DEVELOPMENT OF NEW VALIDATED SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF RABEPRAZOLE SODIUM AND DOMPERIDONE MALEATE IN BULK AND CAPSULE DOSAGE FORM

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ABSTRACT

A method for the simultaneous determination of rabeprazole sodium and domperidone maleate in bulk and capsule dosage form was developed. The method employs formation and solving of simultaneous equations using 259.4 and 284.4 nm as two analytical wavelengths. The absorbance maxima of rabeprazole sodium and domperidone maleate were found to be 259.4 nm and 284.4 nm respectively in 0.1N H_2SO_4. The linearity range lies between 4-40 µg/ml for rabeprazole sodium and 5-35 µg/ml for domperidone maleate at their respective wavelength. Both the drugs obey Beer's law. The molar absorptivity and sandell's sensitivity were found to be 8.87×10^3 and 0.0431 respectively for Rabeprazole sodium and for Domperidone maleate 9.99×10^3 and 0.0427 respectively. The recovery studies confirmed the accuracy of the developed method.

INTRODUCTION

Rabeprazole sodium, 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]methyl] sulfinyl]-1*H*–benzimidazole sodium salt[1], is a proton-pump inhibitors that suppress gastric acid secretion by specific inhibition of the gastric H^+, K^+-ATPase enzyme system at the secretory surface of the gastric parietal cell. The drug is not yet official in any of the pharmacopoeia. A survey of literature reveals that only HPLC[2-5] (in plasma) methods have been reported for the estimation of Rabeprazole sodium. Domperidone maleate is official in British Pharmacopoeia (BP). The method of analysis given in B.P is non-aqueous titration. Methods such as Spectrophotometric and HPLC[6-12] have been reported in the literature.

Even though various methods were reported in the literature for estimation of rabeprazole sodium and domperidone maleate individually or in combination with other drugs no method has been reported for simultaneous estimation of these two drugs using simultaneous equations in bulk drug and capsule dosage form. The present study was aimed at simultaneous estimation of rabeprazole sodium and domperidone maleate by simultaneous equation method. This method was validated according to the ICH guidelines[13].

MATERIAL AND METHODS
Instrument
Shimadzu UV-1800; UV spectrophotometer with Spectral bandwidth of 1.8 nm, wavelength accuracy of 2 nm and Matched quartz cells of 10 mm optical path length.

Drug Sample
Rabeprazole sodium and Domperidone maleate were obtained as gift sample from Torrent Pharmaceutical Pvt. Ltd., Ahmedabad (Gujarat). The tablets were procured from the market.

Chemicals and Reagents
Methanol G.R grade was procured from Loba Chem. Ltd., Mumbai. Double distilled water was used for making 0.1N H_2SO_4

Procedure
Rabeprazole sodium (10 mg) and domperidone maleate (10 mg) separately were dissolved in methanol (50 ml) and volume made up to 100ml with methanol to get a stock solution of 100 g/ml. From these stock solutions, working standard solutions were prepared. These were scanned in the entire UV range to determine ë max. The ë max of rabeprazole sodium and domperidone maleate were found to be 259.4 nm and 284.4 nm respectively. The overlain spectra of both the drugs are shown in Figure 1.
The regression analysis of the calibration curves suggests the level of precision of the method and the optical characteristics such as Beer's law limits, detection limit, molar absorptivities and Sandell's sensitivities as presented in Table 1

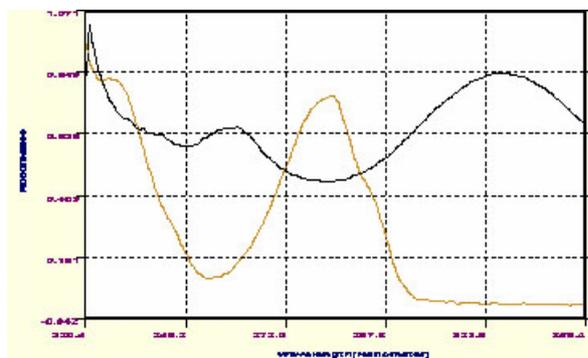***Correspondence :** convener_pharmacy@seedlingacademy.com

Fig. 1: Overlain spectra of rabeprazole sodium and domperidone maleate in 0.1N H$_2$SO$_4$

Table 1. Optical and regression characteristics of rabeprazole sodium and domperidone maleate

Parameters	Rabeprazole sodium		Domperidone maleate	
	259.4 nm	284.4 nm	284.4 nm	259.4 nm
Beers's law limit (μg/ml)	4-40	4-40	5-35	5-35
Molar absorptivity (l mole^{-1} cm^{-1})	8.87 x 10^3	6.88 x 10^3	9.99 x 10^3	2.0 x 10^3
Sandell's sensitivity (mg/cm^2/0.001abs.unit)	0.0431	0.056	0.0427	0.211
Regression equation (y= a + bc) Slope (b) Intercept (a)	0.025 - 0.0049	0.0156 + 0.0304	0.0256 - 0.0274	0.0042 +0.0077
Correlation coefficient	0.9992	0.9987	0.9994	0.995

Preparation of API

The API mixture and synthetic mixture of rabeprazole sodium and domperidone maleate were prepared in ratio of 2:3. For API mixture, accurately weighed 10 mg of rabeprazole sodium and 15 mg of domperidone maleate were transferred to a 100 ml volumetric flask, dissolved and diluted upto the mark with methanol. The API mixture was based upon the dosage strength of combination, which is available in the market.

Preparation of calibration curve

Standard solutions of rabeprazole sodium (0.4, 0.8, 1.2, 1.6, 2, 2.4, 2.8, 3.2, 3.6, and 4.0 ml) and standard solutions of domperidone maleate (0.5, 1, 1.5, 2, 2.5, 3.0, and 3.5) were transferred to a series of 10 ml volumetric flasks. The volumes in each were adjusted with 0.1N H$_2$SO$_4$. The absorbances of the solutions were measured at 259.4 nm and 284.4 nm against 0.1N H$_2$SO$_4$ as blank.

Estimation of rabeprazole sodium and domperidone maleate in API mixture

The API mixtures solution were transferred and diluted to mark with 0.1N H$_2$SO$_4$. The absorbances of these mixtures were measured at 259.4 nm and 284.4 nm. Amounts of rabeprazole sodium and domperidone maleate were determined by solving the simultaneous equations. Two simultaneous equations were formed using absorptivity coefficient values.

$$A_1 = 23.323 \ C_1 + 4.458 \ C_2 \quad\text{——— (1)}$$

$$A_2 = 18.127 \ C_1 + 24.220 \ C_2 \quad\text{——— (2)}$$

Where C$_1$ and C$_2$ are concentrations of rabeprazole sodium and domperidone maleate respectively, in gm/liter in the sample solution. A$_1$ and A$_2$ are the absorbances of the mixture at 259.4 nm and 284.4 nm respectively.

Recovery Studies and Method Validation

To study the validation parameters; accuracy, reproducibility, reliability, interference and recovery experiments were carried out according to ICH Q2A Guidelines by standard addition. The recovery of added standard (80%, 100%, and 120%) was found at four same concentration levels for each drug. From the total amount of drug found, the percentage recovery was calculated.

Estimation of drugs from dosage forms

Twenty tablets (of same respective batch number) of two pharmaceutical companies were accurately weighed and powdered. A quantity of powder equivalent to 10 mg of rabeprazole sodium or 15 mg of domperidone maleate were transferred to 100 ml volumetric flask, dissolved in 50 ml of methanol and volume made up to mark with methanol. The solution was sonicated for 10 minutes and filtered through Whatman filter paper No. 40. One ml of filtrate were transferred to a series of 10 ml volumetric flasks and diluted up to mark with 0.1N H$_2$SO$_4$. The absorbance of the solutions were measured at 259.4 nm and 284.4 nm using 0.1N H$_2$SO$_4$ as blank. The results are shown in Table 2.

Table 2. Content of marketed capsule dosage form

Brand	Drug	Label claim (mg/cap)	Amount Found (mg/cap)	% Recovery[*]	S.D	% C.V.
A	RAB	20.00	19.09	95.49	0.266	1.59
	DOM	30.00	30.00	100	30.00	1.39
B	RAB	20.00	19.25	96.29	0.162	0.84
	DOM	30.00	29.88	99.62	0.405	1.37

[*]Average ± standard deviation of three determinations

RESULT AND DISCUSSION

The molar absorptivity and Sandell's sensitivity values show the sensitivity of rabeprazole sodium and domperidone maleate at respective wavelengths, while precision is confirmed by % RSD. The reproducibility, repeatability and accuracy of these methods were found to be good, as evident from low standard deviation.
Thus, the proposed method for simultaneous estimation of rabeprazole sodium and domperidone maleate in bulk and capsule dosage form was found to be simple, accurate, sensitive and economical. Therefore, the method can be useful in routine quality control analysis.

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