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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF ITOPRIDE AND RABEPRAZOLE IN COMBINED DOSAGE FORM

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ABSTRACT

Two simple, rapid and accurate methods have been developed for the estimation of itopride and rabeprazole in the mixture. Itopride has absorbance maxima at 257.5 nm and rabeprazole has absorbance maxima at 292 nm in 0.01N NaOH. The linearity range was observed in 5-25µg/mL for itopride and rabeprazole. First method is based on simultaneous equation and second method is based on Q absorbance ratio. Absorbances at isoabsorbtive point 271.9 nm and at λ_{max} of rabeprazole were measured for Q absorbance ratio method. These methods were validated statistically. The recovery study confirmed the accuracy of proposed methods.

Key words: Itopride, Rabeprazole, UV-Spectrophotometer, Simultaneous estimation.

INTRODUCTION

Itopride[1], N - [(4 - (2 dimethylaminomethoxy) phenyl]methyl] - 3, 4 - dimethoxybenzamide is an inhibitor of D_2 receptor at parasympathetic nerve ends and thereby increases the release of acetylcholine and decreases the metabolism of acetylcholine by inhibiting enzyme acetylcholinesterase by maintaining higher ACh levels. Itopride increases the esophageal sphincter pressure, which accelerates gastric emptying and improves the gastro-duodenal coordination. Because of its dopamine D_2 receptor antagonistic action, it also exerts antiemetic action.

Rabeprazole[2-5], 2-[(4-(3-methoxy propoxy)3-methyl-2-pyridinyl]methyl sulfinyl]-1H benzimidazole is a proton pump inhibitor that suppresses gastric acid secretion by the specific inhibition of the H^+/K^+ ATPase system. No method is reported for simultaneous

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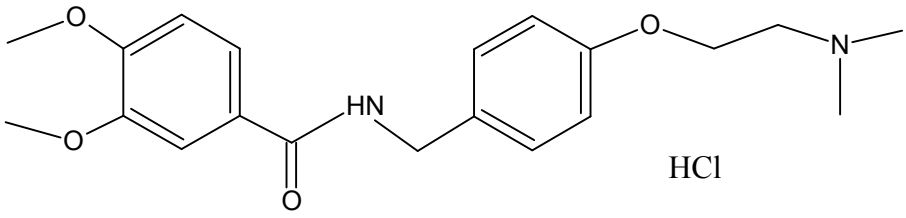
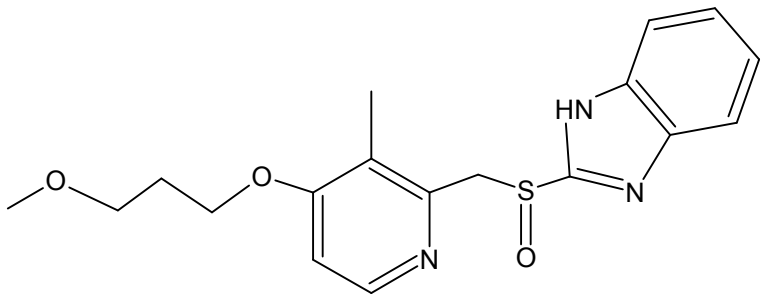
estimation of these drugs in combination by spectrophotometry and hence, the present work was undertaken.



Itopride



Rabeprazole

EXPERIMENTAL

In this study, two simple, rapid, accurate and economical methods have been developed for simultaneous estimation of itopride and rabeprazole in combination. Itopride (100 mg) and rabeprazole (100 mg) were accurately weighed and dissolved in 0.01N NaOH to give stock solution having concentration of 1000 µg/mL. From the stock solution working standard solution with 10 µg/mL concentration were prepared by appropriate dilution. Working standard solutions were scanned in the entire UV range to determine the λ_{max} using 0.01N NaOH as blank. The λ_{max} of the itopride and rabeprazole was found to be 257.5 and 292 nm, respectively. Five standard dilutions of each drug were prepared having concentrations of 5, 10, 15, 20 and 25 µg/mL for itopride and rabeprazole separately from the working standard. The absorbances of these standards were measured at 257.5 nm and 292 nm and the calibration curves were plotted at these wavelengths. The absorptivity coefficients of two drugs were determined. The overlain spectra of itopride and rabeprazole are represented in Fig.1.

Simultaneous equation method[6]

The absorbance and absorptivity values at particular wavelength were substituted in following equation to obtain concentration-

$$\text{(i) } C_x = A^2 a_x^1 - A^1 a^2_y / a_x^2 .a_y^1 - a_x^1 a_y^2.$$

$$\text{(ii) } C_Y = a_x^2 A^1 - a_x^1 A^2 / a_x^2 .a_y^1 - a_x^1 a_y^2.$$

Where $A^{1,} A^2$ are absorbance of the mixture, a_x^1, a^2_x are absorptivities of x, a_y^1, ay^2 denote the absorptivities of y at 257.5 nm and 292 nm, respectively; Where C_x is the concentration of itopride and C_y is the concentration of rabeprazole. Thus, concentration of C_x and C_y can be obtained as-

$$C_x = A^2 111.3 - A^1 383.3/-105683.17.$$

$$C_Y = A^1 130.8 - A^2 313.8/-105683.17.$$

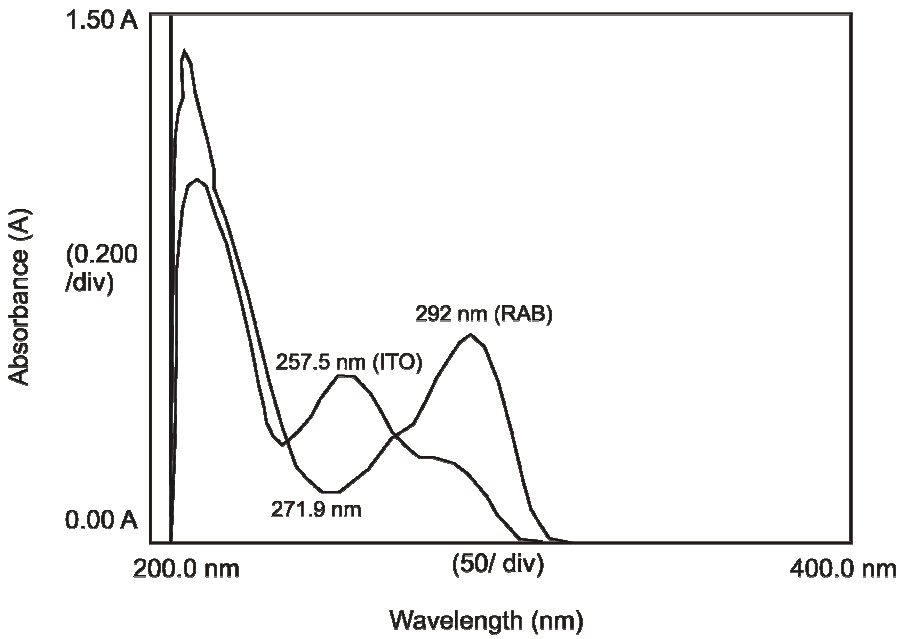


Fig. 1: Overlain spectra of itopride and rabeprazole

Q Absorbance ratio method[7]

Absorbance ratio method uses ratio of absorbances at two selected wavelengths; one at isoabsorptive point and other being at the λ_{max} of one of the components. From the

overlain spectra of two drugs, it was evident that itopride and rabeprazole have isoabsorptive point at 271.9 nm and λ_{max} of rabeprazole is at 292 nm. Three standard solutions of each drug having concentration 10 µg/mL each were prepared separately in 0.01N NaOH and absorbances at 271.9 nm (isoabsorptive point) and 292 nm (λ_{max} of rabeprazole) were measured and absorptivity coefficients were calculated.

Concentration of two drugs in the mixture can be calculated using equation-

$$C_1 = \frac{Q_M - Q_Y}{Q_M - Q_Y} \times \frac{A_1}{aI_1}$$

$$C_R = \frac{Q_M - Q_X}{Q_Y - Q_X} \times \frac{A_2}{aR_1}$$

Where the A_1 and A_2 are the absorbances of the mixture at 271.9 nm and 292 nm; aI_1 and aR_1 are absorptivities of itopride and rabeprazole, respectively at 271.9 nm; aI_2 and aR_2 are absorptivities of itopride and rabeprazole, respectively at 292 nm and $Q_M = A_2/A_1$, $Q_Y = aR_2/ aR_1$ and $Q_X = aI_2/ aI_1$.

Table 1. Analysis of tablet formulation

Method	Formulation	Label claim (mg/tab)		Amount found (mg/tab)		% of label claim	
		ITO	RAB	ITO	RAB	ITO	RAB
I	Tab I	150	20	150.07	19.10	100.04	95.50
	Tab II	150	20	147.85	19.92	98.56	99.6
II	Tab I	150	20	149.89	19.08	99.92	95.40
	Tab II	150	20	143.31	19.92	95.54	99.60

ITO: Itopride; RAB: Rabeprazole; Tab I: Rabiros IT ; Tab II: Itorab

A mixture of the combination of both the drugs was prepared containing 25 mg itopride and 10 mg rabeprazole. Above mixture was taken in the 100 mL volumetric flask containing 0.1 N NaOH. The flask was subjected to sonication so as to dissolve the mixture and volume was made up by 0.1 N NaOH (Stock solution). From the stock solution, 1 mL of sample was taken in 10 mL volumetric flask and the volume was made up by 0.1 N NaOH. The absorbances at selected wavelengths were recorded. The

concentrations of itopride and rabeprazole were worked out utilizing the equations developed. The diluted solutions were also used for the recovery studies.

Assay of marketed formulation

Twenty tablets were accurately weighed. An accurately weighed quantity of powder equivalent to 25 mg itopride and 3.3 mg rabeprazole was taken into 100 mL volumetric flask. In order to minimize the dose difference, appropriate quantity of rabeprazole was added to the mixture so as to make the amount 10 mg. 0.1 N NaOH was added to the flask and flask was subjected to sonication. Volume was made up with 0.1 N NaOH (Stock solution). From this stock solution, 1 mL of sample was withdrawn and taken into 10 mL volumetric flask. Volume was adjusted to 100 mL with 0.1 N NaOH and absorbance was measured at 257.5 nm, 292 nm and 271.9 nm (isoabsorptive point). The diluted solutions were also used for the recovery studies.

RESULTS AND DISCUSSION

The validation parameters were studied at all the three wavelengths for both the methods. Accuracy was determined by calculating the recovery and the mean was determined (Table 2). By observing the validation parameters, both the methods were found to be specific, accurate and precise. Hence, both the methods can be employed for routine analysis of these two drugs in combinations.

Table 2. Recovery study data

Method	Conc. of drug in tablet (μg/mL)		Conc. added to the tablets sample (μg/mL)		Amount recovered		% Recovery	
	ITO	RAB	ITO	RAB	ITO	RAB	ITO	RAB
I	5	2	20	8	19.67	8.21	98.35	102.62
	20	8	5	2	4.94	2.10	98.80	105.00
II	5	2	20	8	19.72	8.14	98.90	101.75
	20	8	5	2	4.97	2.08	99.40	104.00

ITO: Itopride RAB: Rabeprazole

Table 3. Statistical evaluation

Method	Formulation	Standard deviation		Coefficient of variation		Standard error	
		ITO	**RAB**	**ITO**	**RAB**	**ITO**	**RAB**
I	Tab I	0.4528	0.9743	0.4498	1.033	0.2025	0.9743
	Tab II	0.5448	0.9956	0.5553	0.9969	0.2436	0.4452
II	Tab I	1.3765	0.5311	1.3752	0.5575	0.6156	0.5311
	Tab II	0.4379	0.1926	0.4623	0.1929	0.1694	0.0861

(i) The results are mean of five readings (n = 5)

(ii) Tab I: Rabiros IT Tab II: Itorab

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