Extractive Spectrophotometric Methods for the Determination of Etoricoxib in Tablets

KAMAL SHAH^{*}, ALKA GUPTA[§] and PRADEEP MISHRA[#]

[#]Dr. Hari Singh Gour University, Sagar, (M.P.), India.

[§]IPS College of Pharmacy, Gwalior, (M.P.), India.

^{*}GLA, Institute of Pharmaceutical Research, Mathura (U.P.), India.

kamal0603@gmail.com

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Abstract: Two simple, rapid, sensitive, precise and economic spectrophotometric methods have been developed for the estimation of etoricoxib in tablet formulation. During the course of study, it was observed that acidic solution of the drug formed colored ion-association complexes with Bromocresol Green (BCG) and Bromocresol Purple (BCP) which were soluble in chloroform. This property of the drug was followed for the development of colorimetric methods for analysis of drug. The complex of etoricoxib with BCG and BCP showed λ_{max} at 416 nm and 408 nm respectively. These methods were validated statistically. Recovery studies gave satisfactory results indicating that none of common additives and excipients interfere the assay method. The proposed methods are found to be simple, accurate and reproducible that was successfully applied for the analysis of tablet formulation.

Keywords: Etoricoxib, Colorimetric analysis, BCG, BCP, Extractive spectrophotometry,

Introduction

Etoricoxib is 5-chloro-2-(6-methyl pyridin-3-yl) 3-(4-methyl sulfonyl phenyl) pyridine. It is used as a non-steroidal anti-inflammatory agent¹. It has selective inhibition of COX-2 that decreases GI toxicity and without effects on platelet function². It is commonly used for osteoarthritis, rheumatoid arthritis, primary dysmenorrhoea, post operative dental pain and acute gout.

Etoricoxib

The therapeutic importance of this drug has prompted the development of many methods for its assay. This drug is not official in any pharmacopoeia. Several methods have been reported for the analysis of etoricoxib in pharmaceutical dosage form as well as in the biological fluids and tissues, *i.e.* spectrophotometric methods³⁻⁴, chromatographic methods HPLC⁵⁻⁷, LC/Mass spectrophotometry⁸⁻¹¹. As there is no visible spectrophotometric methods for the analysis of etoricoxib in either biological fluids or pharmaceutical formulations were reported in the literature.

Experimental

Apparatus

A GBC Cintra 10 double beam UV-Visible spectrophotometer equipped with 10 mm matched quartz cells was used in the present investigation. A sartorius analytical balance was used.

Reagents

All chemicals used were of analytical reagent grade and double distilled water was used throughout. BCG and BCP reagent supplied by BDH chemicals, India. Aqueous solution of BCG (0.1% w/v), alkaline solution of BCP (0.1%) and buffer solutions¹² from 2.2 to 4 pH were prepared. Etoricoxib as generously supplied by M/s Systopic Laboratories Pvt. Ltd., New Delhi, India was used as such without further purification. The commercially available tablets of etoricoxib were procured from local market labeled to contain 60 mg etoricoxib/tablet.

Preparation of standard solutions

About 100 mg of accurately weighed etoricoxib was dissolved in 100 mL of 0.1 N HCl to get 1 mg/mL of standard stock solution. The working standard solution (100 µg/mL) for method A and B were prepared suitably by stepwise dilutions of the above stock solution with 0.1 N HCl.

Procedure

Varying quantities of working standard drug solution representing 2-18 and 4-20 µg/mL of etoricoxib, 2 mL of dye solution (BCG or BCP), 3 mL of buffer solution (pH 2.2) were added finally volume made up with 0.1 N HCl, transferred into separating funnel, chloroform (5 x 2 mL) was added to the separating funnel and contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 416 nm and 408 nm for method A and method B respectively, then calibration curve plotted for both (2-18 µg/mL for BCG and 4-20 µg/mL for BCP). The sample solutions prepared were also treated in similar manner and the exact amount of etoricoxib present was deduced from the calibration graph.

Optimization of conditions

Condition under which reaction of etoricoxib with dyes fulfils the essential requirements was investigated. All conditions studied were optimized at room temperature ($32 \pm 2^\circ\text{C}$).

Selection of suitable pH buffer solution

Buffer solutions of different pH (2.2, 2.8 and 4) were prepared. The stock solution was diluted with distilled water to give the drug concentration $100 \mu\text{g/mL}$. A 2 mL portion of this diluted solution was pipette out and added to three separating funnels. Two mL of BCG solution and 3 mL of buffers were added to each. Shaken well and extracted with $4 \times 2 \text{ mL}$ of chloroform. Later the extracts were taken into 10 mL volumetric flasks and volume made up, then absorbances were measured at 416 nm. Same procedure was applied for the BCP then absorbances were measured at 408 nm. It was found that drug with BCG and BCP gave maximum absorbance at pH 2.2 (Table 1).

Table 1. Optimization of parameters.

Time, min.	Absorbances					
	BCG-Drug complex at different pH			BCP-Drug complex at different pH		
	2.2	2.8	4	2.2	2.8	4
0	1.0312	0.5601	0.5565	0.9526	0.6579	0.6586
30	1.0296	0.5596	0.5419	0.9525	0.6220	0.6474
60	1.0291	0.5589	0.5387	0.8439	0.6189	0.6419
90	1.0294	0.5597	0.5308	0.8124	0.6070	0.6227
120	1.0293	0.5011	0.5301	0.7929	0.6067	0.6221

Stability study of drug dye complexes

The stability of the drug dye complexes was determined individually for both the dyes (BCG and BCP). A 2 mL portion drug concentration $100 \mu\text{g/mL}$ was pipette out and added to a separating funnel. Two mL of BCG solution (0.1% w/v) and 3 mL of buffers were added to each. Shaken well and extracted with $4 \times 2 \text{ mL}$ of chloroform. Later the extracts were taken into 10 mL volumetric flasks and volume made up. The absorbances were measured periodically at an interval of 30, 60, 90 and 120 minutes at 416 nm. Same procedure was applied for the BCP then absorbances were measured at 408 nm. Finally it was found that BCG drug complex was stable for 2 h, whereas BCP drug complex was stable for more than 1 h and 30 min Table 1.

Procedure for pharmaceutical formulation

Twenty tablets were accurately weighed and powdered. The tablet powder equivalent to 60 mg of etoricoxib was extracted with methanol in ($4 \times 20 \text{ mL}$) in 100 mL volumetric flask. This solution was suitably diluted with 0.1 N HCl and then preceded as described above for pure drug. The nominal content of the tablets was determined either from the calibration curve or using the regression equation.

Results and Discussion

During the course of study, it was observed that acidic solution of the drug formed coloured ion-association complexes with bromocresol green and bromocresol purple which were soluble in chloroform. This property of the drug was followed for the development of colorimetric methods for analysis of drug. The complex of etoricoxib with BCG and BCP showed λ_{max} at 416 nm and 408 nm respectively. These developed for the estimation of

etoricoxib from two formulations (ETOCOX and ETOBRIX). Both methods involve formation of ion-associated complex with BCG and BCP at pH 2.2 exhibiting $\lambda_{\max}$ at 416 nm and 408 nm respectively (Figure 1 and Figure 2). The method commonly used in the determination of certain amines and quaternary ammonium compounds that absorb weakly in the ultraviolet region¹³. The proposed method was based on addition of an amine in its ionized form to an ionized dye, yield a salt (ion-pair) that was extracted into an organic solvent such as chloroform or dichloromethane. The indicator dye was added in excess and the pH of the aqueous solution was adjusted to a value where both the amine and dye were in the ionized forms. The ion pair was separated from the excess indicator by extraction into the organic solvent. In these methods Beer's law was obeyed with BCG and BCP in the concentration range of 2-18 $\mu\text{g/mL}$ and 4-20 $\mu\text{g/mL}$ respectively. Optical characteristics of etoricoxib were given in the Table 2.

Figure 1. Colorimetric scan of drug-BCG complex.

Figure 2. Colorimetric scan of drug-BCP complex.

Table 2. Optical characteristics.

Parameters	BCG	BCP
$\lambda_{\max}$, nm	416	408
Beer Lambert's law limits, $\mu\text{g/mL}$	2-18	4-20
Molar absorptivity, (L/mol/cm)*	1.9331×10^4	1.6642×10^4
Sandell's sensitivity, $\mu\text{g/cm}^2/0.001$	0.01856	0.02155
Absorbance unit*		
Regression equation $y=mx+c$	$y = 0.0512x + 0.0193$	$y = 0.0473x - 0.0095$
Slope (m)	0.0512	0.0473
Intercept (c)	0.0193	0.0095
Correlation coefficient (r)	0.9994	0.9992

* Average of nine determinations.

The molar absorptivity and sandell's sensitivity showed that the methods were sensitive. The optimum conditions for colour development had been established by varying the different parameters involved. The result of analysis of commercial formulation significantly showed low values for standard deviation, standard error of mean, coefficient of variance and percentage range of error (within 95% confidence limits), thus showed precision of the methods given in Table 3. For testing the accuracy and reproducibility of the proposed methods, recovery studies were performed. The data obtained by recovery studies indicate non-interference from the excipients used in the formulation shown in Table 4. The percentage recoveries were close to 100%. This study revealed that the common excipients and other additives such as lactose, starch, gelatine, talc and magnesium stearate that are usually present in the tablet dosage forms do not interfere in the analysis. Thus, it can be concluded that the proposed methods are found to be simple, rapid, sensitive and accurate that can be used for the determination of etoricoxib in their pharmaceutical dosage forms in a routine manner.

Table 3. Statistical analysis of commercial formulations.

Method	Brand	Amount Proposed mg/tab	Amount found* mg/tab	SD*	COV*	SE*	t* Calcd	t* Theor
A	ETOCOX	60	59.99 ± 0.03	0.0404	0.0673	0.0164	0.6063	
	ETOBRIX	60	60.00 ± 0.04	0.0606	0.1009	0.0247	0.8084	
B	ETOCOX	60	60.01 ± 0.04	0.0622	0.1036	0.0253	0.3938	
	ETOBRIX	60	60.00 ± 0.06	0.0828	0.1379	0.0338	0.1774	1.476

* Average of six determinations

SD= Standard deviation, COV= Coefficient of variation, SE = Standard error. * Theoretical 't' values are calculated at 95% confidence level for (n-1) degrees of freedom 't' (0.10,5) = 1.476

Table 4. Drug recovery studies.

Method	Brand	% Recovery $\pm$ S.D.*
A	ETOCOX	99.73 ± 0.11
	ETOBRIX	99.91 ± 0.10
B	ETOCOX	100.04 ± 0.13
	ETOBRIX	100.08 ± 0.13

* Average of six determinations

S. D : Standard Deviation

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