Simultaneous Estimation of Paracetamol and Domperidone in Tablets by Reverse Phase HPLC Method

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A simple, fast, precise and accurate liquid chromatographic method was developed for the simultaneous estimation of paracetamol and domperidone in combined dosage forms. This combination is used for antiemetic and pain associated with gastrointestinal disorders. Drugs are chromatographed on a reverse phase Kromasil C18 column using a mobile phase, 20 mM phosphate buffer (pH 7.0±0.1) and acetonitrile in the ratio of 60:40%v/v. Diclofenac potassium was used as an internal standard. The retention time of paracetamol, domperidone, and diclofenac potassium was 2.94, 8.30, 5.67 min, respectively. The validation of the proposed method was also carried out. The method was found to be linear (r>0.99), precise (%RSD: 0.49% for paracetamol and 0.89% for domperidone), accurate (overall average recovery yields: paracetamol 99.1% and domperidone 98.36%) and selective. Due to its simplicity and accuracy the proposed method can be used for routine quality control analysis of these drugs in combined dosage form.

Domperidone (DMP) is chemically 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl) propyl]-piperidin-4-yl]-1,3-dihydro-2*H*-benzimidazol-2-one used as antiemetic drug. Paracetamol (PAR), chemically 4-hydroxy acetanilide, is a centrally and peripherally acting non-opioid analgesic and antipyretic. A combination of these drugs, DMP (20 mg), and PAR (500 mg) is available as tablets for clinical practice. This combination is used for antiemetic and pain associated with gastrointestinal (GIT) disorders. Many methods[1-8] have been described in the literature for the determination of DMP, PAR, individually. However, there is no HPLC method reported for the simultaneous determination of these drugs either as active pharmaceutical ingredient or from dosage forms. The present work describes a simple, precise and accurate reverse phase HPLC method for simultaneous estimation of PAR and DMP in combined dosage forms.

The drug samples, PAR, DMP and diclofenac potassium were obtained as gift samples from the Karnataka Antibiotics and Pharmaceutical Ltd., Bangalore. Sodium dihydrogen orthophosphate AR, orthophosphoric acid AR, acetonitrile of HPLC grade, and methanol HPLC grade were supplied by S. D. Fine Chemicals, Mumbai. Water HPLC grade was obtained from a milli-Q RO water purification system.

A gradient high-pressure liquid chromatograph (Shimadzu HPLC Class VP series) with two LC-10AT VP pumps, variable wavelength programmable UV/Vis detector SPD-10AVP, SCL-10AVP system controller (Shimadzu) and operating software Shimadzu Class VP version 6.12 SP2 data station was used for the analysis.

The method was carried out on a Kromasil C18 (250 mm×4.6 mm i.d., 5µ) column as a stationary phase. The mobile phase consisted of acetonitrile:20 mM phosphate buffer (40:60 pH-7) at the flow rate of 1 ml/min. The mobile phase was filtered through a 0.45 µ membrane filter and degassed before analysis. A rheodyne 7725 injector with a 20 µl loop was used for the injection of samples. Detection was done at 230 nm and separation was carried out at the room temperature of about 25°.

Standard stock solution of PAR, DMP, and diclofenac (100 µg/ml) were prepared separately by using methanol as a solvent. From the standard stock solutions, mixed standard solution was prepared containing 25 µg/ml of PAR, 1 µg/ml of DMP and 25 µg/ml of diclofenac as internal standard.

Ten marketed tablets, Dompon P (manufactured by Finecure Pharmaceuticals, Ahmedabad), each containing 500 mg of PAR and 20 mg of DMP, were weighed and average weight calculated and finely powdered. A quantity of powder equivalent to 25 mg of PAR and 1 mg of DMP were weighed accurately and transferred in to a 100 ml volumetric flask and extracted using three quantities of methanol of about 25 ml and the volume was made up using methanol. To this 1 ml of diclofenac (250 µg/ml) was added and then the mixture was sonicated for 20 min and then filtered. The combined extracts were made upto 100 ml with methanol and further dilutions (10 times) were made to get a concentration of 25 µg/ml of PAR, 1 µg/ml of DMP and 25 µg/ml diclofenac (theoretical value). The content was vortexed, filtered through a 0.45 µ membrane filter and injected in triplicate. The ratio of peak area of drug to that of internal standard was calculated. The mixed standard solution was subjected to proposed HPLC method of analysis for finding out intra and interday variations. The recovery studies were carried out by adding known amount of standard drug to the pre-analyzed samples and subjecting them to the proposed HPLC method of analysis.

The present study was carried out to develop a simple and rapid HPLC method for the simultaneous estimation of PAR and DMP, using most widely used Kromasil C_{18}

TABLE 1: RECOVERY STUDIES

Drug	Amount added (µg/ml)	Amount recovered (µg/ml)	Recovery (%)	Average recovery (%)
PAR	17.478	17.281	98.87	
	24.987	24.779	99.17	99.1
	32.235	31.995	99.26	
DMP	0.698	0.669	95.84	
	0.987	0.990	100.30	98.36
	1.312	1.298	98.93	

Recovery experiment data for PAR and DMP showing the amounts of drug added and recovered from sample solution at each level (n=3), percentage recovery and the average percentage recovery. PAR stands for paracetamol and DMP stands for domperidone

column. The retention time of DMP, PAR and diclofenac was found to be 8.30, 2.94, and 5.67 min, respectively. The assay concentration of 25 µg/ml of PAR and 1 µg/ml DMP was selected according to the labeled claim. The peaks were well resolved and the resolution between PAR and diclofenac was found to be 8.58 whereas between diclofenac and DMP was 6.34.The peak of internal standard was 5.7 min and it was well resolved from the other analytes. The asymmetry factors of all the peaks were lesser than 2.0 and it showed that all peaks were symmetrical in shape. The precision of the proposed method was lesser than 2% for all the three drugs including internal standard when it was injected 6 times and there was good repeatability of the proposed method. The % CV of PAR, DMP was found to be 0.49%, 0.89%, respectively and it showed that the method was highly precise. The regression equation was found to be linear in the 70 to 130% of assay concentration. Accuracy of method was calculated by % mean recovery studies (n=3). The recovery studies were carried out by the addition of standard analyte to the preanalysed sample. The concentrations of standard spiked to the sample were 17.5-32.5 µg/ml of PAR and 0.7-1.3 µg/ml of DMP. The recovery studies are showed in the Table 1. The mean % recovery was found to be 99.1% for PAR and 98.36% for DMP. Assay of the combination in tablet dosage form was found to be DMP 100.78% and 101.14% of PAR. The estimated amount was within the acceptable limits of the labeled claim of the formulation. The total run time of the proposed method was 20 min and no peaks were found after 10 min. System suitability and linearity results were showed in the Table 2.

The proposed HPLC method was simple and precise because of the commonly used buffer, easier extraction procedures and shorter runtime. The proposed method is highly accurate which showed good recovery of the drug samples and there was no interference from the excipients at the retention time of all three drugs which showed that it was specific and the analysis was less time consuming. The proposed method can be used in routine quality control of combined dosage form containing PAR and DMP in tablets.

TABLE 2: LINEARITY RESULTS AND SYSTEM SUITABILITY STUDIES

Parameter	PAR	DMP
Concentration range (µg/ml)	17.5-32.5	0.7-1.3
Capacity factor	10.90	22.50
Theoretical plates per meter	5900	26800
Asymmetry (10%)	1.09	1.91
Resolution between drug and IS	8.58	6.34

The system suitability results are the average values calculated based on the validation experiments

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