International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.2, No.2, pp 1563-1568, April-June 2010

Simultaneous Spectrophotometric Estimation of Rabeprazole Sodium and Domperidone in combined dosage forms

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ABSTRACT: Rapid, precise, accurate and specific ratio spectra derivative spectrophotometry and a simple UV spectrophotometry using simultaneous equation method were developed for the simultaneous determination of rabeprazole sodium and domperidone in combined pharmaceutical dosage forms. For ratiospectra derivative spectrophotometry, the amplitudes were measured at 249 nm for rabeprazole sodium and at 271.5 nm for domperidone. In the simultaneous equation method, the signals were measured at 258 nm and 287 nm corresponding to the absorbance maxima of rabeprazole sodium and domperidone respectively in 0.05 M methanolic HCl. Concentration of each drug was obtained by using the absorptivity values calculated for both the drugs at two wavelengths, 258 and 287 nm. Commercial tablet formulations were successfully analyzed using the developed methods.
KEY WORDS: Rabeprazole; Domperidone; Spectrophotometry; Pharmaceutical formulations.

INTRODUCTION

Rabeprazole sodium[1] (RS), 2-[[[4-(-methoxypropoxy)-3-methyl-2-pyridinyl]methyl]sulfinyl]-IH benzimida zole sodium salt, is a class of antisecretary compounds that selectively inhibits gastric acid secretion by inhibiting the H^+, K^+ ATPase at secretary surface of the gastric parietal cell. Domperidone[2] (DMP), 5-chloro-l-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazole-l-yl) propyl]-4- piperidinyl]-1, 3-dihydro-2H-benzimidazol-2-one is a class of antiemetic compounds that stimulates gastric muscle contraction by antagonizing the inhibitory effects of dopamine on postsynaptic cholinergic neurons in the myenteric plexus. The combination therapy is used for the treatment of gastric acidosis and emesis. The literature reports many analytical methods like spectrophotometric[3], chromatographic[4-9], electro chemical[10] and fluorimetric[ll] for the determination of DMP alone or in combination with other drugs. Analytical methods like spectrophotometric[12], chromatographic[13-18] and electrochemical[19] have also been reported for determination of RS alone, in tablet formulation in human plasma. Few chromatographic[20, 21] methods have been reported till date for the simultaneous determination of these two drugs in their binary mixture but no spectroscopic method has been developed for the same. In the present investigation, ratio spectra derivative spectrophotometry and simultaneous equation methods were developed for the simultaneous determination of RS and DMP in their combined dosage form.

MATERIALS AND METHODS

Spectrophotometric analysis was carried out on a Shimadzu 1601 double beam spectrophotometer with a fixed slit width (2 nm). The system software of the instrument was used for obtaining the ratiospectra and tracing the 1st derivative of the ratio spectra. Pure drug sample of RS and DMP was kindly gifted by M/s Alembic Ltd., Vadodara. Methanol analytical reagent grade and Hcl analytical reagent grade was procured from Allied Chemical Corporation, Vadodara. Methanolic Hcl, 0.05 M, was prepared using I.P.[22] procedure. Commercial pharmaceutical preparations (Rabetic-DSR®, Wisdom Pharma, New Delhi and Rabekind ™ –DSR®, Mankind Pharrna, New Delhi) were procured from commercial source.

Preparation of standard stock solutions of RS and DMP

About 50 mg each of RS and DMP were accurately weighed and dissolved in 50 ml of methanol. Five millilitres of the above solution was separately diluted to 50 ml with methanol to produce 100µg/ml each of RS and DMP in methanol.

Ratiospectra derivative spectrophotometry

Suitable aliquots of the standard stock solutions were separately diluted with methanol to produce solutions of 10µg/ml of RS and 25µg/ml of DMP for obtaining divisor spectra. Different binary mixture solutions containing RS and DMP in 2: 3 ratio (very near to clinical dose ratio 20 mg: 30 mg of RS: DMP) were prepared by mixing different aliquots of the standard stock solutions of RS and DMP and diluting with methanol. The absorption spectra of 10µg/ml of RS and 25µg/ml of DMP were recorded in the range of 200 nm to 400 nm and stored in the memory of the instrument as divisor spectra. Also, the absorption spectra of the binary mixture solutions of RS and DMP were recorded in the range of 200 nm to 400 nm and were stored in the memory of the instrument. The stored absorption spectra of the binary mixture solutions were then divided by a previously stored divisor spectrum of 25µg/ml of DMP to get the ratiospectra of RS (Fig. 1). The first derivative of the ratio spectra (Fig. 2) were traced with $\Delta\lambda$=3 interval, multiplication factor =10 and the amplitudes at 249 nm were plotted against the respective concentrations of RS. Similarly, the stored absorption spectra of binary mixture solutions were divided by a previously stored divisor spectrum of 10µg/ml of RS to get the ratiospectra of DMP (Fig. 3). The first derivative of the ratio spectra (Fig. 4) were traced with $\Delta\lambda$=3 interval, multiplication factor =20 and the amplitudes at 271.5 nm were plotted against the respective concentrations of DMP.

Simultaneous Equation Method

Standard stock solutions of RS and DMP were separately diluted with 0.05 M methanolic Hcl to obtain series of' 5 to 30 µg/ml solutions of RS and DMP. From the overlain spectra two wavelengths, 258 and 287 nm, were selected for the formation of simultaneous equation. The absorptivity values, E (1 %, 1 cm), of both the drugs at both the wavelengths were determined. Five binary mixture solutions of RS and DMP were prepared in 2:3 ratio (very near to clinical dose ratio 20 mg: 30 mg of RS: DMP) and the dilution of 5:7.5 µg/ml was prepared. The quantitative estimation of the drugs were carried out by solving the simultaneous equations, $Cx=A_2ay_1 - A_1ay_2 / (ax_2\ ay_1 - ax_1\ ay_2)$...(1), $Cy= A_1ax_2 - A_2ax_1 / (ax_2\ ay_1 - ax_1\ ay_2)$…(2), where A_1 and A_2 are absorbance of the mixture at 258 and 287 nm respectively, ax_1 and ax_2 are absorptivities of x at 258 and 287 nm respectively, ay_1 and ay_2 are absorptivities of y at 258 and 287 nm respectively and Cx is the concentration of RS and Cy is the concentration of DMP.

Analysis of tablets:

A total of 20 tablets were accurately weighed, average weight determined and finely powdered. An amount equivalent to one tablet (20 mg of RS and 30 mg of DMP) was taken, dissolved in 20 ml of solvent (methanol for ratiospectra derivative spectrophotometric method and 0.05 M methanolic HCI for simultaneous equation method) and stirred for 5 min. The mixture was then centrifuged at 1000 rpm for 5 min. The supernatant was transferred to a 100 ml volumetric flask through a Whatman No. 40 filter paper. The residue was washed thrice with solvent and the combined filtrate and washings were made up to the mark with the solvent. The sample solution thus prepared was diluted with the solvent to get the solution containing 5µg/ml of RS and 7.5µg/ml of DMP. The above solution was analyzed for the content of RS and DMP using both the methods described above.

RESULTS AND DISCUSSION

Ratiospectra derivative spectrophotometric method and simultaneous equation method for simultaneous determination of RS and DMP in their binary mixture were successfully developed. In ratio spectra derivative spectrophotometry, the method showed good linearity for RS (Table 1) in the range of 2 to 10 µg/ml with co-relation co-efficient, 0.9999, slope, 0.1025 intercept, 0.0086 and 3 to 15 µg/ml for DMP (Table 1) with correlation coefficient, 0.9995, slope, 0.0611, and intercept, 0.0085. The instrumental parameters like divisor spectra, smoothing factor ($\Delta\lambda$) for tracing the 1st derivative of ratiospectra and multiplication factor were optimized for the reliable

determination of subject components. Some divisor concentrations were tested for selecting the standard solution as divisor at an appropriate concentration, and it was observed that the standard solution of 10µg/ml of RS was suitable for determination of DMP and 25µg/ml of DMP was suitable for determination of RS. The smoothing factor $\Delta\lambda$= 3 was found to be optimum for tracing the first derivatives of the ratio spectra as far as linearity and sensitivity is concerned. The experiment was repeated five times in a day for intraday and on five different days for interday precision. The method was found to be precise as % RSD for intraday and interday precision were 0.826, 1.182 for RS and 0.940, 1.088 for DMP respectively. The reproducibility of the method was determined by using methanol from three different manufacturers (Allied Chemical Corporation, Vadodara, S.D. fine Chemicals, Mumbai and Qualigens, Mumbai) for the preparation of standard stock solutions of drugs. The average value of % RSD, 0.722 for RS and 0.931 for DMP reveals the reproducibility of the method. The accuracy of the method was determined by performing recovery studies by standard addition method in which preanalyzed samples were taken and standard drug was added at five different levels. The % recovery ±SD lies in the range of 98.21± 845 to 100.58±1.102 for RS and 97.68±0.91 to 100.87±0.43 for DMP (Table 2). The analysis of commercially available tablet formulations revealed satisfactory results as evident from the results shown in Table 3.

For simultaneous equation method, the overlain spectra of both the drugs showed the λ_{max} at 258 nm for RS and 287 nm for DMP in 0.05 M methanolic HCI, hence these wavelengths were selected for estimation of RS and DMP. Absorbance was determined at these wavelengths and RS and DMP showed linearity in the concentration range of 5 to 30µg/ml and the correlation coefficient was less than one in both the case. The absorptivity was then calculated and along with absorbance, these values were submitted in the equations 1 and 2 to obtain concentration of drugs. The experiment was repeated five times in a day for intraday and on five different days for interday precision. The method was found to be precise as % RSD for intraday and interday precision were 0.58, 1.37 for RS and 1.823, 1.76 for DMP respectively. The reproducibility of the method was determined by using methanol from three different manufacturers for the preparation of standard stock solution of drugs. The average value of % RSD 0.623 for RS and 1.495 for DMP reveals the reproducibility of the method. The accuracy of the method was determined by performing recovery studies by standard addition method in which preanalyzed samples were taken and standard drug was added at five different levels. The % recovery±SD lies in the range of 98.33±0.823 to 101.05±1.042 for RS and 97.30±0.698 to 99.21±0.425 for DMP (Table 2). The analysis of commercially available tablet formulations revealed satisfactory results as evident from the results shown in Table 3.

By observing the validation parameters viz., accuracy, intraday and interday precision expressed as % RSD, reproducibility (% RSD), specificity, linearity and range, both the methods were found to be specific, accurate, precise and reproducible. Hence both the methods can be employed for simultaneous determination of RS and DMP in their combined tablet dosage forms.

Table 1: Calibration Curve Data for Ratiospectra Derivative Spectroscopy

Mixture	Concentration (µg/ml)		Average amplitude		%RSD	
	RS	DMP	RS*	DMP**	RS*	DMP**
a	2	3	0.215	0.185	2.30	2.61
b	4	6	0.416	0.379	0.72	2.11
c	6	9	0.622	0.557	1.10	1.02
d	8	12	0.829	0.749	0.48	0.66
e	10	15	1.035	0.918	0.68	0.76

* Amplitude at 249 run when 25 µg/ml of DMP was used as divisor.

** Amplitude at 271.5 nm when 10 µg/ml of RS was used as a divisor.

Table 2: Recovery Study Data

Level of Standard addition (%)	% Recovery ±SD***			
	Method 1*		Method 2**	
	RS	DMP	RS	DMP
80	98.90±0.912	98.51±0.58	99.00±0.48	99.21±0.43
90	98.21±0.845	98.77±0.82	99.45±0.63	97.30±0.70
100	100.58±1.102	100.87±0.43	99.52±0.56	98.48±0.27
110	98.31±1.13	97.68±0.91	101.05±1.04	97.42±0.73
120	98.66±0.745	99.31±0.73	98.33± 0.82	97.34±1.02

*Ratiospectra derivative spectroscopy
** Simultaneous equation method
***Mean for three determinations

Table 3: Analysis of Commercial Tablet Formulations

Tablet	Label claim (mg)		Method 1*				Method 2**			
			Conc. Found (mg)		% Recovery***		Conc. found (mg)		% Recovery***	
	RS	DMP	RS	DMP	RS	DMP	RS	DMP	RS	DMP
A	20	30	19.64	29.69	98.20	98.93	20.44	29.32	102.4	97.75
B	20	30	19.84	30.12	99.20	100.4	20.36	30.48	101.8	102.1

* Ratiospectra derivative spectroscopy
** Simultaneous equation method
*** Mean for three determinations.
A=Rabetic-DSR® B=Rabekind ™–DSR®

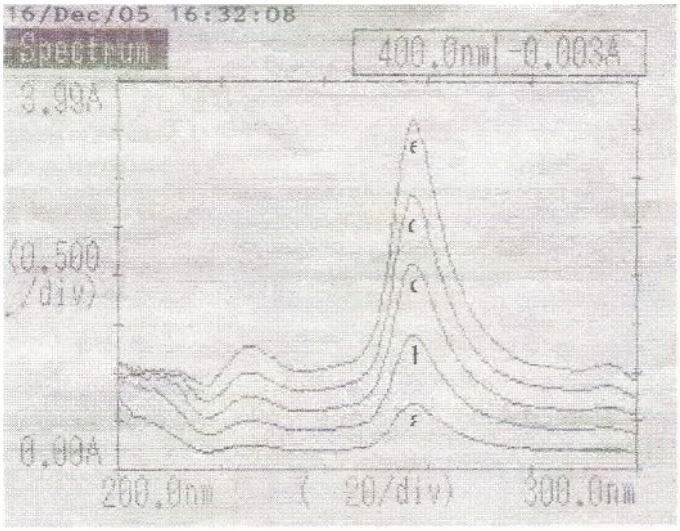

Fig 1: Ratiospectra of RS when 25 µg/ml of DMP was used as divisor
RS:DMP = (a) 2:3 (b) 4:6 (c) 6:9 (d) 8:12 (e) 10:15

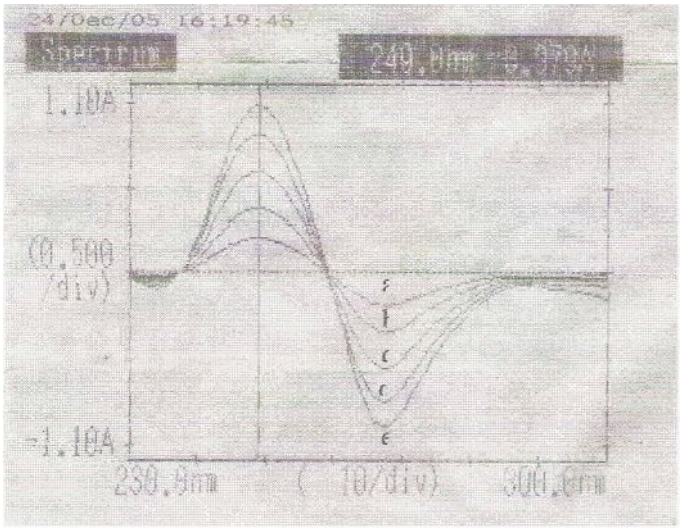

Fig 2: First derivative of the ratiospectra of RS when 25 µg/ml of DMP was used as divisor.
RS:DMP = (a) 2:3 (b) 4:6 (c) 6:9 (d) 8:12 (e) 10:15

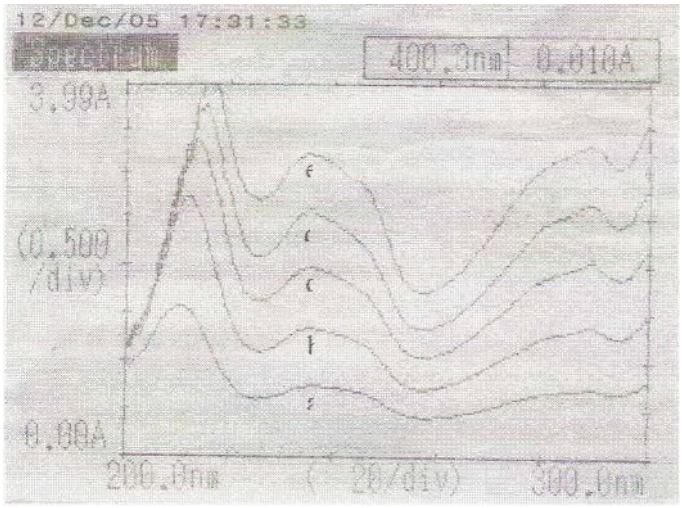

Fig 3: Ratiospectra of DMP when 10 µg/ml of RS was used as divisor.
RS:DMP = (a) 2:3 (b) 4:6 (c) 6:9 (d) 8:12 (e) 10:15

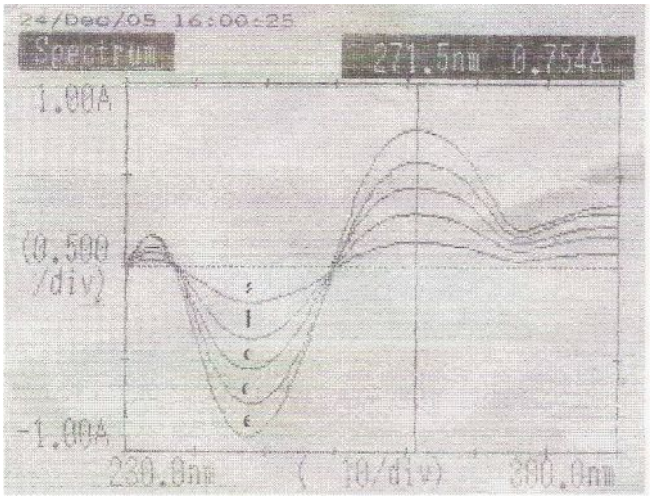

Fig 4: First derivative of the ratiospectra of DMP when 10 µg/ml of RS was used as divisor.
RS:DMP = (a) 2:3 (b) 4:6 (c) 6:9 (d) 8:12 (e) 10:15

ACKNOWLEDGEMENTS

The authors are grateful to M/s. Alembic Ltd. for providing rabeprazole sodium and domperidone pure drug as gift sample. One of the authors, R Baldha, is grateful to University Grant Commission (UGC) for providing financial support in the form of junior research fellowship (JRF) during the work. The authors owe a great debt of gratitude to Prof A.N. Mishra, Head, Pharmacy Department, The Maharaja Sayajirao University of Baroda for providing the necessary facilities.

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