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Review Article

A Review on the Analytical Techniques for the Quantification of Etoricoxib

Boddepalli Amar Srikar and Mukthinuthalapati Mathrusri Annapurna*

GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India

***Corresponding Author:** Mukthinuthalapati Mathrusri Annapurna, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, India.

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Abstract

Etoricoxib is a non-steroidal anti-inflammatory drug which belongs to an oxicam class. It belongs to second-generation COX-2 inhibitors. Etoricoxib is insoluble in water and readily soluble in alkaline aqueous solutions. In the present paper the authors have reviewed the analytical methods already published till now in the literature for the estimation of Etoricoxib in pharmaceutical formulations and in biological samples.

Keywords: Etoricoxib; Fluids; Molecular Weight

Introduction

Etoricoxib (CAS no 202409-33-4), chemically 5-chloro-2-(6-methylpyridin-3-yl)-3-(4-methylsulfonylphenyl) pyridine is a methyl sulphone derivative. Etoricoxib is also a bipyridine derivative. Etoricoxib is generally administered through oral route and it is a COX-2 inhibitor. Etoricoxib (Figure 1) has a molecular formula $C_{18}H_{15}ClN_2O_2S$ and molecular weight 358.8419 g/mole and it is a white or off white powder with bitter taste [1-4]. The pKa values of Etoricoxib are found to be 3.9 and 4.6.

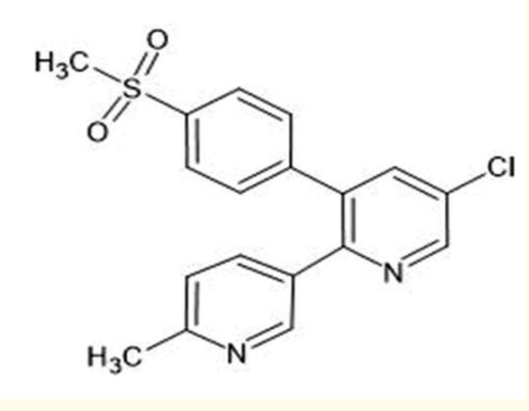

Figure 1: Chemical structure of Etoricoxib.

Etoricoxib is available as tablets with brand names KRETOS (Label claim: 90 mg; 120 mg) (Glenmark Pharmaceuticals Ltd) and NUCOXIA (Label claim: 60 mg; 90 mg) (Zydus Cadila) in India. Etoricoxib is available in combination with Thiocolchicoside as tablets in market.

This article summarizes the analytical techniques proposed by different authors for the quantification of Etoricoxib using spectrophotometry, HPLC, LC-MS/MS, UPLC-MS/MS, HPTLC and Capillary electrophoresis in pharmaceutical dosage forms and biological fluids.

Shahi SR., *et al.* [5] and Shipra Singh., *et al.* [6] developed the spectrophotometric methods in 0.1N HCl for the assay of Etoricoxib and the linearity was followed 2-24 µg/ml and 0.1-0.5 µg/ml respectively. Juyal., *et al.* and Garlapati Manideep., *et al.* used methanol as the solvent with λ_{max} at 284 nm [7] and 234 nm [9] respectively. Manish Kumar Thimmaraju., *et al.* [8] used an organic solvent chloroform (λ_{max} at 247 nm) for the development of the spectrophotometric method and the linearity was 1-40 µg/ml.

Reverse phase liquid chromatographic methods were developed and validated by many authors [10-13] for the estimation of Etoricoxib in its tablet formulations using different mobile phases. Muhammad Alzweiri., *et al.* studied [14] the stability of Etoricoxib using RP-HPLC method by incorporating an internal standard, Celecoxib keeping the mobile phase pH at 6.0. Ashok KS and Nooman AK developed HPLC method for the determination of Etoricoxib in human plasma [15] Liberato Brum Junior proposed LC- MS/MS method for the estimation of Etoricoxib in human plasma using Piroxicam as an internal standard and a mixture of acetonitrile: water (95: 5)/0.1% acetic acid (90:10) as mobile phase along with another HPLC method using a mixture of 0.01M Phosphoric acid (pH 3.0 adjusted with sodium hydroxide 3 M: Acetonitrile (62:38) for the assay of pharmaceutical formulations and the linearity range was 1-500 ng/ml for both the methods [16].

Liberato Brum Junior., *et al.* proposed LC-MS/MS method in human plasma with atmospheric pressure chemical ionisation technique using automated on-line solid-phase extraction [17]. A mixture of acetonitrile: water (95:5)/10 mM ammonium acetate (pH 4.0) was used as mobile phase and the calibration curve was linear over the concentration range 1-500 ng/ml. Xiaoran Zhang., *et al.* proposed UPLC-MS/MS method for the quantitative analysis of Etoricoxib in human plasma on gradient mode and a pharmacokinetic study was continued with the Chinese healthy volunteers [18] and the linearity was observed over the concentration range 5 - 500 ng/ml only.

Gourab Maheshwari., *et al.* proposed a HPTLC technique in presence of an internal standard, Rofecoxib using a mixture of toluene: 1, 4-dioxane: methanol (8.5:1.0:0.5) as mobile phase and in this method the detection was selected at 235 nm and the linearity was observed as 0.1-1.5 µg per spot [19]. A capillary zone electrophoresis [20] method was proposed by Maximiliano da Silva Sangoi., *et al.* for the comparative determination of Etoricoxib in pharmaceutical formulations using 25 mM tris-phosphate solution (pH 2.5) as background electrolyte with UV detection at 234 nm using PDA detector and the linearity was observed over the concentration range 2-150 µg/ml.

The significant parameters observed in spectrophotometry and liquid chromatographic methods were highlighted in table 1 and 2 respectively.

Reagent	Linearity (µg/ml)	λ_{max} (nm)	Reference
0.1N HCl	2-24	233	[5]
0.1M HCl	0.1-0.5	233	[6]
Methanol	2-24	284	[7]
Chloroform	1-40	247	[8]
Methanol	1-11	234	[9]

Table 1: Review of spectrophotometric methods.

Conclusion

The present review helps the readers to do research in a new field apart from the presenting existing analytical techniques for the non-steroidal anti-inflammatory drug Etoricoxib. The significant parameters observed during the review of Etoricoxib are important to carry out any analytical study.

Mobile phase (v/v)	Detection wavelength (nm)	Linearity (µg/ml)	Comment	Reference
Acetonitrile: Potassium dihydrogen phosphate buffer (pH 4.2) (46: 54)	280	0.5-85	HPLC	[10]
Acetonitrile: (0.05M) KH_2PO_4 buffer (50: 50)	283	0.5-85	HPLC	[11]
Acetonitrile: Methanol: 10mM Potassium dihydrogen phosphate (pH 3.0 adjusted with ortho phosphoric acid)	234	0.025-0.4	HPLC	[12]
Methanol	233	20-55	HPLC	[13]
Methanol: Phosphate buffer (pH 6)(70:30) Celecoxib (Internal standard)	215	1-8	HPLC	[14]
Aq. buffer containing tri ethyl amine and ortho phosphoric acid): Acetonitrile (62:38)	284	0.015-3.2	HPLC (Human plasma)	[15]

Acetonitrile: Water (95: 5)/0.1% Acetic acid (90:10) and Piroxicam (Internal standard) 0.01M Phosphoric acid (pH 3.0 adjusted with sodium hydroxide 3 M: Acetonitrile (62:38)	- 234	0.001-5	LC-ESI-MS/MS (Human plasma) HPLC	[16]
Acetonitrile: Water (95:5)/ 10 mM Ammonium acetate (pH 4.0)	-	0.001-5	LC-APCI/MS/MS (Human plasma)	[17]
Acetonitrile: 2 mM Ammonium acetate (Gradient mode)	-	0.005-5	UPLC-MS/MS (Human plasma)	[18]
Toluene: 1,4-dioxane: Methanol (8.5:1.0:0.5) Rofecoxib (Internal standard)	235	0.1–1.5 per spot	HPTLC	[19]

Table 2: Review of liquid chromatographic methods.

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