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Spectrophotometric Simultaneous Determination of Rabeprazole Sodium and Domperidone in Combined Tablet Dosage Form

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Abstract

A simple, economical, precise and accurate method for simultaneous determination of Rabeprazole Sodium (RAB) and Domperidone (DOM) in combined tablet dosage form has been developed. The method is based on Ratio Spectra Derivative Spectrophotometry. The amplitudes in the first derivative of the corresponding ratio spectra at 230 nm and 250 nm were selected to determine Rabeprazole Sodium and Domperidone respectively. Beer's law is obeyed in the concentration range of 10-30 µg mL^{-1} for RAB and 5-15 µg mL^{-1} for DOM. The % assay for commercial formulation was found to be 99.82 $\pm$ 0.552 for RAB and 99.63 $\pm$ 0.791 for DOM. The method was validated with respect to linearity, precision and accuracy.

Key words: Rabeprazole Sodium, Domperidone, Ratio Spectra Derivative Spectrophotometry.

1. Introduction

Rabeprazole sodium (RAB), 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl] sulfinyl] 1H-benzimidazole, is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the gastric H+ K+ ATPase enzyme system at the secretory surface of the gastric parietal cell [1]. Domperidone (DOM) chemically is 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)propyl]-piperidin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one. It is a unique gastro kinetic and antiemetic drug and is official in *British Pharmacopeia* [2]. It increases the duration of antral and duodenal contractions thus stimulating gastric emptying both in animals and in man and is also effective in relief of symptoms of reflux oesophagitis [3].

Literature survey reveals chromatographic methods for determination of RAB in tablet dosage form [4,5] as well as spectrophotometric method for RAB determination in combination with other drug [6]. Stability indicating [7] and bioanalytical chromatographic methods [8-11] for

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quantification of RAB are also reported. *British Pharmacopeia* describes HPLC method for determination of Domperidone [2]. HPLC [12 -14], Spectrophotometric [15-17] and HPTLC [17,18] methods have also been developed for the determination of DOM either in single or in combination with other drugs. Spectrophotometric methods have been reported for determination of Rabeprazole sodium and Domperidone maleate in combined tablet dosage form [19]. Extensive literature survey revealed that no method is available for simultaneous determination of Rabeprazole Sodium and Domperidone in combined dosage form by ratio spectra derivative spectrophotometry. Aim of the present work was to develop simple, economical, precise and accurate method for simultaneous determination of binary drug formulation. The proposed method is optimized and validated as per the International Conference on Harmonization (ICH) guidelines [20].

2. Materials and Methods

2.1. Instrumentation

The instrument used in the present study was JASCO double beam UV/Visible spectrophotometer (Model UV-530) with fixed slit width of 2 nm. All weighing were done on electronic balance (Model Shimadzu AY -120).

2.2. Reagents and chemicals

Analytically pure samples of RAB (Purity 99.74 % w/w) and DOM (Purity 100.18 % w/w) were kindly supplied by Burgeon Pharmaceuticals Pvt. Ltd. (Pondicherry, India) and used as such without further purification. The pharmaceutical dosage form used in this study was Rioz-DMP tablets (Aeon Therapeutics Pvt. Ltd, Chennai, India) labeled to contain 20 mg of Rabeprazole sodium and 10 mg of Domperidone/tablet.)

2.3. Theory

The method involves dividing the spectrum of mixture by the standardized spectra of each of the analyte and deriving the ratio to obtain spectrum that is independent of concentration of analyte used as a divisor [21].

Using appropriate dilutions of standard stock solution, the two solutions were scanned separately. The ratio spectra of different RAB standards at increasing concentrations (Scaling factor 10) were obtained by dividing each with the stored spectrum of the standard solution of DOM (10 µg mL^{-1}) with the aid of Spectra Manager (Version 1.53.01) software as shown in Fig 1(A) and the first derivative of these spectra traced with the interval of $\Delta\lambda$ = 4 nm (the influence of $\Delta\lambda$ on the first derivative of the ratio spectra was tested to obtain the optimum wavelength

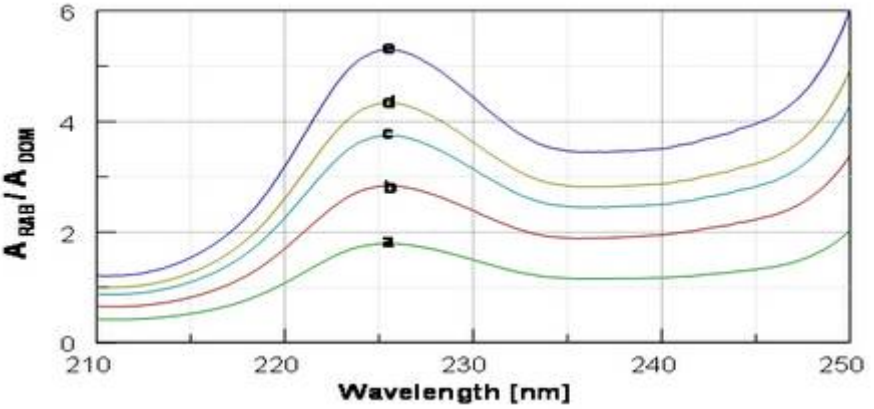
interval, Δλ = 4 nm was considered to be suitable) are illustrated in Fig 1(B). Wavelength 230 nm was selected for the quantification of RAB in RAB + DOM mixture. The ratio and ratio derivative spectra of the solutions of DOM at different concentrations (Scaling factor 10) were obtained by dividing each with the stored standard spectrum of the RAB (20 µg mL^{-1}) with the interval of $\Delta\lambda$ = 4 nm (Fig. 2(A) and 2(B) respectively). Wavelength 250 nm was selected for the quantification of DOM in RAB + DOM mixture. Measured analytical signals at these wavelengths are proportional to the concentrations of the drugs. The amount of RAB and DOM in tablets was calculated by using following equations-

At 230 nm: $C_{RAB} = d/d\lambda [A_{RAB} / A_{DOM}]$ – Intercept (C) / Slope (m) …… (1)

At 250 nm: $C_{DOM} = d/d\lambda [A_{DOM} / A_{RAB}]$ – Intercept (C) / Slope (m) …… (2)

The coincident first derivative ratio spectra of pure and sample solution for determination of RAB and DOM are shown in the Fig 3(A) and 3(B).

(A)



(B)

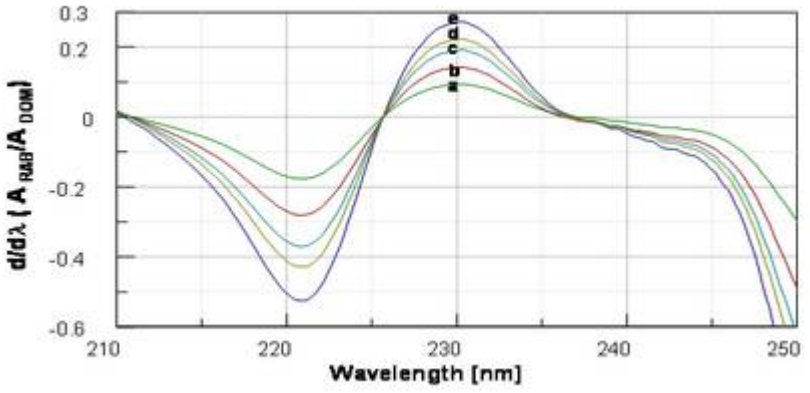
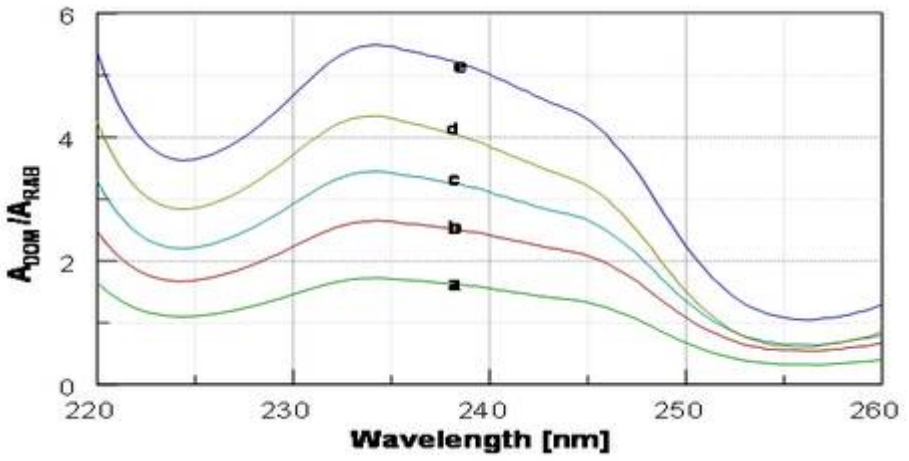


Fig 1. Ratio spectra (A) and first derivative of the ratio spectra (B) ($\Delta\lambda$ = 4 nm) of (a) 10, (b) 15, (c) 20 , (d) 25 and (e) 30 µg mL^{-1} solution of RAB when 10 µg mL^{-1} solution of DOM is used as divisor. (A)



(B)

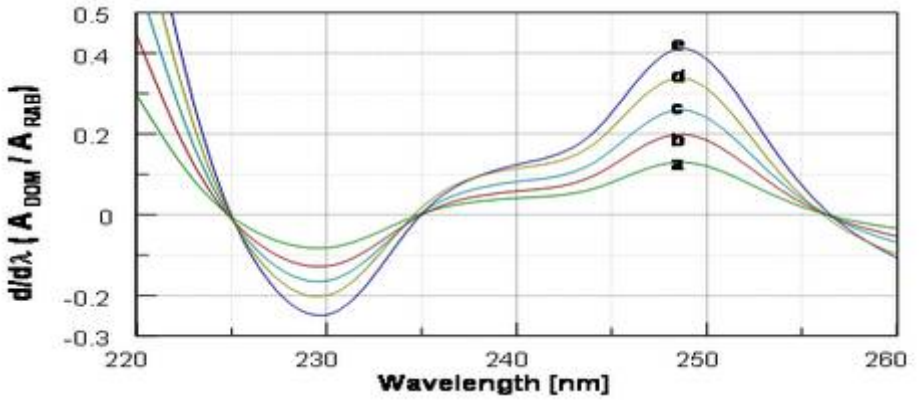


Fig 2. Ratio spectra (A) and first derivative of the ratio spectra (B) ($\Delta\lambda$ = 4 nm) of (a) 5, (b) 7.5, (c) 10 , (d) 12.5 and (e) 15 µg mL^{-1} solution of DOM when 20 µg mL^{-1} solution of RAB is used as divisor.

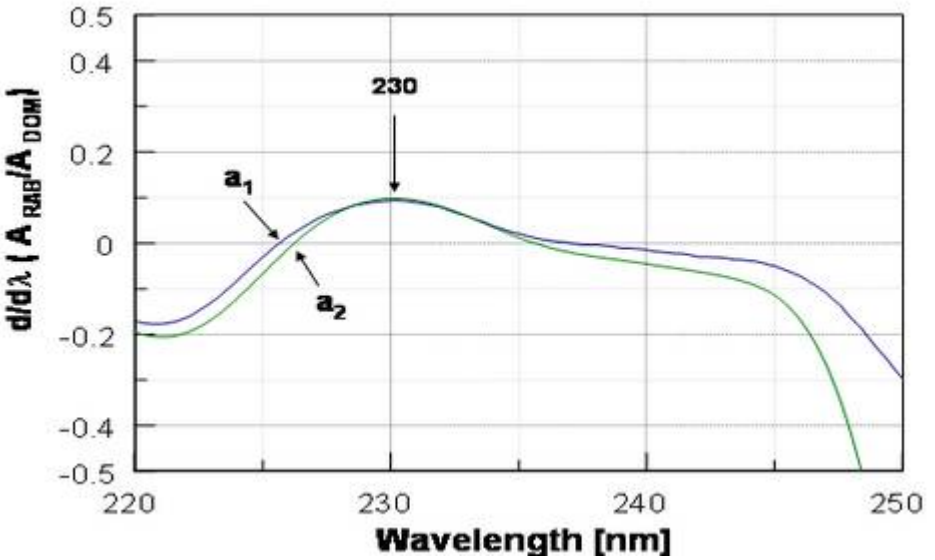


Fig 3. (A) Coincident first derivative ratio spectra of (a_1) 10 µg mL^{-1} of pure RAB and (a_2) sample solution (5 µg mL^{-1} of DOM and 10 µg mL^{-1} of RAB); 10 µg mL^{-1} DOM as a divisor

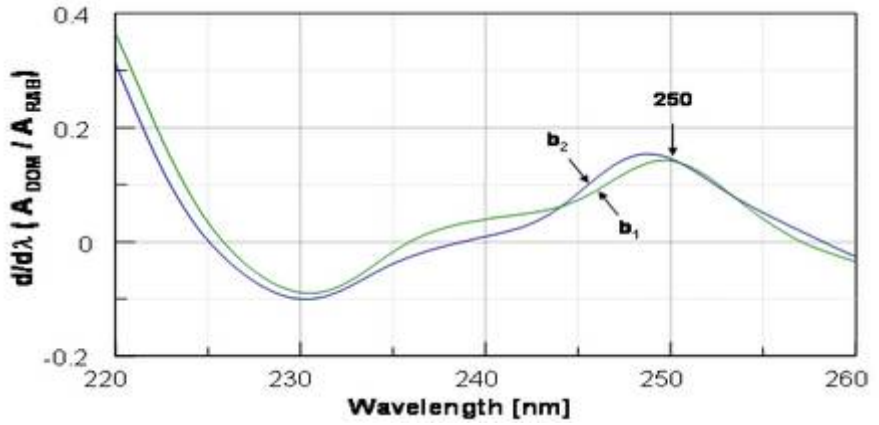


Fig 3. (B) Coincident first derivative ratio spectra of (b_1) 5 µg mL^{-1} pure DOM and (b_2) sample solution (5 µg $mL^{-1}$of DOM and 10 µg mL^{-1} of RAB); 20 µg mL^{-1} RAB as a divisor.

2.4. Preparation of Standard Stock Solutions

Standard stock solutions of pure drug containing 200 µg mL^{-1} of RAB, 100 µg mL^{-1} of DOM were prepared by dissolving 20 mg of pure RAB and 10 mg of pure DOM in 50 mL of methanol in a 100 mL volumetric flask and volume was made up to the mark with methanol separately. The working standard solutions of these drugs were obtained by dilution of the respective stock solution with methanol. Beer's law obeyed in the concentration range of 10-30 µg mL^{-1} for RAB and 5-15 µg mL^{-1} for DOM.

2.5. Preparation of Sample Stock Solution

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 20 mg of RAB (10 mg of DOM) was weighed and dissolved in the 50 mL of methanol with the aid of ultrasonication for 5 min and volume was filtered through Whatman paper No. 41 to a 100 mL volumetric flask. Filter paper was washed with methanol, adding washings to the volumetric flask and volume was made up to the mark with methanol**.** 0.5 ml of this solution was further diluted to 10 ml with methanol to get required final concentration of RAB (10 µg mL^{-1}) and DOM (5 µg mL^{-1}).

2.6. Recovery studies

The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (80 %, 100 % and 120 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 10 µg mL^{-1} of RAB and 5 µg mL^{-1} of DOM.

3. Results and Discussion

Under experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient is shown in Table 1. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy and precision. Beer's law obeyed in the concentration range 10-30 µg mL^{-1} and 5-15 µg mL^{-1} with correlation coefficient of 0.997 and 0.999 for RAB and DOM, respectively. The proposed method was also evaluated by the assay of commercially available tablets containing RAB and DOM (n = 6). The % assay was found to be 99.82 % for RAB and 99.63 % for DOM as presented in Table 2. Results of recovery studies are shown in Table 3. For RAB, the recovery study results ranged from 99.32 % to 100.59 % with % RSD values ranging from 0.228 % to 0.612 %. For DOM, the recovery results ranged from 99.87 % to 101.23 %, with % RSD values ranging from 0.216 % to 0.560 %. The accuracy and reproducibility is evident from the data as results are close to 100 % and standard deviation is low.

Table 1. Optical characteristics of the proposed method

Parameter	**RAB**	**DOM**
λ (nm)	230	250
Beer's law limit (µg mL^{-1})	10-30	5-15
Molar absorptivity*	3.343 x 10^{3}	1.172 x 10^{3}
Regression Equation (y = mx + c)		
Slope (m)	0.0087	0.0015
Intercept (c)	0.0094	0.006
Correlation coefficient	0.997	0.999

*obtained from the first derivative ratio spectra

Table 2. Results of commercial formulation analysis

Drug	Label Claim (mg/tablet)	% of Label Claim Estimated*	Standard Deviation (±)	Standard Error	% R.S.D.
RAB	20	99.82	0.552	0.225	0.553
DOM	10	99.63	0.791	0.323	0.794

*average of six determinations

Table 3. Recovery studies of RAB and DOM

Level of % Recovery	Sample (μg mL^{-1})		Standard Drug Spiked (μg mL^{-1})		% Mean Recovery*		Standard Deviation		% R.S.D.	
	RAB	DOM	RAB	DOM	RAB	DOM	RAB	DOM	RAB	DOM
80	10	5	8	4	99.32	100.74	0.226	0.564	0.228	0.560
100	10	5	10	5	100.59	101.23	0.616	0.289	0.612	0.286
120	10	5	12	6	99.49	99.87	0.349	0.215	0.351	0.216

* average of three determinations
R.S.D. is relative standard deviation

4. Conclusion

The validated spectrophotometric method employed here proved to be simple, economical, precise and accurate. Thus it can be used for routine simultaneous determination of RAB and DOM in tablet dosage form.

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