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Spectrophotometric Estimation of Valdecoxib in Pure Form and Tablets

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Simple UV and third derivative spectrophotometric methods have been developed for the determination of valdecoxib in bulk drug and its tablets. In simple UV spectrum of valdecoxib in 0.1 N sodium hydroxide, it exhibits absorption maxima (λ_{max}) at 243 nm where as in third derivative spectrum it shows maxima at 221.2 nm and minima at 213.6 nm. Both the methods were found to be simple, economical, accurate, reproducible and can be adopted in routine analysis of valdecoxib in bulk drug and its tablets.

Valdecoxib (VXB) is a new NSAID, which chemically is 4-[5-mehtyl–3-phenylisoxazole-4-yl] benzenesulfonamide. It is active at low dose and has less gastric toxicity. It inhibits synthesis of prostaglandins by inhibiting the activity of the enzyme, cyclooxygenase-2 (COX-2) [1-4]. It is 28,000 times more selective for COX-2 than COX-1[5]. Valdecoxib 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[6-7]. It is mainly used for the osteoarthritis, rheumatoid arthritis and dysmenorrhea[8-10]. The drug is available in tablet form and is not yet official in any pharmacopoeia.

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So far only solid-phase extraction–liquid chromatography–tandem mass spectrometry method has been reported for the estimation of valdecoxib[11]. But this method is comparatively time consuming and expensive when compared to simple spectrophotometric method. The aim of the present investigations is to develop a simpler, rapid and cost-effective analytical method for the determinations of valdecoxib in bulk drug and in its various dosage forms. The present investigation illustrates two simple, sensitive and accurate simple UV method and third derivative spectroscopic method for the analysis of valdecoxib in bulk drug and in tablets.

A Shimadzu UV–1601PC UV/Vis spectrophotometer was used for all absorbance measurement. Valdecoxib was obtained as a gift sample from Cadila Pharma Ltd., Ahmedabad. Stock solution of valdecoxib (1 mg/ml) was pre-

pared in 0.1 N sodium hydroxide solution. Working solution (30 μg/ml) was prepared by appropriate dilutions of the stock solution in 0.1 N sodium hydroxide.

In simple UV method, aliquots of working solution of valdecoxib (1–5 ml, 30 μg/ml) were transferred into a series of 10 ml volumetric flasks and volume was made up to the mark with 0.1 N sodium hydroxide solution. The absorbances of the resulting solutions were measured at 243 nm against a reagent blank solution (prepared similarly without drug). Calibration curve was prepared by plotting concentration versus absorbance.

In derivative spectroscopic method, aliquots of working solution of valdecoxib (1–7 ml, 30 μg/ml) were transferred into a series of 10 ml volumetric flask. These solutions were diluted with 0.1 N sodium hydroxide solution up to the mark and third derivative curves were obtained which showed maxima at 221.2 nm and minima at 213.6 nm. Third derivative spectrum of valdecoxib in 0.1N sodium hydroxide solution (12 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) and percentage range of error at 95% confidence limit of both methods were incorporated in Table 1.

The values obtained by simple UV method and third derivative method for the estimation of valdecoxib 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 three 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 tablets and the mixtures were analyzed by proposed methods. The data of recovery studies are incorporated in Table 3.

Sharp peaks were not observed in first derivative and second derivative spectrum. There was no linearity of amplitude in first and second derivative spectroscopic method while in third derivative spectroscopic method, there was good amplitude as shown in fig. 1 and linearity was also observed. So, third derivative spectroscopy method was selected for analysis.

Both proposed methods are rapid, economical, accurate and precise for the determination of valdecoxib in bulk

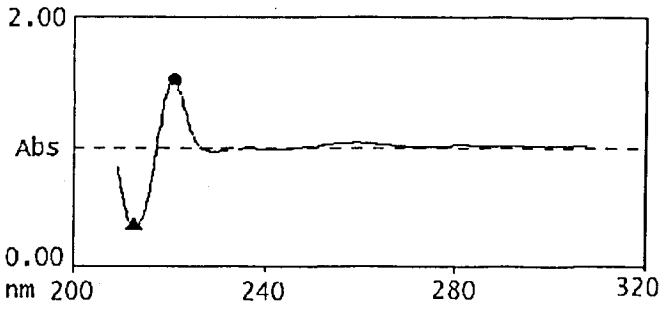

Fig. 1: Third derivative spectrum of valdecoxib.

Third derivative spectrum of valdecoxib in 0.1N NaOH solution (12 μg/ml) which shows maxima at 221.2 nm (●) and minima at 213.6 nm (▲).

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Simple UV method	Third Derivative method
Absorption maxima (λ_{max})	243 nm	221.2 nm
Absorption minima (λ_{min})	-	213.6 nm
Beer's law limit	3-15 μg/ml	3-21 μg/ml
Molar absoptivity (lit/mole/cm)	1.45×10^{4}	7.73×10^{4}
Sandell's sensitivity (μg/ml/cm²/0.001 abs. unit)	2.16×10^{-2}	4.06×10^{-3}
Regression equation (Y)*		
Slope (b)	0.0547	0.238
Intercept (a)	0.0117	0.0349
Correlation coefficient (r)	0.9998	0.9997
Relative standard deviation (%)**	0.578	0.424
% Range of error (0.05 level)	0.467	0.532

*Y=a+bc, where C is concentration in μg/ml and Y is absorbance units. **Seven replicate samples.

TABLE 2: ANALYSIS OF PHARMACEUTICAL FORMULATION

Sample	Labeled value (mg)	Amount found		t-value (Calculated)	F-value (Calculated)
		Simple UV method (mg)*	Third derivative method (mg)*		
Tablet-1	10	10.1±0.48	11.2±0.52	0.012	0.265
Tablet-2	10	9.61±0.76	9.23±0.58	0.126	0.572
Tablet-3	10	10.9±0.71	11.2±0.93	0.411	0.566

*Average ± standard deviation of six determinations. The t-value and F-value refer to compression of the simple UV method with third derivative method. Theoretical value at 95% confidence limit: t = 2.57 and F = 6.61. Tablet-1 stands for tablet of Glenmark Pharmaceuticals Ltd., Nasik (brand name-Vorth-10, strength-10 mg), tablet-2 stands for tablet of Torrent Pharmaceuticals Ltd., Ahmedabad (brand name-Valz-10, strength-10 mg) and tablet-3 stands for tablet of Mepro Pharmaceuticals Ltd, Surendranagar (brand name-Valed-10, strength-10 mg).

TABLE 3: RECOVERY FROM TABLETS

Sample	% Recovery*			
	By simple UV method		By third derivative method	
	I	II	I	II
Tablet-1	99.3±0.43	99.2±0.64	99.2±0.3	100±0.51
Tablet-2	100±0.35	100±0.11	98.3±0.24	99.3±0.27
Tablet-3	98.8±0.56	98.3±0.24	100±0.36	101±0.56

* Recovery of 4 mg added to the pharmaceutical preparation (average of six determinations). I and II indicates two replicate measurements. Tablet-1 stands for Vorth-10 from Glenmark Pharmaceuticals Ltd., tablet-2 stands for Valz-10 from Torrent Pharmaceuticals Ltd and tablet-3 stands for Valed-10 from Mepro Pharmaceuticals Ltd.

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 statistical 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 valdecoxib in its dosage forms. Interference studies revealed that the common excipients and other additives usually present in the dosage forms did not interfere in the both 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 valdecoxib in its tablets and in bulk drug.

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