TABLE 2: DISSOLUTION PROFILE OF DIFFERENT FORMULATIONS OF CELECOXIB IN PHOSPHATE MEDIUM PH 7.4

Formulations	% Release of drug						Rate constant $K_1 min^{-1} \times 10^{-3}$	DE_{15} (%)
	5	10	15	30	45	60		
M1	2.3(0.88)	3.7(1.62)	4.2(1.42)	4.3(1.35)	4.4(1.48)	4.5(1.52)	3.7	2.8
M2	2.4(1.21)	4.0(1.83)	4.6(1.72)	4.9(1.17)	5.2(1.67)	5.3(1.47)	4.2	2.9
CB-1	1.1(1.36)	2.8(1.49)	4.2(1.93)	6.3(1.61)	8.9(1.82)	10.7(1.85)	2.8	3.1
CB-2	2.7(2.04)	4.8(1.55)	6.3(1.68)	8.5(1.31)	10.9(1.46)	11.6(1.92)	4.8	8.6
CB-3	12.3(1.22)	17.8(1.57)	21.6(1.43)	24.3(1.03)	29.5(1.41)	32.8(1.53)	17.7	12.7
CB-4	17.4(1.72)	25.8(1.54)	34.5(1.37)	42.0(1.45)	50.4(1.25)	55.2(1.51)	25.9	19.2

n=6, K_1=dissolution rate constant, M1=marketed sample 1, M2=marketed sample 2, CB-1=capsule containing plain drug, CB-2= capsule containing physical mixture, CB-3= capsule containing drug-cyclodextrin inclusion complex, CB-4=capsule containing drug-cyclodextrin inclusion complex and sodium bicarbonate, DE_{15} (%)=dissolution efficiency of percent drug release, compared at 15 min.

Since all the formulations showed best release in phosphate buffer media, therefore this medium was chosen for further study-comparison of drug release rate with commercial formulations M_1 and M_2. The results are given in Table 2. Here again, we observed the superior performance of the laboratory-made formulations as compared to the commercial ones. The test formulations CB-2, CB-3 and CB-4 gave faster and higher dissolution of celecoxib than M_1 and M_2. A similar order, as before was followed here: CB-4>CB-3>CB-2>CB-1. The present study serves to highlight the need for proper formulation development of poorly-water soluble drugs such as celecoxib. With proper design, the formulation can be optimized for good performance both *in vitro* and *in vivo*.

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Spectrophotometric Estimation of Etoricoxib in Bulk Drug and Dosage Forms

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Accepted 29 October 2005

Revised 18 February 2005

Received 4 January 2005

Simple UV and first derivative spectrophotometric methods have been developed for the determination of etoricoxib in bulk drug and its pharmaceutical formulations. In simple UV spectrum of etoricoxib in 0.1 N sodium hydroxide, it exhibits absorption maxima (λ_{max}) at 284 nm where as in first derivative spectrum it shows maxima at 301.0 nm and minima at 266.8 nm. Both the methods were found to be simple, economical, accurate, reproducible and can be adopted in routine analysis of etoricoxib in bulk drug and its pharmaceutical formulations.

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Etoricoxib[1-2] is a new NSAID, which is chemically 5-chloro-6'-methyl-3-[4-(methylsulfonyl) phenyl]-2,3'-bipyridine. It is active at low dose and has less gastric toxicity[3]. It inhibits synthesis of prostaglandins by inhibiting the activity of the enzyme, cyclooxygenase-2 (COX-2)[1-2]. It has highest COX-2 selectivity and better safety profile[1]. Prostaglandins are involved in mediating inflammation, swelling, pain and fever. Etoricoxib is preferred over conventional NSAIDs as they may lead to serious gastrointestinal complications such as ulcer, severe bleeding and perforation, resulting in hospitalization and even death[4]. It is mainly used for the osteoarthrities, rheumatoid arthritis and acute gouty arthritis[5-7]. The drug is available in tablet form (60 mg, 90 mg or 120 mg)[2] and is not official in any pharmacopoeia. So far only solid-phase extraction–liquid chromatography–tandem mass spectrometry method has been reported for the estimation of etoricoxib[8-10]. But this method is comparatively time consuming and expensive than simple spectrophotometric method. The aim of the present investigations is to develop a simple, rapid and cost-effective analytical method for the determination of etoricoxib in bulk drug and in its various dosage forms. The present investigation illustrates two simple, sensitive and accurate simple UV method and first derivative spectroscopic method for the analysis of etoricoxib in bulk drug and in tablets.

Shimadzu UV–160A UV/Vis spectrophotometer was used for all absorbance measurement. Etoricoxib was obtained as a gift sample from Sun Pharmaceuticals Limited, Vadodara. Stock solution of etoricoxib (500 μg/ml) was prepared in methanol.

In the simple UV method, aliquots of stock solution of etoricoxib (1–5 ml, 500 μg/ml) were transferred into a series of 100 ml volumetric flasks and volume was made up to the mark with 0.1 N sodium hydroxide solution. The absorbance of the resulting solutions was measured at 284 nm against the reagent blank solution (prepared similarly without drug). Calibration curve was prepared by plotting concentration versus absorbance.

In the derivative spectroscopic method, aliquots of stock solution of etoricoxib (1–6 ml, 500 μg/ml) were transferred into a series of 100 ml volumetric flasks. These solutions were diluted with 0.1 N sodium hydroxide solution up to the mark and first derivative curves were obtained which showed maxima at 301.0 nm and minima at 266.8 nm. First derivative spectrum of etoricoxib in 0.1 N sodium hydroxide solution (15 μg/ml) is shown in fig. 1. The calibration curve was prepared by plotting the absorbance difference between maxima and minima (i.e. amplitude) versus concentration.

The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation (calculated from the seven measurements containing three fourth of the concentration of the upper Beer's law limit) of both methods were determined (Table 1).

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION DATA

Parameters	Simple UV method	First Derivative method
Absorption maxima (λ_{max}), nm	284.0	301.0
Absorption minima (λ_{min}), nm	-	266.8
Beer's law limit (μg/ml)	5-25	5-30
Molar absoptivity (l/mole/cm)	1.44×10^{4}	0.8616×10^{4}
Sandell's sensitivity(μg/ml/cm²/0.001 abs. unit)	2.50×10^{-2}	2.50×10^{-3}
Regression equation (Y)[p]		
Slope (b)	0.0400	0.0660
Intercept (a)	0.0002	0.0245
Correlation coefficient (r)	0.9998	0.9998
Relative standard deviation (%)[q]	0.08	0.15
Recovery (%)	98.81-101.47	99.74-101.40

[p]means Y=a+bc, where c is concentration in μg/ml, a is the intercept and Y is absorbance units. [q]means seven replicate samples.

TABLE 2: RESULTS OF ANALYSIS OF PHARMACEUTICAL FORMULATIONS.

Dosage Forms	Labeled value (mg)	% Amount found		t-value (Calculated)	F-value (Calculated)
		Simple UV method (mg)[a]	First derivative method (mg)[a]		
Tablet-1	60	99.74±1.11	100.1±2.31	0.780	0.374
Tablet-2	90	102.8±1.96	98.52±1.97	0.184	0.998
Tablet-3	120	99.97±2.02	99.70±2.32	0.925	0.861
Tablet-4	90	101.7±1.97	101.5±1.10	0.871	0.474

[a]means average±standard deviation of three determinations. The t-value and F-value refer to compression of the simple UV method with first derivative method. Theoretical value at 95% confidence limit: t=4.30 and F=18.50. Tablet-1 stands for tablets of Dr. Reddy Laboratories, Hyderabad (Retoz, strength-60 mg), tablet-2 stands for tablets of Wockhardt Limited, Mumbai (Etobrix-90, strength-90 mg), tablet-3 stands for tablets of Torrent pharmaceuticals Ltd., Ahmedabad (Torcoxia-120, strength-120 mg) and tablet-4 stands for tablets of Bergen Healthcare, Mumbai (Alcoxib-90, strength-90 mg)

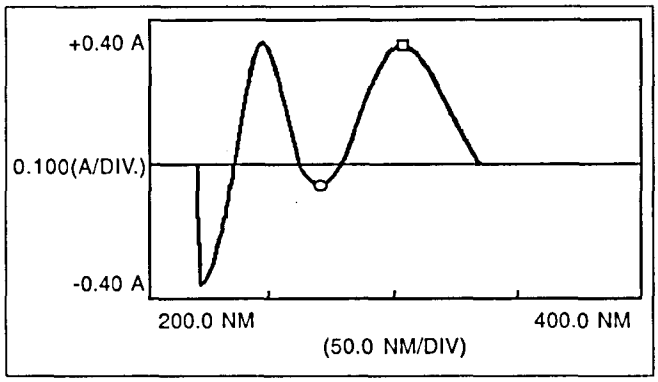

Fig. 1: First derivative spectrum of etoricoxib.

First derivative spectrum of etoricoxib in 0.1N NaOH solution (15μg/ml) which shows maxima at 301.0 nm (□) and minima at 266.8 nm (O)

The values obtained by simple UV method and first derivative method for the estimation of etoricoxib in marketed tablets are compared by using student t-test (paired, two sided) and F-test at 95% confidence limit. The results of analysis of four different brands of marketed tablets by both the methods are shown in Table 2.

For recovery study, known amounts of pure drug was added to the previously analyzed pharmaceutical preparation and the mixtures were analyzed by proposed methods. The data of recovery studies are incorporated in Table 3.

Sharp peaks were observed in first derivative as compared to second and third derivative spectrum. There was no linearity of amplitude at other wavelengths except 266.8 and 301.0 nm in first derivative spectroscopic method. *Therefore, 266.8 and 301.0 nm wavelengths were selected* for analysis in first derivative spectroscopic method. The good amplitude and linearity were observed over the given concentration range (fig. 1).

Both proposed methods are rapid, economical, accurate and precise for the determination of etoricoxib in bulk drug and in its dosage forms. In results of analysis of marketed tablets by both methods, t-calculated values and F-calculated values were less than the corresponding statis-

TABLE 3: RECOVERY STUDY OF PHARMACEUTICAL FORMULATIONS.

Initial Conc. (μg/ml)	Added Conc. (μg/ml)	Total Conc. (μg/ml)	% Recovery[a]	
			Simple UV method	First derivative method
10	5	15	101.97±2.52	100.7±1.23
10	10	20	100.3±1.06	99.31±0.72
10	15	25	98.81±0.90	101.4±1.64

[a]means Recovery of average of three determinations.

tical values indicating no significant difference in means and variances of results obtained by either of the proposed methods. Both proposed methods produce comparable results and can be used for precise and accurate analysis of etoricoxib in its dosage forms. Interference studies revealed that the common excipients and other additives usually present in the dosage forms did not interfere in both the proposed methods. The values of standard deviations were satisfactory and % recovery was close to 100 % indicating the reproducibility and accuracy of both the methods. Both proposed methods can be employed as a quality control tool for the analysis of etoricoxib in bulk drug and its dosage forms.

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Studies on the Antimicrobial Activity of *Cadaba indica* Lam

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Accepted 30 October 2005

Revised 18 February 2005

Received 5 January 2004

Leaves of *Cadaba indica,* family Capparidaceae were extracted with petroleum ether, chloroform, ethanol and water. The crude extracts were investigated for its antibacterial activity against *Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and antifungal activity against *Candida albicans, Candida krushi.* The extracts showed significant antibacterial and antifungal activity in the order ethanol, water, chloroform, petroleum ether against all the microorganisms tested and the effect so produced was compared with the standard drugs ampicillin and cotrimoxazole. However, the antibacterial, antifungal activity of the ethanol extract of the leaves was found to be most effective against all the organisms.

Cadaba indica (Capparidaceae) is an unarmed, branched shrub up to 3 m height. Leaves simple or trifoliate, size- 12-15 by 8-12 mm, entire, elliptic, oblong or ovate, muccronate dull green. It is locally called as kattagatti, villi and medicinally used for treating skin diseases, uterine obstruction, anthelmentic, purgative, deobstruent, emmenagogue and antisyphillictic[1]. The leaves of the plant are rich in lactones, steroids, flavonoids, alkaloids, reducing sugar and tannins[2-4]. The present study was taken up to evaluate antibacterial and antifungal activity of the petroleum ether, chloroform, ethanol and water extracts of the leaves of *C. indica.*

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C. indica plant was collected from outskirts of Trichy district, Tamil Nadu in the month of June, identified from the