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Simultaneous HPLC Estimation of Pantoprazole and Domperidone from Tablets

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Abstract: The present work describes a simple reverse phase HPLC method for the determination of pantoprazole and domperidone from tablet formulations. The determination was carried out on a Hypersil, BDS, C-18 (150×4.6 mm, 5 micron) column using a mobile phase consisting of 0.05 M, 4.70 pH, potassium dihydrogen phosphate buffer - acetonitrile (720:280 v/v) at a flow rate and run time of 1.0 ml/min and 10 min, respectively. The eluent was monitored at 280 nm. The method was reproducible, with good resolution between pantoprazole and domperidone. The detector response was found to be linear in the concentration range of 10-60 µg/ml for pantoprazole and 5-30 µg/ml for domperidone.

Key words: Pantoprazole ,Domperidone, HPLC Estimation

Introduction

Pantoprazole (PP), 5-(difluoromethoxy)-2-[[(3, 4-dimethoxy-2-pyri-dinyl) methyl] sulphinyl]-1H-benzimidazole, is a selective and long-acting proton-pump inhibitor used for treatment of acid-related gastrointe-stinal disorders. According to the literature HPLC has been used for deter-mination of PP in serum and plasma[1] and in tablet dosage forms[2], and for enantioselective separation of Pantoprazole and three analogues on different chiral stationary phases[3]. Chiral resolution of PP and related sulphoxides has been performed by capillary zone electrophoresis using bovine serum albumin as the chiral selector[4]. Separation of the enan-tiomers of PP by multidimensional HPLC[5] has also been reported. Domperidone (DP), 5-chloro-1-[1-[3-(2, 3-dihydro-2-oxo-1H-benz-imidazol-1-yl) propyl]-4-piperidinyl]-1, 3-dihydro-2H-benzimidazol-2-one, is a potent dopamine antagonist used for treatment of nausea and vomiting. DP does not cross the blood–brain barrier and therefore has fewer adverse CNS effects than other dopamine antagonists[6, 7]. DP has been determined in human plasma[8], human serum and human milk[9], and rat plasma[10], has been evaluated in coevaporates by HPLC[11], and has been determined, with cinnarizine, in tablets, by HPLC[12].

Experimental

Standard samples of pantoprazole and domperidone, which were prepared from reference standard procured from a pharmaceutical company (Nosch Laboratories Ltd, Hyderabad). HPLC grade acetonitrile manufactured by E. Merck was procured from commercial sources. Double distilled water was prepared in the laboratory. Tablet formulations, DYOFLUX, (Dyota) PEPMARK-SRD (Unimark) PENTALINK D (Lincoln) containing both Pantoprazole and domperidone were obtained from local market.

A Shimadzu HPLC (Kyoto, Japan) system was used coupled with SPD 10A UV detector. Separations were carried out on a Hypersil BDS C18 column (150×4.6 mm I.D) packed with 5 µ particle size as the stationary phase. The mobile phase consisting of potassium dihydrogen phosphate buffer - acetonitrile (720:280 v/v) was pumped at a flow rate 1 ml per min, the detection was monitored at 280 nm and the run time was 10 min.

Preparation of Standard solutions

Pantoprazole and domperidone (50 mg each) were weighed accurately in two 100 ml volumetric flasks separately and both standards were dissolved in about 20 ml of solvent solution (50 volumes of water and 40 volumes of acetonitrile). The volume was made up to 100 ml with solvent solution (stock solution). In case of pantoprazole varying amounts (1, 2, 3, 4, 5 and 6 ml) of the above solution (500 µg/ml) was taken in six different 50 ml volumetric flasks and the volume was made upto the mark with the solvent solution. An aliquot of 20 µl of the solution from each flask was injected two times. In case of domperidone 10 ml was taken from stock solution (500 µg/ml) and diluted to 100 ml with the solvent solution (50 µg/ml). Varying amounts (1, 2, 3, 4, 5 and 6 ml) of the above solution (50 µg/ml) was taken in six different 10 ml volumetric flasks and the volume was made upto the mark with the solvent solution. An aliquot of 20 µl of the solution from each flask was injected two times. Calibration curves were constructed by plotting mean peak areas against the corresponding drug

concentrations. The detector response was found to be linear in the concentration range of 10-60 µg/ml for Pantoprazole and 5-30 µg/ml for domperidone.

Twenty tablets were powdered finely. A quantity equivalent to two tablets was transferred to a 100 ml volumetric flask and 30 ml of solvent solution was added. The flask was shaken for 15 min and then contents were diluted to 100 ml and filtered through Whatman No.1 filter paper. One ml of this solution was then diluted to 10 ml with solvent solution. Results of the triplicate analysis are given in table 1.

This method was validated for statistical parameters i.e. precision, accuracy, specificity, linearity and range, stability of analytical solutions and ruggedness criteria. Results of the method validation experiments are given in table 2. The precision of the method was determined by knowing percentage RSD of means of three replicate solutions of all the three dependent samples.

The accuracy of method is determined by adding known amount of standard to that of sample (above and below the normal level) at 3 different levels to cover both above and below (75 to 125%) the normal levels expected in the sample. The normal expected level for the assay of Pantoprazole and domperidone is about 20 µg/ml. So the study range was 15, 20 and 25 µg/ml both.

The linearity of analytical method was studied by analyzing response of standard with predetermined concentration range, linearity curve was plotted for response areas against the concentration of the solution. Regression coefficient was calculated using above plot. For Pantoprazole, prepared solutions were within concentration range of 10 to 50 µg/ml at 5 constant consecutive concentration levels i.e. 10, 20, 30, 40 and 50 µg/ml. For domperidone, prepared solutions were within concentration range of 5 to 30 µg/ml at constant consecutive concentration levels i.e. 5, 10, 15, 20, 25 and 30 µg/ml. The regression coefficient of area of above consecutive concentrations was calculated.

The stability of analytical solutions of the method studied by a series of samples and standards were prepared and analysed immediately. They were stored at normal lab conditions and in a dark refrigerator, then reanalyzed 120 h later against freshly prepared standard solutions. The ruggedness of analytical method for Pantoprazole and domperidone in assay determination was studied by analyzing the samples by two sets. (i.e. different analyst, different reagents and solutions and differentdays).

A typical chromatogram obtained in the present investigation is shown in figure 1. The results obtained were summarized in table 1. Prior to the analysis, the method was subjected to system suitability tests. The resolution factor was found to be 6.55, which indicated that there is good resolution between Pantoprazole and domperidone. This method is highly sensitive to estimate Pantoprazole and domperidone in tablet formulations.

Discussion: The statistical parameters in method validation studies for precision, accuracy, specificity, stability of analytical solutions and ruggedness were justified the validity of the proposed method. The results of the assay and method validation studies given in table 1, table 2, have shown that the method is simple, accurate and precise and non-interference from tablet excipients[13].

Table 1: Analysis of Tablets containing Pantoprazole and Domperidone

Formulation	Label Content mg/tablet	Mean amount Found	Mean % drug mg/tablet	Standard deviation found
Pantoprazole				
Brand 1	40	40.02	100.2	0.58
Brand 2	40	40.01	99.99	0.60
Brand 3	40	39.98	99.98	0.61
Domperidone				
Brand 1	30	29.99	100.1	0.59
Brand 2	30	30.03	99.99	0.61
Brand 3	30	30.01	99.98	0.62

Table 2: Results of method validation experiments of Pantoprazole and Domperidone

Performance parameters		Results	Acceptance Limits
Precision	Pantoprazole	1.95 %	RSD NMT 2.0 %
	Domperidone	1.96 %	
Accuracy	Pantoprazole	3.20 %	% Bias NMT 5.0
	Domperidone	2.24 %	
Linearity (regression coefficient-r^2)	Pantoprazole	0.997	Linear NLT 0.996%
	Domperidone	0.998	
Stability of Analytical solutions (Normal conditions)	Pantoprazole	0.89 %	RSD NMT 2.0 %
	Domperidone	0.94 %	
Stability of Analytical solutions (in a dark refrigerator)	Pantoprazole	0.66 %	RSD NMT 2.0 %
	Domperidone	0.72 %	
Ruggedness	Pantoprazole	0. 60 %	RSD NMT 2.0 %
	Domperidone	0.64 %	

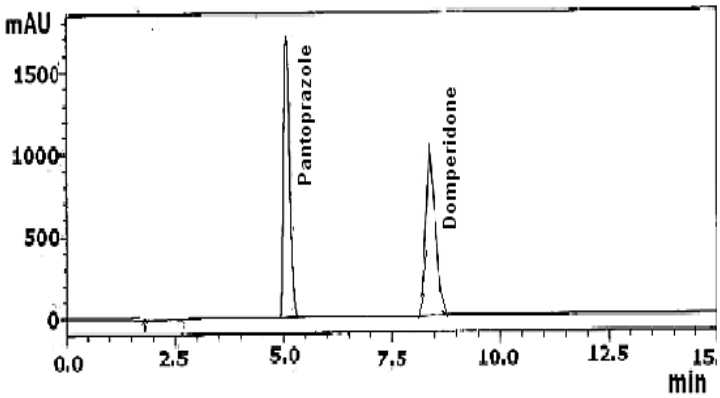

Figure 1: Standard chromatogram of Pantoprazole and Domperidone

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