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Spectrophotometric simultaneous determination of Rabeprazole Sodium and Itopride Hydrochloride in capsule dosage form

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Abstract

A new simple, economical, rapid, precise and accurate method for simultaneous determination of rabeprazole sodium and itopride hydrochloride in capsule 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 231 nm (minima) and 260 nm were selected to determine rabeprazole sodium and itopride hydrochloride, respectively. The method was validated with respect to linearity, precision and accuracy.

Keywords: Rabeprazole sodium; Itopride hydrochloride; 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]. Itopride hydrochloride (ITO) is *N*-[4-[2-(dimethylamino)ethoxy]-benzyl]-3,4-dimethoxybenzamide hydrochloride. It is a gastrokinetic agent. It increases the release of acetylcholine (Ach) through dopamine D2 receptor antagonistic action and inhibits decomposition of Ach through its acetylcholinesterase inhibitory action, resulting in enhancement of gastrointestinal motility [2].

Literature survey reveals chromatographic methods for determination of RAB in tablet dosage forms [3,4] as well as spectrophotometric methods for RAB determination in combination with other drugs [5,6]. Stability indicating [7] and bioanalytical chromatographic methods [8–11] for quantification of RAB are also reported. Two HPLC methods for detection of ITO in blood serum using fluorescence detector have been reported [12,13]. Also analytical HPLC method for determination of ITO in tablet dosage form and bulk drug has been reported [14]. Extensive literature survey revealed that no method is available for simultaneous determination of rabeprazole sodium and itopride hydrochloride in capsule dosage form by ratio spectra derivative spectrophotometry. Aim of present work was to develop simple, economical, rapid, precise and accurate method for simultaneous determination of binary drug formulation.

2. Experimental

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. Weighing was done on electronic balance (Model Shimadzu AY-120).

2.2. Reagents and chemicals

Analytically pure samples of RAB and ITO 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 a Rabium Plus capsules labeled to contain 20 mg of rabeprazole sodium as enteric coated tablet and 150 mg of itopride hydrochloride as two sustained release film coated tablets/capsule.

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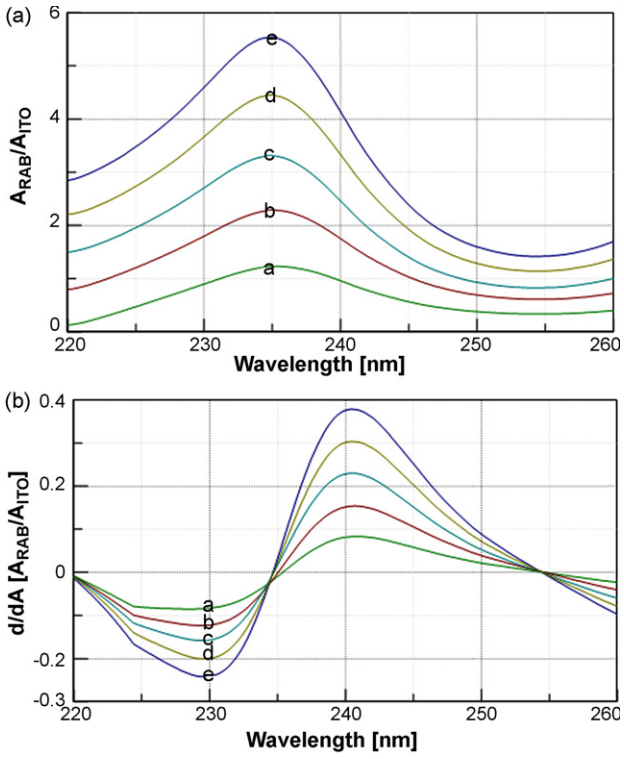

Fig. 1. (a) Ratio spectra of solutions of RAB when 5 μg/ml solution of ITO is used as divisor (Δλ = 21 nm) a–e (4–20 μg/ml). (b) First derivative of the ratio spectra of solutions of RAB when 5 μg/ml solution of ITO is used as divisor (Δλ = 21 nm) a–e (4–20 μg/ml).

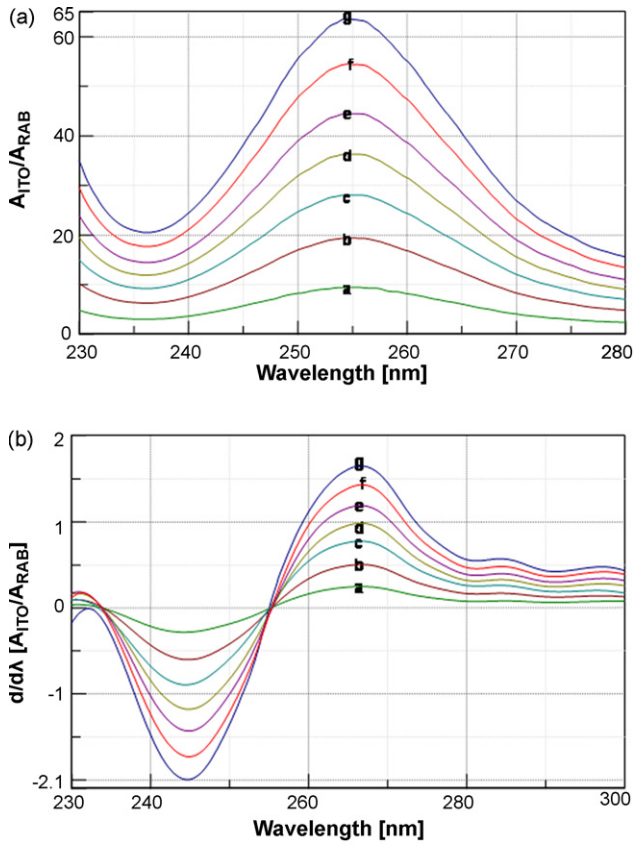

Fig. 2. (a) Ratio spectra of solutions of ITO when 2 μg/ml solution of RAB is used as divisor (Δλ = 21 nm) a–g (10–70 μg/ml). (b) First derivative of the ratio spectra of solutions of ITO when 2 μg/ml solution of RAB is used as divisor (Δλ = 21 nm) a–g (10–70 μg/ml).

2.3. Theory

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

Using appropriate dilutions of standard stock solution, the two solutions were scanned separately. The ratio spectra of different RAB standards at increasing concentrations were obtained by dividing each with the stored spectrum of the standard solution of ITO (5 μg/ml, scaling factor 1) with the aid of computer (Fig. 1a) and the first derivative of these spectra traced with the interval of Δλ = 21 nm (the influence of Δλ for the first derivative of the ratio spectra was tested to obtain the optimum wavelength interval, Δλ = 21 nm was considered to be suitable) are illustrated in Fig. 1b. Wavelength 231 nm (minima) was selected for the quantification of RAB in RAB + ITO mixture. The ratio and ratio derivative spectra of the solutions of ITO at different concentrations were obtained by dividing each with the stored standard spectrum of the RAB (2 μg/ml, scaling factor 1) as divisor with the interval of Δλ = 21 nm (Fig. 2a and b, respectively). Wavelength 260 nm was selected for the quantification of ITO in RAB + ITO mixture. Measured analytical signals at these wavelengths are proportional to the concentrations of the drugs. The amount of RAB and ITO in capsules was calculated by using following equations

$$\text{At } 231\text{ nm}: \quad C_{RAB} = \frac{d}{d\lambda}\left[\frac{A_{RAB}}{A_{ITO}}\right] - \frac{\text{Intercept}(C)}{\text{Slope}(m)} \qquad (1)$$

Table 1
Optical characteristics of the proposed method

Parameter	RAB	ITO
λ_{max} (nm)	231 (minima)	260
Beer's law limit (μg/ml)	4–20	10–70
Molar absorptivity[a]	-1.78×10^4	0.195×10^3
Regression equation ($y = mx + c$)		
Slope (m)	−0.0473	−0.0094
Intercept (c)	−0.0463	−0.0414
Correlation coefficient	0.9997	0.9996

[a] Obtained from the first derivative ratio spectra.

$$\text{At } 260\text{ nm}: \quad C_{ITO} = \frac{d}{d\lambda}\left[\frac{A_{ITO}}{A_{RAB}}\right] - \frac{\text{Intercept}(C)}{\text{Slope}(m)} \qquad (2)$$

The coincident first derivative ratio spectra of pure and sample solution for determination of RAB and ITO are shown in the Fig. 3.

2.4. Preparation of standard stock solutions

Standard stock solutions were prepared by dissolving separately 10 mg of each drug in 100 ml of 0.1N NaOH to get concentration of 0.1 mg/ml. Beer's law is obeyed in the concentration range of 4–20 μg/ml for RAB and 10–70 μg/ml for ITO.

Table 2
Results of commercial formulation analysis

Drug	Label claim (mg/capsule)	% of label claim estimated[a]	Standard deviation	Standard error	% R.S.D.
RAB	20	99.67	0.568	0.232	0.569
ITO	150	99.36	0.752	0.307	0.757

[a] Average of six determinations.

Table 3
Recovery studies of RAB and ITO

Level of % recovery	% mean recovery[a]		Standard deviation		% R.S.D.	
	RAB	ITO	RAB	ITO	RAB	ITO
80	99.19	99.94	0.606	0.420	0.611	0.420
100	99.38	100.48	0.269	0.344	0.271	0.342
120	99.48	99.73	0.386	0.511	0.388	0.512

[a] Average of three determinations, R.S.D. is relative standard deviation.

2.5. Preparation of sample stock solution

Contents of 20 capsules were weighed accurately and powdered. Powder equivalent to 20 mg of RAB and 150 mg of ITO was weighed and dissolved in 50 ml of 0.1N NaOH with the aid of ultrasonication for 5 min. The solution was filtered through Whatman filter paper no. 41 to a 100 ml volumetric flask. Filter paper was washed with 0.1N NaOH, adding washings to the volumetric flask and volume was made up to the mark with 0.1N NaOH to get sample stock solution which was further diluted with 0.1N NaOH to get required concentration in the linearity range.

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 within the range of linearity for both the drugs.

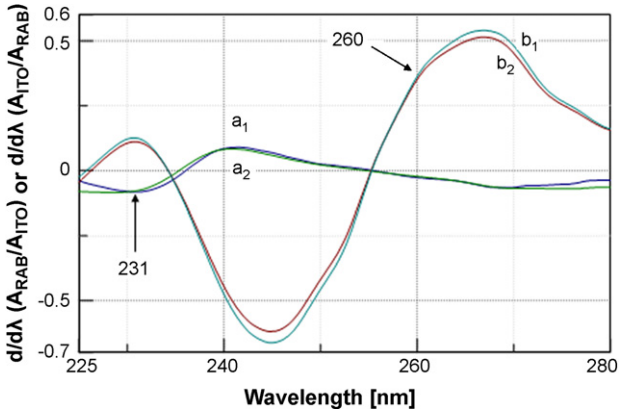

Fig. 3. Coincident first derivative ratio spectra of (a_1) sample solution (30 μg/ml of ITO and 4 μg/ml of RAB) and (a_2) 4 μg/ml of pure RAB; 5 μg/ml ITO as a divisor and (b_1) sample solution (30 μg/ml of ITO and 4 μg/ml of RAB) and (b_2) 30 μg/ml of pure ITO; 2 μg/ml of RAB as a divisor.

3. Results and discussion

Under experimental conditions described, calibration curve, assay of capsules and recovery studies were performed. A critical evaluation of proposed method was performed by statistical analysis of data where slopes, intercepts, correlation coefficients are shown in Table 1. The proposed method was also evaluated by the assay ($n = 6$) of commercially available capsules containing RAB and ITO. The % assay was found to be 99.67% for RAB and 99.36% for ITO is presented in Table 2. Results of recovery studies are shown in Table 3. For RAB, the recovery study results ranged from 99.19% to 99.48% with % RSD values ranging from 0.271% to 0.611%. For ITO, the recovery results ranged from 99.73% to 100.48%, with % RSD values ranging from 0.342% to 0.512%. The accuracy and reproducibility is evident from the data as results are close to 100% and low standard deviation. The proposed method is simple, economical, rapid, precise and accurate. Hence it can be used for routine analysis of RAB and ITO in capsule formulation.

4. Conclusion

The validated spectrophotometric method employed here proved to be simple, economical, rapid, precise and accurate. Thus it can be used for routine simultaneous determination of RAB and ITO in capsule dosage form instead of processing and analyzing each drug separately.

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