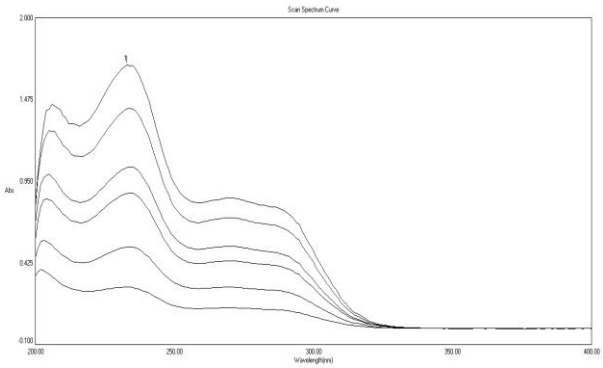

Fig 2: Overlay Linearity Spectra for Etoricoxib (2 to 20 µg/ml solutions)

3.2 Accuracy

The accuracy of an analytical procedure is the closeness of agreement between the accepted true value or reference value and the found value. It is calculated from precision experiment results and percent accuracy at three levels across the range. According to ICH guideline Q2R1, accuracy is determined at three concentration levels (QC standards) across the range. Percent accuracy is determined from measured concentrations and correspondent nominal concentrations. In this assay, Etoricoxib tablets were used, with an average weight of 0.1447 gm. The tablet powder was crushed, weighed, sonicated, diluted, and filtered. The final concentration was 10 µg/ml (Figure 3).

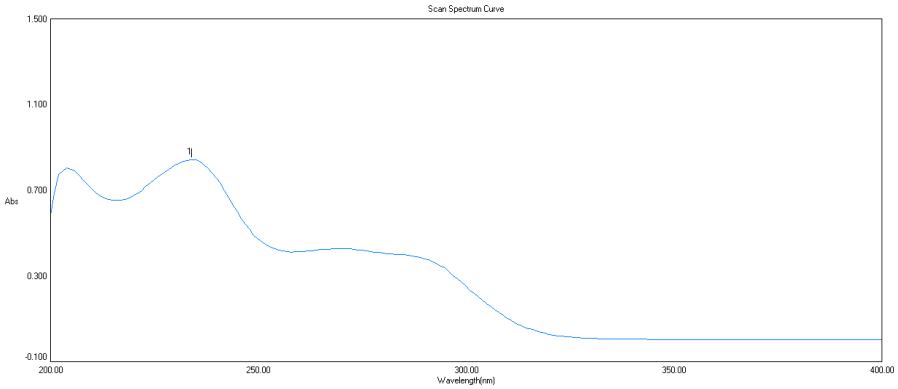

Fig 3: Accuracy graph

3.3 Recovery Studies

In this parameter, Accuracy was conducted by analyzing sample solution spiked with known amounts of the bulk drug or standard at three kinds of concentration levels of 50, 100 and 150% of each at a specified limit. For all three levels, percentage recoveries were measured and found to be within the limit. The accuracy and reliability of the developed method were established (Table 1).

Table 1: Recovery Studies

Level	Standard Stock solution taken	Tablet Stock Soluti taken	Diluted with Solvent mixture	Etoricoxib (in µg/ml)
I (50%)	0.05 ml	0.1 ml	10 ml	15
II (100%)	0.10 ml	0.1 ml	10 ml	20
III (150%)	0.15 ml	0.1 ml	10 ml	25

3.4 Precision

Precision is the assessment of the accuracy of measurements under the same conditions. Three QC standards were selected: LQC, MQC, and HQC, based on calibration range. LQC was chosen for its concentration slightly higher than the lowest linearity concentration, while MQC was chosen for its concentration near the middle concentration. HQC was chosen for its concentration near the highest concentration but less than the highest concentration. The method's precision was tested for intra-day and inter-day precision by diluting standard stock solution with solvent mixture and scanning in the 400-200 nm range using a UV-Vis spectrophotometer (Figure 4).

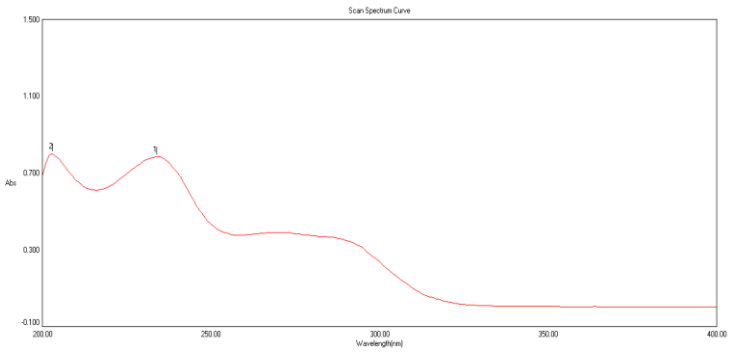

Fig 4: Precision graph

3.5 Robustness

The study evaluated the robustness of an analytical method by analyzing the absorbance of 10µg/ml concentration of Etoricoxib under various conditions, including temperature, wavelength, and solvent mixture composition. The results showed minimal variation in absorbance after deliberate changes in temperature, wavelength, and composition. The method's consistency throughout customary usage was also assessed. The results showed no significant variation in absorbance despite deliberate changes in temperature, wavelength, and solvent mixture composition. This suggests the method's robustness and accuracy.

4. Conclusions

A method has been developed for estimating Etoricoxib in both pure drug and formulation. The UV spectrum of Etoricoxib was scanned to obtain the maximum wavelength at 234 nm. The method was validated according to ICH guidelines and showed good reproducibility with a % RSD below 1.0%. The method is simple, economical, accurate, and reproducible, and can be used for routine analysis of Etoricoxib in oral dosage formulations. The method follows ICH guidelines and is applicable for determining Etoricoxib in pharmaceutical dosage formulations.

5. Conflict of Interest

None

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