Development and Validation of Derivative Spectrophotometric Method for Simultaneous Estimation of Domperidone and Rabeprazole Sodium in Bulk and Dosage Forms

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ABSTRACT

The use of first order derivative spectroscophotometry allowed simultaneous determination of domperidone and rabeprazole sodium, in fixed dose combination products. The absorbance values at 253.2 nm and 266.4 nm of first derivative spectrum was used for the estimation of domperidone and rabeprazole sodium, respectively without mutual interference. This method obeyed beer's law in the concentration range of 9-45 µg/ml and 6-30 µg/ml for both domperidone and rabeprazole sodium, respectively. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method.

Keywords: Domperidone, Rabeprazole Sodium, Sodium hydroxide solution, Ultra-violet spectrophotometry, Derivative spectrophotometry.

1. INTRODUCTION:

Domperidone (DOM) is peripheral dopamine antagonist. It is official in British Pharmacopoeia and European Pharmacopoeia [1,2]. Chemically it is 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl]-piperidin-4-yl]-1,3-dihydro-2*H* benzimidazol-2-one[3]. Literature described HPLC method[4], HPTLC method[5], and LC-MS method[6], extractive spectroscopic method[7] for its determination in plasma, serum and pharmaceutical preparations when present with other drugs. Rabeprazole sodium (RAB) is proton pump inhibitor and is not official in any of the Pharmacopoeias and is chemically 2-({[4-(-3-mehotxypropoxy)-3-methyl-2- pyridyl] methyl} sulfinyl)-1H-benzimidazole sodium. HPLC[8], Capillary electrophoresis[9], and LC-MS method[10] have been reported for the estimation of RAB in plasma, and in pharmaceutical preparations. HPLC[11] and dual wavelength Spectrophotometric method[12] were reported for the simultaneous estimation of DOM and RAB in combined dosage forms[13]. The present paper describes a simple, rapid, accurate and responsible method for the simultaneous estimation of DOM and RAB in bulk and dosage forms by first order derivative spectrophotometric method.

2. MATERIALS AND METHODS

Both DOM and RAB were gift sample from Astron Pharmaceuticals. Sodium hydroxide AR Grade was procured from Rankem Chemicals.

2.1 Instrumentation:

Derivative spectrophotometric method has been developed for the simultaneous determination of domperidone (DOM) and rabeprazole sodium (RAB) by using zero crossing first derivative methodology. The derivative UV spectra of standard and test solutions were recorded in 1 cm quartz cells using a Shimadzu UV/Vis-1700 double beam UV/Vis spectrophotometer (Japan) with a fixed slit width of 2 nm. The zero order and first derivative absorption spectra were recorded over the wavelength range 200-400 nm against the solvent blank. Shimadzu Libror AGE 220 balance was used for weighing the samples.Class'A' volumetric glassware were used.

2.2 Development of the method:

The standard stock solutions of 1.5 mg/ml of domperidone and 1.0 mg/ml of rabeprazole sodium in methanol were prepared. Further dilutions were made in 0.1N NaOH to obtain concentrations ranging from 9-45 µg/ml for

DOM and 6-30 µg/ml for RAB.The absorbance of resulting solutions was measured at 266.4 and 253.2 nm for DOM and RAB and the calibration curves were plotted at these wavelengths. The overlain zero order spectra DOM and RAB (fig. 1) showed that the absorption maxima of DOM and RAB lie in close proximity and at absorption maxima of one, another exhibits substantial absorbance. This clearly indicates the existence of spectral interference in estimation of DOM and RAB. To overcome this, spectra of these two drugs were derivatised to first order between 200-400 nm with Δλ= 2 nm.The overlain first derivative spectra of DOM and RAB (fig. 2) reveal that RAB concentration is proportional to the first derivative signals at 266.4 nm (zero-crossing point for DOM) and DOM can be estimated at 253.2 nm (zero-crossing point for RAB).

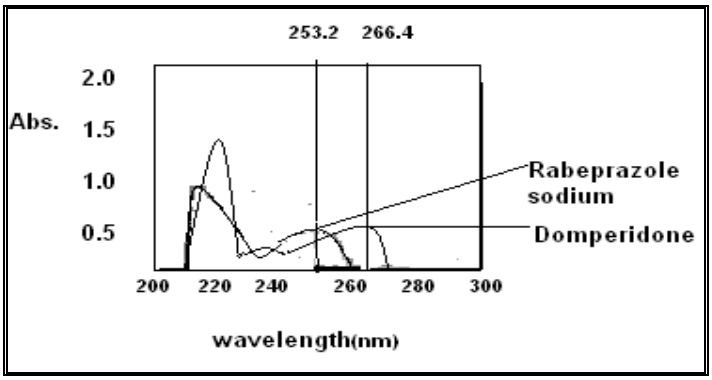
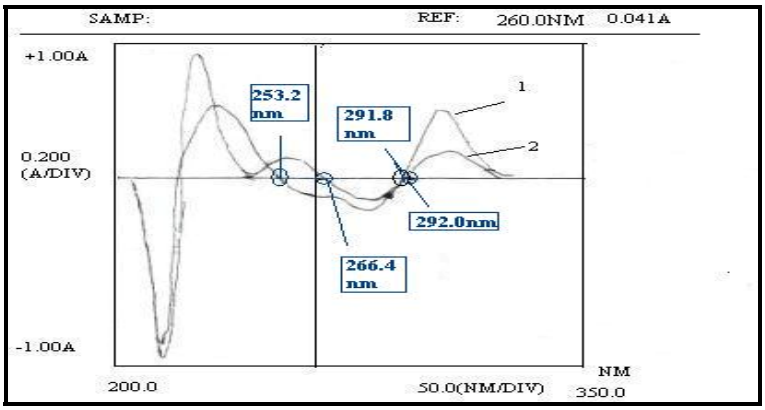


Fig. 1: Overlain zero order spectra of DOM and RAB. The spectra of the DOM and RAB were taken for their 9 µg/ml and 6 µg/ml solution.



Peak 1: Rabeprazole sodium, Zero crossing pt: 253.2 & 292.0 nm
Peak 2: Domperidone, Zero crossing pt: 266.4 & 291.8 nm

Fig.2 first order derivative spectra for each Domperidone and Rabeprazole sodium

2.3 Linearity:

Standard stock solutions were prepared by dissolving 37.5 mg domperidone and 25 mg of rabeprazole sodium in 25 ml volumetric flask and the volume was made up with methanol to get a concentration of 1.5 mg/ml and 1.0 mg/ml.From this, suitable dilutions were made in 0.1N NaOH to get the working standard solutions of 9-45 µg/ml for DOM and 6-30 µg/ml for RAB. The absorbances of the derivatised spectra were measured at 253.2 nm and 266.4 nm for DOM and RAB, respectively. Six replicate analysis were carried out. Absorbance Vs concentration were plotted to obtain the calibration graph. Both drugs obey the Beer's law with the above concentration range with R^2 value of 0.9993 and 09995 for DOM and RAB, respectively.

2.4 Limit of detection and limit of quantitation:

LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determinations, y intercept was calculated and the standard deviation of the y intercept was computed. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation LOD and (LOQ) were determined on the basis of response and slope of the regression equation.

2.5 Analysis of synthetic mixture of DOM and RAB

Solution in0.1N NaOH containing various proportions of DOM and RAB were prepared and their first derivative spectra were recorded. From the derivative spectra, the absorbance at 253.2 nm and 266.4 nm were noted for the estimation of DOM and RAB, respectively. From these absorbance values, the concentrations of DOM and RAB were determined using calibration graph (Table 1).

Table: 1.Analysis of Synthetic Mixtures of Domperidone and Rabeprazole sodium

Sample No.	Concentration of DOM (µg/ml)		% Recovery	Concentration of RAB (µg/ml)		% Recovery
	Theoretical	Experimental		Theoretical	Experimental	
1	9	8.72	96.8	6	5.9	100.7
2	18	17.88	99.3	12	12.15	101.6
3	27	26.70	99.7	18	17.92	98.1
4	36	36.22	100.8	24	23.69	100.3
5	45	44.06	97.9	30	30.1	98.8

2.6 Recovery studies (accuracy):

It is defined as the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. It is measure of exactness of analytical method. Accuracy should be expressed as % recovery by the assay of known added amount of analyte in the sample or as the difference between the mean and the accepted true value together with the confidence intervals. Accuracy should be established across the specified range of the analytical procedure. It was determined by calculating the recovery of domperidone and rabeprazole sodium by standard addition method. To the fixed amount of solution (18 µg/ml of domperidone and 18 µg/ml of rabeprazole sodium) an increasing aliquots from working standard solution of domperidone and rabeprazole sodium were added. The solutions were measured at 253.2 nm for domperidone and 266.4 nm for rabeprazole sodium and % recovery of the sample were calculated (Table 2 and 3).

Table: 2.Accuracy Data of Determination of Rabeprazole sodium in the Presence of Domperidone (18µg/ml) Using First Derivative Spectroscopy

Amount of Domperidone (µg/ml)	Amount of added Rabeprazole sodium (µg/ml)	Total amount found Mean ± S.D.	Accuracy (%)
18	6	5.9±0.14	100.7
18	12	12.15±0.38	101.6
18	18	17.92±.25	98.1
18	24	23.69±0.25	100.3
18	30	30.1±0.39	98.8

Table: 3. Accuracy Data of Determination of Domperidone in the Presence of Rabeprazole sodium (12µg/ml) Using First Derivative Spectroscopy

Amount of Rabeprazole sodium (µg/ml)	Amount of added Domperidone (µg/ml)	Total amount found Mean ± S.D.	Accuracy (%)
12	9	8.72±0.23	96.8
12	18	17.88±0.30	99.3
12	27	26.7±0.51	99.7
12	36	36.22±0.42	100.8
12	45	44.06±0.55	97.9

3. RESULT AND DISCUSSION:

Zero-order absorption spectra of domperidone and rabeprazole sodium showed overlapping peaks that interfere with the simultaneous determination of this formulation (Fig. 1). Derivative spectroscopy, based on a mathematical transformation of the spectra zero-order curve into the derivative spectra, allows a fast, sensitive and precise resolution of a multicomponent mixture and overcomes the problem of overlapping of a multi-component system. Derivative spectroscopy on the basis of zero-crossing measurements involves measurement of the absolute value of the total derivative spectrum at an abscissa value corresponding to the zero-crossing wavelength of the derivative spectra of individual components, which should be only a function of the concentration of other component. The spectroscopic parameters including derivative order, wavelength and $\Delta\lambda$ values should be optimized to obtain maximum resolution, sensitivity and reproducibility. In this study first-derivative technique (D_1) traced with $\Delta\lambda$= 2 nm was used to resolve the spectral overlapping. Zero-crossing points of 200-300 nm is presented in fig. 2. The optimums D1values without interference for domperidone and rabeprazole sodium were 253.2 and 266.4 nm, respectively (Fig. 3).

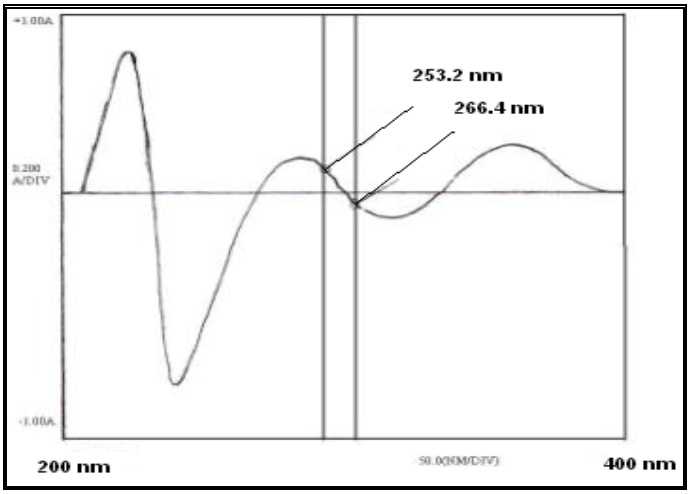


Fig. 3: Overlain first derivative spectra of DOM and RAB.

The DOM and RAB were estimated at the marked wavelengths 253.2nm and 266.4 nm respectively

The linearity of the method was established form first-derivative spectra by measurement of the absorbance of standard solutions containing varying concentrations of each compound in the presence of constant concentration of the other one. The calibration curves were constructed by plotting the D_1value against domperidone and rabeprazole sodium concentration at the zero-crossing wavelength of rabeprazole sodium (253.2 nm) or domperidone (266.4 nm), respectively. The analytical results of synthetic mixtures obtained are summarized in Table 1. The linearity of the calibration curves and the adherence of the method to Beer's law are validated by the high value of the correlation coefficient and the value of intercept on ordinate which is close to zero.

The limit of detection that was found to be 0.68 µg/ml and 0.45 µg/ml for domperidone and rabeprazole sodium. The accuracy and precision were determined by using synthetic mixture of domperidone and rabeprazole sodium in the laboratory. The mean recoveries and SD are illustrated in Tables 2 and 3. Data of these tables showed a good accuracy and precision over the entire concentration range .The data indicate that the proposed derivative spectroscopic method is highly precise during one analysis and between different runs.

The percentage of recovery in each case was calculated. The results obtained from the recoveries of both drugs (Tables 2 and 3) showed excellent accuracy. The influence of excipients was studied by mixing two formulations containing 9 µg/ml of domperidone and 6µg/ml of rabeprazole sodium. No interference was observed from the presence of excipient in the amounts, which are commonly present in tablet dosage forms. Study of stability of domperidone and rabeprazole sodium in the solutions during analysis showed that analytes were stable at least for 72 h in solutions. The validation of results is summarized in Table 4.The proposed method was successfully applied to analyze preparation containing domperidone and rabeprazole sodium.

Table: 4.Validation of The Proposed Method

Sample No.	Parameters	Experimental Values	
		DOM	RAB
1	Precision (%C.V.) 1. Repeatability 2. Intraday precision 3. Interday precision	 0.54 % 1.27-2.47% 1.90-3.25%	 1.01 % 1.44-2.41% 2.23-3.46 %
2	Linearity Range	9-45 µg /ml	6-30µg/ml
3	Accuracy(%Recovery)	96.8-100.8%	98.1-101.6%
4	Limit of Detection(µg/ml)	0.68µg/ml	0.45µg/ml
5	Limit of Quantification(µg/ml)	2.00µg/ml	1.36 µg/ml
6	Correlation coefficient	0.9993	0.9995

4. ACKNOWLEDGEMENTS:

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