

SIMULTANEOUS DETERMINATION OF RABEPRAZOLE AND DOMPERIDONE IN DOSAGE FORMS BY RP-HPLC

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ABSTRACT

A rapid and accurate high performance reverse phase liquid chromatography has been developed for the simultaneous determination of rabeprazole and domperidone in pharmaceutical dosage forms. Chromatography was carried out on a C-18 column (4.6 mm × 250 mm, 5 μm) using a mixture of phosphate buffer (pH 7.4) and acetonitrile in the ratio of 65:35 (v/v) as the mobile phase at a flow rate of 1.5 mL/min and eluents are monitored at 290nm. The calibration curves were linear over the range of 0.1 – 1.0 mg/mL of rabeprazole. The average retention time of rabeprazole and domperidone was found to be 5.45 and 11.07 respectively. The % recovery value for rabeprazole is 100.2% and for domperidone is 102% confirms the non-interferences of the excipients in the formulation. Due to its simplicity, rapidness and high precision, the proposed HPLC method may be used for the simultaneous determination of these two drugs in pharmaceutical dosage forms.

Key words: RP-HPLC, Rabeprazole, and Domperidone.

INTRODUCTION

Rabeprazole sodium is chemically known as 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl] sulfinyl]-1H-benzimidazole sodium salt. It is a proton pump inhibitor and used for the treatment of peptic ulcer or GERD. It is not official in any pharmacopoeia. Domperidone is chemically known as 5-chloro-1-[1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl] piperidin-4-yl]-2, 3-dihydro-1H-benzimidazol-2-one. It is a gastro-kinetic and anti-emetic. It is a peripheral dopamine-2 receptor antagonist. It is official in B.P. The present work describes the development of a validated RP-HPLC method, which can quantify these components simultaneously from a combined dosage form. A few chromatographic methods have been described for the individual determination of rabeprazole and domperidone in both dosage forms and biological fluids¹⁻⁵. The aim of the present work was to develop and validate a precise method for the simultaneous determination of these two drugs in dosage forms. The present RP-HPLC method was validated following the ICH guidelines⁶⁻⁷.

EXPERIMENTAL

Instrumentation: A waters C-18 RP – HPLC instrument with a C-18 analytical column, (4.6 mm × 250 mm, 5 μm) was used for the study. UV detector achieved detection. Using a digital pH meter checked the pH of the solution.

Chemicals and reagents: Pure samples of rabeprazole and domperidone were obtained from Chethana chemicals, Trichur. The commercial samples of rabeprazole D capsules and setgi capsules containing 20 mg of rabeprazole and 30 mg of domperidone were purchased from local market. Water (HPLC) was obtained from a Milli-QRO water purification system. Acetonitrile (HPLC grade), potassium dihydrogen ortho phosphate (A.R. grade) and sodium hydroxide (A.R. grade) were procured from Merck Ltd. (Mumbai, India.).

Preparation of stock solutions: Stock solutions containing 1 mg/mL of rabeprazole and 1 mg/mL of domperidone were prepared by dissolving each 100 mg in a separate 100 mL volumetric flasks containing 100 mL mobile phase. The working concentrations for the determination of both drugs were 1 mg/mL.

Chromatographic conditions: the mobile phase used in this study was a mixture of phosphate buffer pH 7.4 and acetonitrile in the ratio 65:35 % v/v. The mobile phase was filtered before use through a 0.2 μ membrane and degassed for 15min. The mobile phase was pumped from solvent reservoir to the column at a flow rate of 1.5 mL/min. The column temperature was maintained at $\pm 28^{\circ}\text{C}$. The events were monitored at 290nm.

Recommend procedure for standard graph: After a systematic and detailed study of various parameters involved, the following procedure and conditions are recommended for the determination of rabeprazole and domperidone in pure samples and in dosage forms.

Prior to injection of the drug solutions, the column was equilibrated at least for 30 min with the mobile phase flowing through the system. The prepared dilutions containing the concentration of rabeprazole in the range of 0.1 – 1.0 mg/mL maintaining the domperidone concentration at a fixed level (15 $\mu\text{g/mL}$) and 0.1 – 1.0 mg/mL maintaining the rabeprazole concentration at a constant level (10 $\mu\text{g/mL}$). Each of these samples (20 μL) was injected five times into the column and the peak area ratio of drug to that of internal standard was calculated. Standard graph was plotted by taking concentration of drug on x-axis and peak area ratio of drug to that of internal standard on y-axis.

Assay determination of rabeprazole and domperidone from formulations:

Capsules of rabeprazole and domperidone: Twenty weighed capsules of rabeprazole D and setgi were ground separately to a fine powder. From each formulation an amount of powder equivalent to 10 mg was accurately weighed and dissolved with mobile phase in a 25 mL volumetric flask.

Simultaneous quantification of rabeprazole and domperidone: Suitable dilutions of both of the capsules were made with mobile phase so as to obtain a concentration of the two drugs in the range of linearity determined. 20 μL volume of sample was injected into the column. All the determinations were made in triplicate.

METHOD VALIDATION

Linearity: The standard curve was obtained in the concentration range of 0.1 – 1.0 mg/mL for rabeprazole and also for domperidone. The linearity of these methods was evaluated by linear regression analysis, using least squares method.

Precision: The precision of the assay was determined in terms of repeatability (intra-day) and intermediate (inter-day) precision. The intra and inter-day variation in the peak area of drug solution containing 12 $\mu\text{g/mL}$ of rabeprazole and also domperidone were calculated in terms of coefficient of variation (C.V.).

Accuracy: The accuracy of HPLC method was assessed by adding known amount of drug to a drug solution of pre-analyzed sample subjecting the samples to the proposed HPLC method. All solutions were prepared and analyzed in triplicate.

Limit of detection (L.O.D.) and limit of quantification (L.O.Q.): Limit of detection was found to be 0.010 and 0.014 mg/mL for rabeprazole and domperidone and limit of quantification was found to be 0.024 and 0.030 mg/mL.

RESULTS AND DISCUSSION

To estimate the percentage recovery of rabeprazole and domperidone in capsules, typical chromatograms of rabeprazole and domperidone were also recorded individually under identical chromatographic conditions. The order of the elution was rabeprazole followed by domperidone at 5.45 and 11.07 min, respectively. The calibration curve plotted for

rabeprazole and domperidone were later used to determine concentrations of the drug in capsules.

Subjecting with pre-analyzed sample to the proposed HPLC method assessed the accuracy of HPLC method. All the solutions were prepared and analyzed in triplicate. There was a high recovery 100.2 of rabeprazole and 102 of domperidone (Table.1) indicating the proposed method is highly accurate. The HPLC method, developed in the present study is used for simultaneous quantification of rabeprazole and domperidone in capsule dosage forms. High percentage recoveries of rabeprazole ranging from 99.8 to 100.2 and 101.92 to 102 of domperidone (Table.1) were observed with the capsule dosage forms. No interfering peaks were found in the chromatogram indicating the excipients used in capsule formulations did not interfere with the estimation of drug by the proposed HPLC method.

The proposed method is simple, precise, accurate and rapid for the simultaneous quantification of rabeprazole and domperidone in capsule dosage forms. Hence, it can be easily and conveniently adopted for routine quality control analysis.

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TABLE-1
Results of Analysis of formulation and Recovery Studies

Drug	Amount mg/ tab		% Recovery*
	Labelled	Found *	
Rabeprazole	20.0	20.10	100.2
Domperidone	30.0	30.55	102.0

* Average of six determinations

Each tablet containing 20 mg of Rabeprazole and 30 mg of Domperidone

TABLE-2
System Suitability Studies

S. No.	Parameters	Rabeprazole	Domperidone
1	Linearity range	0.1-1.0 mg/mL	0.1-1.0 mg/ mL
2	Theoretical plate/meter	14769	22020
3	Capacity factor	4.44	10.03
4	Asymmetric factor	1.359	1.323
5	Efficiency	1477	2202
6	LOD (mg/mL)	0.010	0.014
7	LOQ (mg/mL)	0.24	0.030

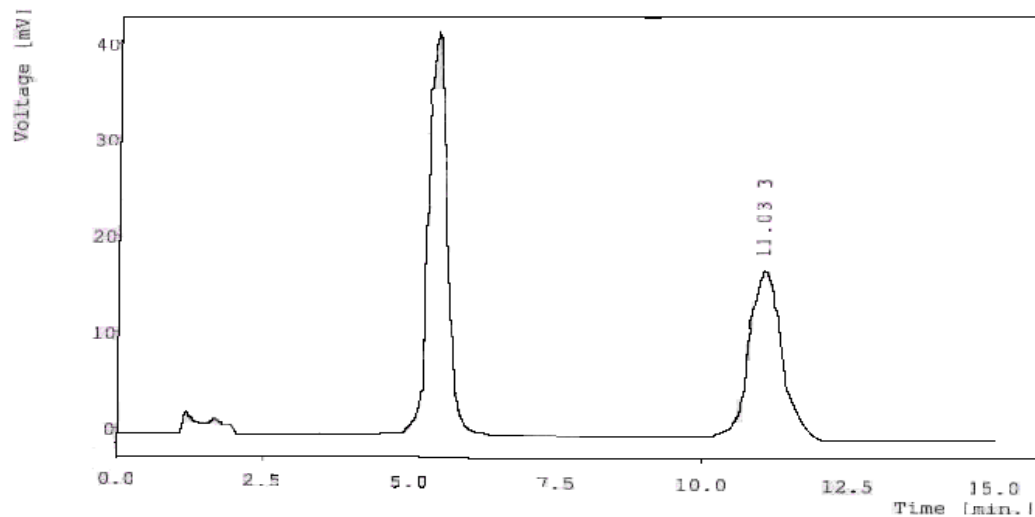


Fig. 1. Typical Chromatogram of Sample Solution

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