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RP-HPLC Method for Simultaneous Estimation of Domperidone in Combination with Rabeprazole Sodium in Solid Dosage Form

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The present work describes a reverse phase high performance liquid chromatographic method for simultaneous estimation of domperidone in combination with rabeprazole sodium in capsule formulation. Chromatography was performed on a Inertsil C_{18} (250 mm × 4.6 mm i.d.) column in isocratic mode with mobile phase containing 0.05 M potassium dihydrogen phosphate:acetonitrile:methanol in the ratio (40:30:30 % v/v/v) and pH of the final mobile phase was adjusted to 7.44 ± 0.03 with 5 M KOH. The flow rate was 1.0 mL/min and the eluent was monitored at 287 nm. The selected chromatographic conditions were found to effectively separate domperidone (run time 9.74 ± 0.33 min), rabeprazole sodium (run time 6.85 ± 0.46 min). Linearity for domperidone and rabeprazole sodium was found in the range of 3-300 and 2-200 µg/mL, respectively. The proposed method was found to be accurate, precise, reproducible and specific and can be used for simultaneous analysis of these drugs in capsule formulation.

Key Words: Domperidone, Rabeprazole sodium, RP-HPLC.

INTRODUCTION

Domperidone (DOM) is 5-chloro-1-[1-{3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl}-piperidin-4-yl]-1,3-dihydro-2*H*-benzimidazole-2-one and rabeprazole sodium (RAB) is 2-[{4-(3-methoxy propoxy)-3-methyl-2-pyridinyl)methyl}-sulfinyl]-1*H*-benzimidazole sodium salt[1].

Domperidone is an antiemetic drug usually given in combination with either rabeprazole or esomeprazole, respectively. The combination is useful in treatment of gastro esophageal reflux disease (GERD)[2]. The marketed capsule formulations contain domperidone and rabeprazole sodium in the ratio of 3:2 (Rablet D, domperidone 30 mg and rabeprazole sodium 20 mg, manufactured by Hetero labs Ltd.). Literature survey revealed spectrophotometric[3] and RP-HPLC[4-7] method for estimation of domperidone alone and in combination with other drugs in pharmaceutical preparations.

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Rabeprazole sodium alone and in combination with other drugs is reported to be estimated by RP-HPLC[8] methods. On the few analytical methods are reported for simultaneous determination of domperidone with rabeprazole sodium. The present work describes validated reverse phase HPLC method for simultaneous determination of these drugs in capsule formulation.

EXPERIMENTAL

An isocratic HPLC system (Jasco) consisting of Jasco PU 1580 intelligent HPLC pump, rheodyne injector (20 µL) loop, Jasco UV-1575 intelligent UV/Vis Detector, an Inertsil C_8 column (250 mm × 4.6 mm ID), 25 µL Hamilton injecting syringe and window based single channel Borwin software 1.21.60 used. Pure drug samples of domperidone and rabeprazole sodium were procured from Abbott pharma, Mumbai and Aurbindo pharma, Daman, respectively.

The capsule formulation Rablet D (manufactured by Hetero labs limited) with a labeled claim of 30 mg domperidone and 20 mg rabeprazole sodium, respectively, was obtained from local drug stores. The solvents acetonitrile, methanol and water used in the investigation were of HPLC grade (LOBA chemicals, Mumbai).

Chromatographic conditions: The column temperature was kept ambient temperature. The flow rate of mobile phase was maintained 1.0 mL/min. The detection was carried out at 287 nm. Injection volume was taken 20 µL and run time was kept 20 min.

Preparation of mobile phase: Potassium dihydrogen phosphate (0.05 M) was prepared by dissolving 6.8045 g in 1000 mL of HPLC grade water; 0.05 M KH_2PO_4 (400 mL), methanol (300 mL) and acetonitrile (300 mL) were mixed and pH of final mobile phase was adjusted to 7.44 ± 0.03 with 5 M KOH and filtered through 0.45 µm membrane filter and sonicated.

Preparation of stock solution of domperidone and rabeprazole sodium: Accurately weighed quantity of domperidone (30 mg) and rabeprazole sodium (20 mg) was weighed and transferred to standard 100 mL volumetric flasks separately, dissolved and diluted to the mark with methanol. The stock solutions were further diluted with mobile phase to get concentration range of 3-300 µg/mL of domperidone and 2-200 µg/mL of rabeprazole sodium. Plotting a graph of peak area *vs.* concentration allowed the checking of linearity of detector response.

Procedure for assay: Assay was performed on marketed formulations containing domperidone and rabeprazole sodium.

Marketed capsules (20), of rablet D (manufactured by Heterolabs limited) were taken and weighed properly. Average weight of capsule was calculated. The pellets from each capsule were crushed properly; a powder equivalent to 20 mg rabeprazole sodium [= 30 mg domperidone] was weighed out in 100 mL volumetric flask containing 40 mL methanol each and shaken properly. The content in volumetric flask was sonicated properly and volume was made up to mark with methanol and filtered with 0.45 µm membrane filter. Further dilutions were made with mobile phase to

get 20 µg/mL for rabeprazole sodium with 30 µg/mL of domperidone in each. 20 µL of sample preparation was injected into injector of liquid chromatographic system. Chromatogram was recorded, further calculations were carried out.

TABLE-1
RESULTS OF ANALYSIS OF CAPSULE FORMULATION

Capsule formulation	Label claim (mg/capsule)		Amount of drug estimated (mg)		% of label claim* ± SD	
	RAB	DOM	RAB	DOM	RAB	DOM
Rablet D	20	30	19.69	29.90	98.45±0.51	99.67±0.42

*Mean of six determinations.

Recovery studies: To study the accuracy, precision of proposed method recovery experiments were carried out. To an accurately weighed quantity of capsule powder, standard domperidone and rabeprazole sodium were added at three different levels (*ca*. 80, 100, 120 % of labeled claim).

TABLE-2
RESULTS OF RECOVERY STUDIES

Amount of drug added (mg)		Amount of drug recovered (mg)		% Recovery*	
RAB	DOM	RAB	DOM	RAB	DOM
16	24	16.29	23.92	101.83	99.66
20	30	20.06	29.74	100.33	99.14
24	36	24.40	35.36	101.66	98.22

*Mean of three determinations.

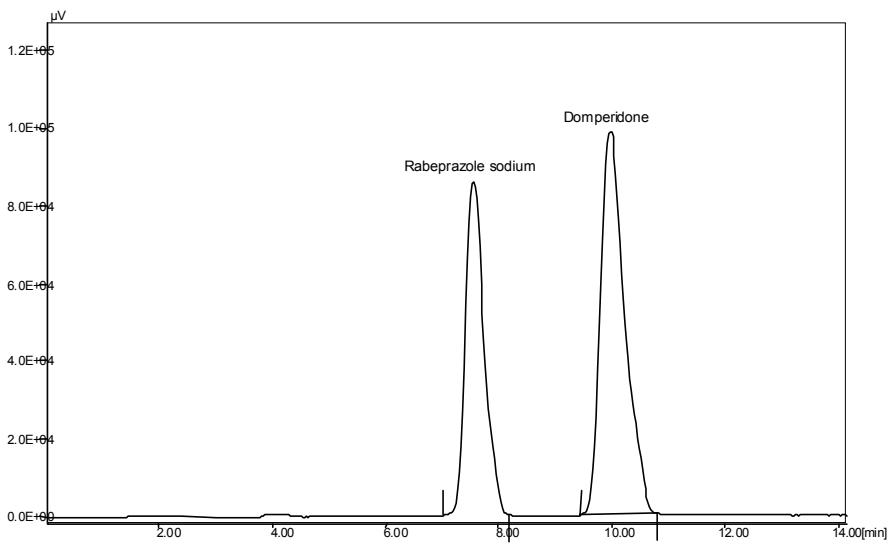

Fig. 1. Chromatogram of rabeprazole sodium [run time 7.42 min] and domperidone [run time 9.81 min]

RESULTS AND DISCUSSION

The values of per cent recovery and low values of standard deviation indicate the accuracy, precision and reproducibility of the proposed method. Ruggedness was carried out using different analysts, intraday and interday studies in which three samples were prepared and analyzed by three different analysts, on same day with 2 h interval and on three different days (Tables 3 and 4).

TABLE-3
SYSTEM SUITABILITY PARAMETERS

Parameter	Rabeprazole	Domperidone
Resolution	8.86	8.86
Capacity factor	3.07	4.33
No. of theoretical plates	17231	16696
Tailing factor	0.95	1.016

TABLE-4
VALIDATION PARAMETERS

Parameter	Rabeprazole	Domperidone
Accuracy: Recovery Studies	101.27 % ± 0.82	99.0 ± 0.73
Precision (RSD, n = 6)	0.0052	0.0042
Linearity and range (µg/mL)	2-200	3-300
Regression equation	Y= 38975x + 297739	Y=26366x + 277338
Slope (m)	38975	26366
Intercept (c)	297739	277338
Correlation coefficient (r^2)	0.9953	0.9942
Limit of detection (ng/mL)	20	30
Limit of Quantitation (ng/mL)	60	90
Intra-day Precision (RSD, n =3)	0.0030	0.0052
Inter-day Precision (RSD, n=3)	0.0031	0.0028
Different analysts (RSD, n=3)	0.0028	0.0020

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