Research Article

First Derivative UV Spectrophotometric Method for the Determination of Etodolac in Solid Dosage Forms

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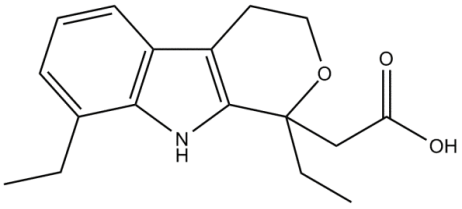
ABSTRACT

Purpose: Simple, accurate, precise and economical spectroscopic method for determination of Etodolac in pure and its tablet dosage form by first order derivative method has been developed for the routine analysis. **Methodology:** Spectroscopic method development for the estimation of Etodolac by first order derivative method was carried out using ethanol as solvent and Shimadzu 1800 Spectronic UV Visible Spectrophotometer. **Findings:** The absorbance maximum in first derivative spectrum was measured at 273 nm and selected as analytical wavelength. Beer's law was obeyed in the concentration range of 10-50 µg/ml. The recovery studies ascertained the accuracy of the proposed method and the results were validated as per ICH guidelines. The results were found satisfactory and reproducible. **Research application:** The method was applied successfully for the estimation of Etodolac in pure drug and tablet dosage form. **Industrial application:** The method can be applied for routine analysis. **Research Value:** The newly developed method is a good alternative for HPLC methods and better than zero orders UV methods. **Conclusion:** The method is simple, rapid, accurate, precise and economic method which can be used without the interference of impurities for the determination of Etodolac in solid dosage forms.

Key words: Etodolac, First derivative method, Spectrophotometric method, UV Estimation,UV determination, Estimation, Tablet assay.

INTRODUCTION

Etodolac is a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory and antipyretic properties. Its analgesic effects are due to its ability to inhibit prostaglandin synthesis. It is designed for relief of signs and symptoms of rheumatoid arthritis and osteoarthritis. Chemically it is 2-{1,8-diethyl-1*H*,3*H*,4*H*,9*H*-pyrano[3,4-b] indol-1-yl}acetic acid. It is official in Indian Pharmacopoeia.[1] There are few methods so far reported for the determination of Etodolac in its single component formulations and bulk drugs. Four HPLC methods,[2-5] three Colorimetric (Visible Spectrophotometric) methods,[6-8] one GC-MS method,[9] one Capillary Electrophoresis method[10] and one LC-MS method[11] are reported so far in literature. No first derivative spectrophotometric method has been reported for routine analysis of Etodolac in its bulk form and formulations. The aim of the present study



Etodolac

was to develop a simple and rapid first derivative spectrophotometric method for the routine determination of Etodolac.

MATERIALS AND METHODS

Materials

Shimadzu 1800 Spectronic double beam UV-visible spectrophotometer with 1 cm matched quartz cells was used for all the measurements. Ethanol (98%) A.R. Grade (Qualigens, Fine Chemicals) was used as the solvent. Commercial brand tablets were obtained from local market.

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Methodology

Preparation of standard stock solution

Standard stock solution of Etodolac was prepared by dissolving accurately weighed quantities (100 mg each) of Etodolac in 40 ml ethanol and transferred into a 100 ml volumetric flask. Volume was made up to mark with ethanol to obtain stock solution of 1000 µg/ml concentration. For obtaining clear solution, further dilutions were made to get the concentration of 100 **µg/ml.**

Determination of λ_{max}

The standard solution of Etodolac (10 µg/ml) was scanned in the wave length range of 200-300 nm and the spectrum was derivatized in first order at N=5 smoothening factor. Absorption maximum was found to be 273 nm wavelength; where the absorption showed higher intensity than other wavelengths for Etodolac. Therefore analytical wavelength was fixed at 273 nm for the analysis of Etodolac (Figure 1).

Stability of Drug in Selected Solvent

The stability of the drugs in the selected solvent was determined by measuring the absorbance of the drug solution (10 µg/ml) at different time intervals. The absorbance was measured after every 10 min. The solutions were found to be stable. The stability study data is given in Table 1.

Study of Beer-Lambert's law

From the standard stock solution of Etodolac, appropriate aliquots were pipette out in to 25 ml volumetric flasks and dilutions were made with ethanol to obtain working standard solutions of concentrations of 2 µg to 60 µg/ml and the difference in absorbance (dA/dλ) of Etodolac was measured in the first derivative mode with N=5 smoothening factor of the instrument at 273.0 nm at the interval of 2 µg/ml concentration. The calibration curve of the drugs was plotted. (Figures 2 to 7) The concentration range over which the drugs followed linearity was chosen as an analytical concentration range i.e. 10-50 µg/ml.

Optimum Parameters for the Calibration Curve

The Optimum parameters of the calibration curves are given in Table 2.

Validation of proposed method

Estimation of drug from dosage form

Twenty tablets of Etodolac is weighed, and finely powdered. A quantity of powder sample equivalent to 200 mg of Etodolac was taken in volumetric flask and dissolved in ethanol. Further dilution was made to get concentration of 25 µg/ml. These concentration was scanned at wavelength 273 nm for in first order derivative mode with N=5 smoothening factor.

The results and statistical parameters for tablet analysis are shown in Table 3.

Accuracy (Recovery Test)

Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts of standard solutions to solutions of tablet. The recovery was performed at three levels, 80, 100 and 120% of Etodolac standard concentration. The recovery samples were prepared. Three samples were prepared for each recovery level. The solutions were then analyzed, and the percentage recoveries were calculated using formula:

$$\% \text{ recovery} = \frac{\text{Observed amount of compound in sample}}{\text{Amount of all compound present in sample}} \times 100$$

The recovery values are summarized in Table 4.

Precision Study

The dilution was made to get concentration of 25 µg/ml of Etodolac and scanned at wavelength 273 nm in first order derivative mode by four different analyst using same laboratory and same instrument. The precision data for Etodolac are given in the following Table 5.

RESULTS AND DISCUSSION

The standard solutions of Etodolac in Ethanol (10 µg/ml) subjected to a scan individually at the series of wavelengths of 200 nm to 300 nm at first order derivative mode and the first order derivative spectra was taken at N=5 smoothening factor of the instrument using Shimadzu 1800 spectronic UV Visible spectrophotometer. Absorption maximum of Etodolac was found to be at 273 nm. Therefore, 273 nm was selected as λ_{max} of Etodolac for the present study. The calibration curve of Etodolac was found to be linear in the range of 10-50 µg/ml at 273 nm. Therefore, it was clear that Etodolac can be determined without interference of any irrelevant substance in single component pharmaceutical products.

With the intention of determining the practicability of the developed technique for the assessment of commercially available brands of medicinal formulations, the technique was initially attempted on bulk drugs in their synthetic sample and concentrations were estimated. Then the technique was subjected to the assay of tablets in three marketed dosage brands that is Brand-A, Brand-B and Brand-C and adequate results were attained within

Table 1: Stability Data for Etodolac

Time (min)	Absorbance
10	0.561
20	0.559
30	0.550
40	0.546
50	0.530
60	0.525

Table 2: Optimum Parameters for the Calibration Plot

Parameter	Etodolac
Linearity range (µg/ml)	10-50 µg/ml
Slope	0.0270
Intercept	0.0425
Regression Coefficient(r^2)	0.999
Sandell's Sensitivity (Specific Extinction Coefficient x Concentration of Analyte in µg/L)	0.0294 µg/ml/cm^2
Limit of Detection (LOD) LOD = 3.3σ/s	0.0099 µg/ml
Limit of Quantitation (LOQ) LOQ = 10σ/s	0.0300 µg/ml

*σ = Standard Deviations of Intercepts s = Slope

Table 3: Assay of Etodolac in Tablet formulation Brand- A, B and C

Drug	Label Claim (mg/cap)	Amount Found (mg/cap)	% of Label Claim	Mean %	SD	CV
Etova 200 mg	200	199.78	99.89	100.07	0.6293	0.3960
	200	199.12	99.56			
	200	200.24	100.21			
Etova 300 mg	200	199.92	99.96	99.91	0.2891	0.0835
	200	202.52	101.26			
	200	199.16	99.58			
	300	298.98	99.66			
	300	299.94	99.98			
	300	299.28	99.76			
	300	301.11	100.37			
	300	300.27	100.09			
	300	298.86	99.62			
Etova 400 mg	400	402.04	100.51	100.12	0.2588	0.0670
	400	401.28	100.32			
	400	399.36	99.84			
	400	399.72	99.93			
	400	400.8	100.20			
	400	399.84	99.96			

Table 4: Results of Accuracy (Recovery) parameter of Etodolac

Level of % Recovery	Amount present (µg/ml)	Amount of standard added (µg/ml)	Total amount recovered (µg/ml)	% Recovery	% mean Recovery	SD	CV
80	200	160	361.69	100.47	100.07	0.3464	0.1203
80	200	160	359.38	99.83			
80	200	160	359.71	99.92			
100	200	200	362.12	100.59	100.20	0.3385	0.1146
100	200	200	359.85	99.96			
100	200	200	360.21	100.06			
120	200	240	361.90	100.53	100.12	0.4050	0.1641
120	200	240	360.39	100.11			
120	200	240	358.99	99.72			

Table 5: Determination of Precision of Etodolac

Sample Number	Assay of Artemether as % of Labeled amount			
	Analyst-I	Analyst-II	Analyst-III	Analyst-IV
1	100.36	100.26	99.86	101.18
2	99.79	101.06	100.26	100.30
3	101.31	99.87	101.13	99.82
4	99.56	99.92	101.14	99.89
5	99.62	100.56	99.96	101.24
6	100.20	99.88	100.20	100.39
Mean%	100.14	100.25	100.42	100.47
S.D	0.6557	0.4779	0.5694	0.6150
CV	0.4300	0.2284	0.3243	0.3782

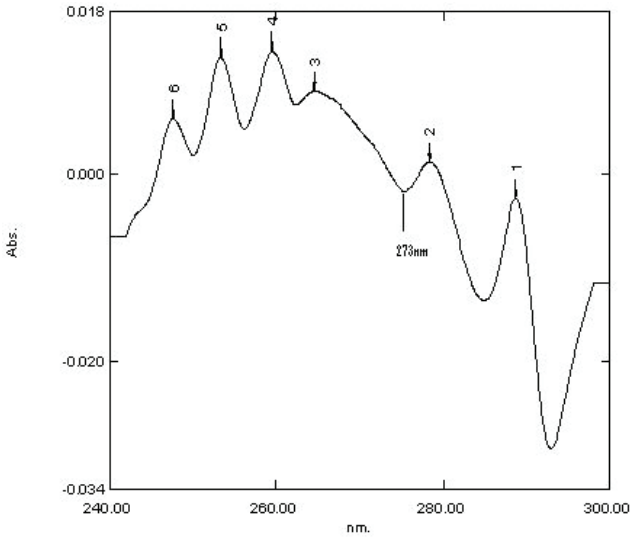

Figure 1: Absorption Maximum of Etodolac at 273 nm

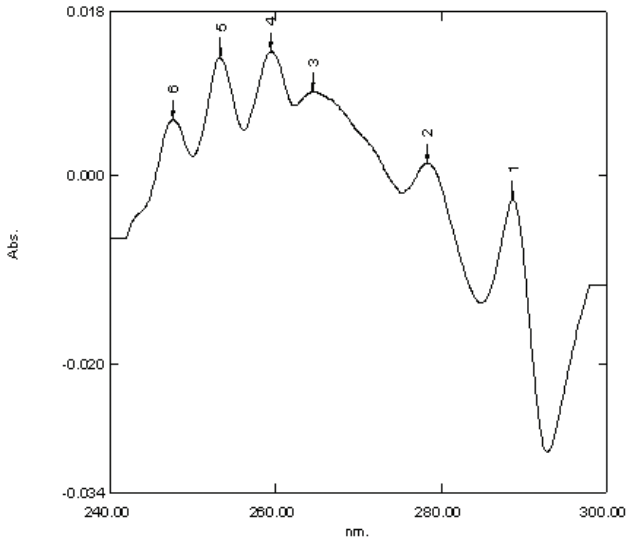

Figure 3: First order derivative spectrum of Etodolac 10 µg/ml

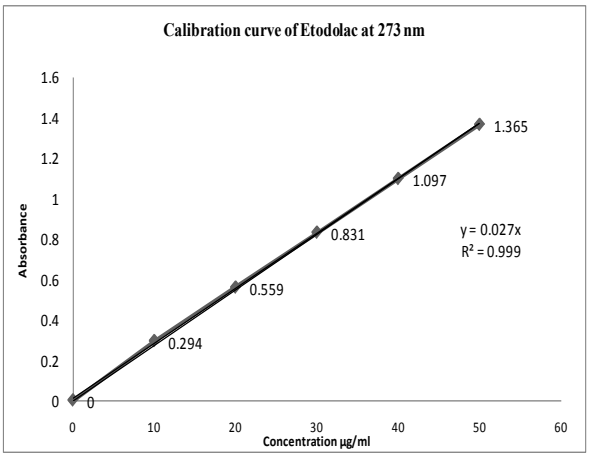

Figure 2: Calibration Plot of Etodolac .

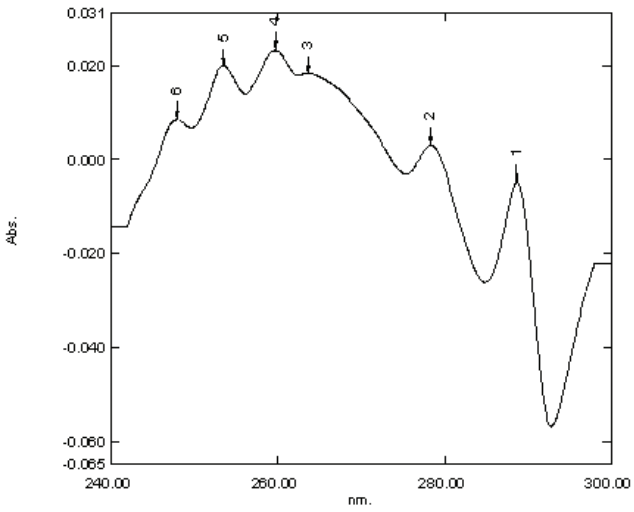

Figure 4: First order derivative spectrum of Etodolac 20 µg/ml

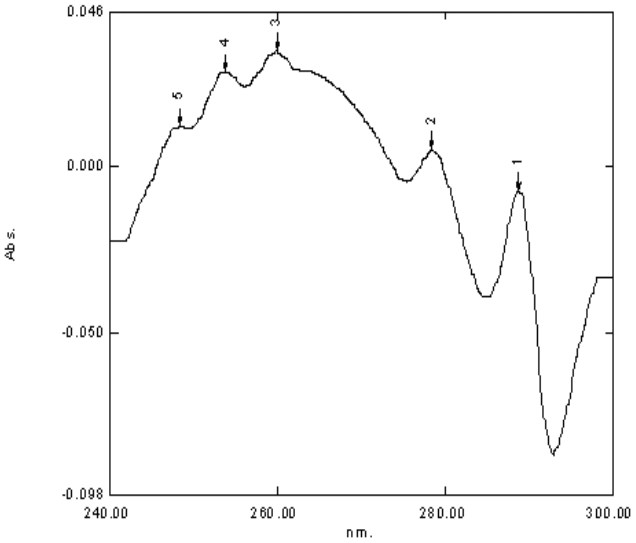

Figure 5: First order derivative spectrum of Etodolac 30 μg/ml

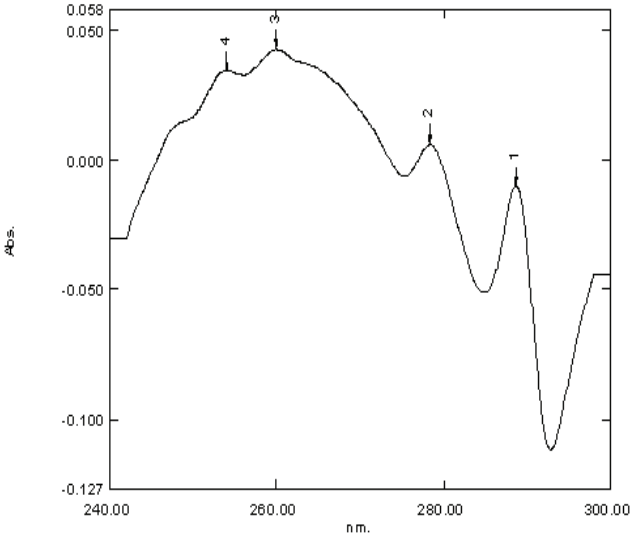

Figure 6: First order derivative spectrum of Etodolac 40 μg/ml

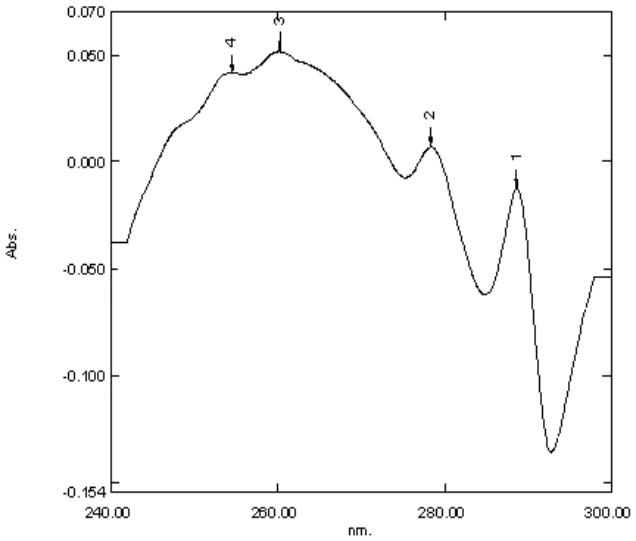

Figure 7: First order derivative spectrum of Etodolac 50 μg/ml

the acceptable limits as per the content of the label claim for Etodolac.

The recovery experiments were conducted by adding known amounts to tablet. The recovery was performed at three levels, 80, 100 and 120% of three brand of Etodolac standard concentration. Three samples were prepared for each recovery level. The solutions were then analyzed, and the percentage recoveries were found to be satisfactory within the acceptable limits as per the content of the label claim for marketed tablet.

The newly developed method was validated as per the ICH guidelines and parameters. The novel method for the quantitative investigation of Etodolac was subjected to different validation parameters like specificity and selectivity in presence of formulation additives and excipients, studied for Linearity and range at different levels of concentrations and calibration standards where the determination range was optimized, accuracy was proved by recovery studies at different concentration levels, precision for Etodolac was established through the analysis of sample by four different analyst using same instrument and same laboratory. The method was developed successfully for Etodolac in its single component dosage forms by first order derivative method.

CONCLUSION

From the experimental studies it can be concluded that first order derivative method is developed for Etodolac in bulk and single dosage form. The proposed method for the selected drug was found to be accurate and precise. The most striking features of spectrophotometric method are their simplicity and rapidity. Results of validation parameters demonstrate that the analytical procedure is suitable for its intended purpose and meet the criteria defined in ICH Q2A/B. The proposed method can be successfully applied for the routine determination of Etodolac, which is an advantage over HPLC and a better method than colorimetric methods comparing accuracy and interference.

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CONFLICT OF INTEREST

Nil.

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