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NOTE

RP-HPLC Method for the Simultaneous Determination of Valdecoxib and Paracetamol in Tablet Dosage Form

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A simple, precise, accurate and rapid RP-HPLC method has been developed and validated for the simultaneous determination of valdecoxib and paracetamol in combined tablet dosage form. The mobile phase used was a mixture of methanol and water (55 : 45) (v/v). The detection of valdecoxib and paracetamol was carried out on dual λ_{max} absorbance detector at 243 and 245 nm, respectively. Results of the analysis were validated statistically and by recovery studies. The proposed method can be successfully used to determine the drug contents of marketed formulation.

Key Words: RP-HPLC, Valdecoxib, Paracetamol.

The combination of valdecoxib and paracetamol has recently been introduced into the market. Valdecoxib[1], chemically 4-(5-methyl-3-phenyl-4-isoxazolyl) benzene sulfonamide, is a diaryl substituted isoxazole. It is a COX-2 inhibitor with a lower incidence of ulcer complication[2]. Paracetamol[3], chemically N-acetyl *p*-amino phenol, is used in the symptomatic treatment of pain and fever. Literature survey reveals that individual HPLC methods[4–6] have been developed for the estimation of both drugs in pharmaceutical dosage forms and in human plasma. Till now no method has been developed for the estimation of these drugs simultaneously. In this communication, a fast, very simple, accurate and reproducible method for the simultaneous estimation of both these drugs in tablet dosage form is reported.

Valdecoxib and paracetamol were obtained from M/s Aristo Pharmaceuticals Ltd., Mumbai, India and M/s. Dr. Reddy's Labs, Hyderabad, India. Methanol of HPLC grade was obtained from M/s. S.D. Fine Chemicals. Ltd., Mumbai, India. The separation was carried out on gradient HPLC system (Waters) with Waters 1525 binary HPLC pump, Waters 2487 UV dual λ absorbance detector, Waters Breeze software and RP-C_{18} column (150 × 4.6 mm I.D; particle size 5 μm).

HPLC Conditions: The mobile phase used was methanol and water in the ratio of 55 : 45 (v/v). The run time and the flow rates were 7 min and 1 mL/min, respectively. Detection wavelengths of valdecoxib and paracetamol were set at 243 and 245 nm, respectively. The injection volume was 20 μL.

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Procedure: Standard stock solutions of 1 mg/mL of valdecoxib and paracetamol were prepared separately in methanol and used for estimation. For construction of calibration graph, stock solutions were further diluted with mobile phase ranging from 0.05–10 μg/mL. This method was applied to determine valdecoxib and paracetamol in two different market samples. For analysis of tablet formulation an accurately weighed tablet powder equivalent to 20 mg of valdecoxib and 500 mg of paracetamol was taken in a volumetric flask (25 mL). The powder was dissolved in 15 mL methanol, shaken thoroughly and made up to the volume with methanol. Then the solution was filtered through Whatmann filter paper (No. 41) and further diluted with methanol to get the concentrations of 0.2 and 5 μg/mL of valdecoxib and paracetamol, respectively. These solutions were injected and the chromatograms were recorded.

The method was validated in terms of linearity, accuracy, inter-day and intra-day precision, reproducibility and specificity. The limit of detection (LOD) and limit of quantitation (LOQ) were also determined. Accuracy of the method was evaluated by carrying out recovery studies. For this, known concentration of standard solution was added to pre-analyzed sample solution and the recovery was calculated. The intra-day precision was determined by analyzing standard solutions in the linearity range of calibration curve in triplicate on the same day, while inter-day precision was determined by analyzing the corresponding standard solutions daily for a period of one week. The RSD or CV of < 2.5% was observed (Table-1). The validated data is furnished in Table-2.

The retention times of valdecoxib and paracetamol are 6.30 and 1.81 min, respectively (Fig. 1). Linearity range for valdecoxib and paracetamol were 0.05–10 μg/mL (r = 0.9976) and 0.05–10 μg/mL (r = 0.9999), respectively. The linear regression equations are Y = 1629.67 + 146849.4X for valdecoxib and Y = 1034335.4 + 1316341.9X for paracetamol. The high percentages of recovery of the drugs indicate that the method is highly accurate. The content and the percentage of drugs in two different market samples (Table-3) indicate that the proposed method is simple, rapid, precise and accurate for the estimation of valdecoxib and paracetamol in its pharmaceutical formulation.

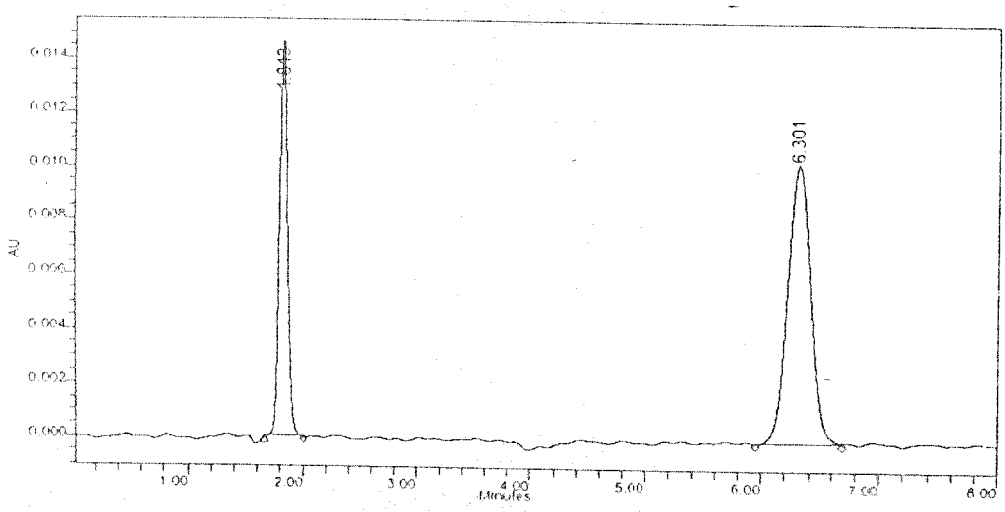

Fig. 1. Typical chromatogram of valdecoxib and paracetamol

TABLE-1
INTER- AND INTRA-DAY PRECISION STUDIES

Concentration	Amount found on			
	Intra-day		Inter-day	
	Mean (n = 5)	C.V.(%)	Mean (n = 5)	C.V.(%)
Valdecoxib (4 μg/mL)	4.03	0.877	3.88	0.783
Paracetamol (4 μg/mL)	3.92	1.239	3.91	0.994

TABLE-2
VALIDATION SUMMARY

System suitability	Results	
	Valdecoxib	Paracetamol
Theoretical plates (N)	5069	3313
Resolution	1.84	—
Linearity range (μg/mL)	0.05–10	0.05–10
Percentage recovery (accuracy)	99.37	98.92
LOD (μg/mL)	0.01	0.01
LOQ (μg/mL)	0.03	0.03
Tailing factor	1.03	1.19
Capacity factor	6.21	1.09
Symmetry factor	1.03	1.09

TABLE-3
ASSAY AND RECOVERY STUDIES

Formu-lation	Drug	Label claim (mg)	Amount found* (%)	Amount of standard added (mg)	Amount recovered*	Recovery (%)
Brand-1	Valdecoxib	20	19.94	10	10.02	100.20
	Paracetamol	500	500.05	50	50.21	102.42
Brand-2	Valdecoxib	20	19.91	10	9.98	99.80
	Paracetamol	500	498.09	50	49.42	98.84

*Mean of five determinations.

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