

RP-HPLC Estimation of Paracetamol and Valdecoxib in Combined Dosage Form

A. S. BHAVSAR, G. S. TALELE*, R. A. FURSULE AND S. J. SURANA

Department of Pharmaceutical Chemistry, R. C. Patel College of Pharmacy, Shirpur-425 405, *JZMDS College of Pharmacy, Mamurabad, Jalgaon-425 001, India.

A reverse phase high performance liquid chromatography method was developed for simultaneous estimation of paracetamol and valdecoxib in tablet formulation. The separation was achieved by Luna C₁₈ column and methanol: phosphate buffer pH 3.5 (60:40 v/v) as eluent, at a flow rate of 1.0 ml/min. Detection was carried out at 242 nm. Etoricoxib was used as an internal standard. The retention time of PAR and VAL was found to be 3.01 and 8.51 min, respectively. The method was validated for linearity, accuracy and precision. Linearity for paracetamol and valdecoxib were in the range 25-150 µg/ml and 1-6 µg/ml, respectively. The developed method was found to be accurate, precise, and selective for simultaneous estimation of paracetamol and valdecoxib in tablets.

Paracetamol (PAR) is chemically 4-hydroxyacetanilide, is a centrally and peripherally acting non-opioid analgesic and antipyretic. PAR is official in IP, BP and USP¹⁻⁴. Valdecoxib (VAL) is [4-(5-methyl-3-phenyl-4-isoxazolyl)benzenesulfonamide] is the newest addition to the group of non-steroidal antiinflammatory drugs (NSAIDs) known as selective Cox-2 inhibitor. This drug has been recently approved by the USFDA for treatment in rheumatoid arthritis, osteoarthritis and pain⁵⁻⁷. VAL is not official in any pharmacopoeia. A tablet formulation containing 500 mg of PAR and 20 mg of VAL has been introduced in to clinical practice. A survey of literature revealed that few HPLC and spectrophotometric methods are reported for determination of VAL individually⁸⁻¹¹. However there is no HPLC method reported for simultaneous determination of PAR and VAL from combine dosage form. The present work describes the

simple, precise and accurate RP-HPLC method for simultaneous estimation of PAR and VAL in tablets.

The drug samples, PAR and VAL were obtained as a gift samples from the Emcure Pharmaceuticals Pvt. Ltd., Pune. HPLC grade methanol was supplied by Merck. Co. Mumbai. Potassium dihydrogen orthophosphate AR and phosphoric acid AR were purchased from Merck and S. D. Fine Chemicals, Mumbai, respectively.

A gradient high performance liquid chromatography (Shimadzu HPLC class LC-10 series) with two LC-10 AT-VP pumps, variable wavelength programmable PDA detector SPD-10 AVP, SCL-10 AVP system controller (Shimadzu) and operating software Shimadzu class LC-10 data station was used. The chromatography column used was reverse phase Luna C₁₈ column (250 mm x 4.6 mm i.d, partical size 5 µ).

A mixture of methanol and 10 mM phosphate buffer

*For correspondence

E-mail: gstalele@rediffmail.com

(adjusted to pH 3.5 using Orthophosphoric acid) in the ratio 60:40 v/v was used as mobile phase and was filtered before use through 0.45 μ Millipore membrane filter. The flow rate of mobile phase was maintained at 1.0 ml/min. Detection was carried out at 242 nm at the room temperature.

Standard stock solution of VAL, PAR and etoricoxib (1 mg/ml) was prepared in methanol. From the standard stock solutions, mixed standard solution was prepared containing 50 μ g/ml of PAR, 2 μ g/ml of VAL and 30 μ g/ml of etoricoxib. Twenty tablets, each containing 500 mg of PAR and 20 mg of VAL were weighed and finely powdered. A quantity of powder equivalent to 500 mg of PAR and 20 mg of VAL was weighed and transferred to 100 ml volumetric flask containing 50 ml methanol. The mixture was sonicated for 10 min. The volume was made up to 100 ml with methanol. Further dilutions were made to get a concentration of 50 μ g/ml of PAR, 2 μ g/ml of VAL and 30 μ g/ml of etoricoxib as internal standard (theoretical value). The contents were vortexed and filtered through 0.22 μ membrane filter. Twenty microliters of the test and standard solutions were injected separately and chromatograms were recorded upto 15 min.

The present investigation was aimed at developing a simple, precise and accurate HPLC method to estimate PAR and VAL in tablet using the widely used RP-HPLC C_{18} column (Luna). The mobile phase was optimized with methanol and 10 mM Potassium dihydrogen ortho phosphate buffer (pH 3.5) in the proportion of 60:40 v/v. With the above mentioned composition of mobile phase a good resolution between PAR and VAL was achieved. UV detection was carried out at 242 nm as both the drugs showed good absorbance at this wavelength.

The retention time of PAR and VAL was found to be 3.01 and 8.51 min, respectively. The capacity factor of VAL was found to be 2.06. The peak shape of both drugs were symmetrical and asymmetric factor was lesser

than 2.0. The response factor (peak area ratio of standard peak area and internal standard peak area) of the standard and test solution was calculated. The proposed method was validated as per ICH guidelines¹². Each of the samples was injected 6 times and the retention time was observed in all the cases. Precision of proposed method (RSD) was found to be 0.041% for PAR and 0.058% for VAL. The low RSD value indicated that proposed method had good precision. Linearity experiments were performed thrice for the both the compounds and the response was found to be linear in the range of 25-150 μ g/ml for PAR and 1-6 μ g/ml for VAL. Linearity of PAR and VAL was plotted by a graph of response factor versus concentration. The correlation coefficient (r) values (n=3) for PAR and VAL were 0.9997 and 0.9998, respectively. Accuracy of the method was calculated by recovery studies (n=3) at three level. Amount of drug recovered at each level (n=3) was calculated. Percent recovery study at each level was calculated. Table 1 shows the data from the recovery data for PAR and VAL. The average recovery of PAR and VAL were 101.1 and 101.7%, respectively. The sample recovery in the formulation was in a good agreement in a label claim. High percentage recovery showed that the method was free from interferences of excipients used in the formulations. Assay of the combination in tablet dosage form was found to be 100.89% of PAR and 100.03% of VAL. The results of study indicate that proposed method is simple, precise, highly accurate and specific.

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TABLE: 1 RECOVERY STUDY

Drug	Assay results		Amount added μ g/ml	Amount recovered μ g/ml (n=3)	Recovery (%)	Average recovery (%)
	Actual concentration mg	Concentration found (%) (n=3)				
PAR	500.00	100.89 \pm 0.512	40.00	40.36	100.9	
VAL	20.0	100.03 \pm 0.412	50.00	51.2	100.5	101.1
			60.00	60.59	100.9	
			1.6	1.63	101.8	
			2.0	2.03	101.5	101.7
			2.4	2.45	102.0	

PAR = Paracetamol, VAL = Valdecosib

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