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Simultaneous Spectrophotometric Estimation of Rabeprazole Sodium and Domperidone Maleate in their Combined Pharmaceutical Dosage Form

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ABSTRACT: Two simple, rapid, economical, specific, precise and accurate spectrophotometric methods have been developed for simultaneous estimation of rabeprazole sodium and domperidone maleate in their combined pharmaceutical dosage forms. Rabeprazole sodium and domperidone shows absorption maxima at 285 nm and 287 nm respectively. The first method is based on the simultaneous equations. In the simultaneous equations, the signals were measured at 285 nm and 287 nm and concentration of each drug was obtained by using the molar absorptivity values calculated for both the drugs at 285 nm and 287 nm. Second method involves analysis of drug by multicmponent mode of the instrument. Both the drugs obeyed beer's law in the concentration ranges of 2 – 30 µg/ml employed for these methods. The results of analysis were validated statistically and by recovery studies. Both of these developed methods were found to be simple, precise and accurate and can be utilize as a quality control tool for the simultaneous estimation of both drugs from their combined marketed formulation.
KEY WORDS: Rabeprazole Sodium and Domperidone Maleate, Simultaneous equation, Multicomponent mode, Pharmaceutical formulation.

1. INTRODUCTION

Chemically Rabeprazole sodium is 2 - [[[4 – (3 – methoxy – propoxy) – 3 – methyl 2 – pyridinyl] methyl] sulfinyl] – 1H – benzimidazole sodium salt. Rabeprazole sodium (RA)[1-3] is a new proton pump inhibitor belongs to a class of antisecretory compounds that do not exhibit anticholinergic or histamine H_2 receptor agonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+/K^+ ATPase at the secretory surface of the gastric parietal cell. Chemically Domperidone maleate is 5 – chloro – 1 - [1 - [3 - (2, 3 – dihydro – 2 – oxo - 1H – benzimidazole – 1 – yl) propyl] piperidin – 4 – yl] –2, 3 – dihydro - 1H – benzimidazol –2 - one, maleate. Domperidone maleate (DMP)[1-5] is an antiemetic drug and is official in BP. The official method was based on the non aqueous titrimetry.

The combination of RA and DMP is widely used for the management of healing of erosive or ulcerative gastro esophageal reflux disease, duodenal disease with nausea and vomiting. Few spectrophotometric, HPLC, HPTLC and Voltametric methods have been reported for the individual estimation of RA and DMP [6-13], but not a single method is available for the simultaneous estimation of rabeprazole sodium and domperidone maleate in their combined pharmaceutical dosage forms. This paper illustrates three simple, economical, accurate, precise and sensitive spectrophtometric methods for simultaneous determination of RA and DMP in their combined dosage forms. The proposed methods were successfully utilized as a quality control tool for simultaneous estimation of RA and DMP in their combined market formulation in quality control laboratory.

2. EXPERIMENTAL

2.1 Apparatus:

Absorbance measurements were made on Shimadzu UV-1601 UV visible spectrophotometer with 10 mm quartz cells. The system software of the instrument was used for the multicomponent analysis. Magnetic stirrer (Remi Equipment Pvt. Ltd., India) was used in the initial steps

of extraction. Whatman filter paper no.42 was used to filter the solutions.

2.2 Reagents and Solutions:

All chemicals were of analytical reagent grade.

2.3 Preparation of Standard Stock Solutions of RA and DMP:

Standard stock solutions of RA and DMP were prepared in methanol AR having concentration of 100 µg/ml. Further dilution was done with methanol AR as per requirement of each method.

2.4 Preparation of Binary Mixture of RA and DMP:

Different binary mixture containing RA and DMP in 2:1 ratio (equal to clinical dose ratio 20:10 of RA and DMP) were prepared by diluting different aliquots of the stock solutions of RA and DMP with methanol.

2.5 Sample Preparation:

Twenty tablets were weighed to obtain the average tablet weigh and made into the fine powder. The quantity equivalent to 20 mg of RA and 10.0 mg of DMP was dissolve in 100 ml methanol. This mixture was allowed to stand for 3 h with intermittent sonication to ensure complete solubility of the drug, and was then filtered. The filtrate was further diluted with methanol to obtained final solution having concentration of RA and DMP were 20 µg/ml and 10 µg/ml.

2.6 Method I: Simultaneous Equation [14]

Different aliquot from the standard stock solution of each drug were transferred to 10 ml volumetric flasks separately and diluted up to mark with methanol to give the concentration in the rang of 1 – 50 µg/ml. The standard solution of 10 µg/ml of each drug was scanned in UV range separately keeping methanol as the blank. The λ_{max} for RA and DMP were found to be 285 nm and 287 nm respectively. The absorbance of 5, 10, 15, 20, 25 and 30 µg/ml of standard solutions of each drug was measured at 285 nm, 287 nm and molar absorptivity were find out at the same wavelengths for both the drugs using the following equation.

$E = A / (b \times C \times 1000)$

Where, E = Absorptivity

A = Absorbance

b = Path length (1 cm)

C = Concentration in µg/ml

$$\text{Molar absorptivity } (\varepsilon) = \frac{E \times \text{molecular weight}}{10}$$

Sample solution containing both RA and DMP were measured at 285 nm and 287 nm. The concentration of RA and DMP was calculated by applying following formula for simultaneous equation.

$$A_{285} = \varepsilon_{RA285} bc_{RA} + \varepsilon_{DMP285} bc_{DMP}$$

$$A_{287} = \varepsilon_{RA287} bc_{RA} + \varepsilon_{DMP287} bc_{DMP}$$

where;

ε_{RA285}, ε_{RA287} *is molar absorptivity of RA compound at* 285*nm and* 287*nm*

ε_{DMP285}, ε_{DMP287} *is molar absorptivity of DMP compound at* 285*nm and* 287*nm*

A_{285}, A_{287} *is absorbanceof the sample solutions at* 285*nm and* 287*nm*

C_{RA} is the concentration of RA in moles per litre in sample solution

C_{DMP} is the concentration of DMP in moles per litre in sample solution

By solving these simultaneous equations the value of C_{RA} and C_{DMP} can be obtained.

$$C_{RA} = \frac{A_{287}\,\varepsilon_{DMP\ 285} - A_{285}\,\varepsilon_{DMP\ 287}}{\varepsilon_{RA\ 287}\,\varepsilon_{DMP\ 285} - \varepsilon_{RA\ 285}\,\varepsilon_{DMP\ 287}}$$

$$C_{DMP} = \frac{A_{285}\,\varepsilon_{RA\ 287} - A_{287}\,\varepsilon_{RA\ 285}}{\varepsilon_{RA\ 287}\,\varepsilon_{DMP\ 285} - \varepsilon_{RA\ 285}\,\varepsilon_{DMP\ 287}}$$

2.7 Method II: Multicomponent Mode [15]

In this method involves analysis by multicmponent mode of the instrument. Analytical wavelengths were selected to be 285 nm and 287 nm, which could be utilized for the simultaneous analysis of RA and DMP using multicomponent mode. Standard solutions of RA and DMP were mixed in definite ratio (as per market formulation) to obtained five mixed standard solutions having concentration of RA in the range of 2, 4, 6, 8 and 10 µg/ml and DMP in 1, 2, 3, 4 and 5 µg/ml respectively. The analytical wavelengths and the concentration of mixed standards were fed into multicomponent mode of the instrument. These mixed standards were scanned in the region of the 400 nm to 200 nm. The concentration of RA and DMP in sample solution was determined using spectral data of mixed standards by the instrument.

2.8 Validation of Analytical Methods

The all developed methods were validated in terms of accuracy, precision (interday and intraday), Limit of detection (LOD), limit of quantification (LOQ) and linearity.

3. RESULTS AND DISCUSSION

The development of new spectrophotometric methods for the simultaneous determination of RA and DMP from their combined dosage form has received considerable attention because of their importance in the quality control of the drug products. The spectra of RA and DMP is shown in figure 1 and figure 2. The λmax for RA and DMP were found to be 285 nm and 287 nm respectively. Molar absorptivity values of the subject analyte were determined at two selected wavelength and malor absorptivity values at 285 nm and 287 nm were calculated to be 14570.62, 14176.22 for RA and 11543.58, 12558.29 for DMP respectively. The method-I show good linearity in the concentration range of 5 – 30 µg/ml for both the drugs with correlation coefficient (R^2), slope and intercept 0.9996, 0.0381 and - 0.0004 at 285 nm as well as correlation coefficient (R^2), slope and intercept were found to be 0.9985, 0.0276 and + 0.0023 at 287 nm. The absorbance of standard binary mixture of RA and DMP was repeated five times a day and the average % RSD was found to be 0.19 for 285nm and 0.18 for 287nm. Similarly, the method was repeated on five different days, the average % RSD was found to be 0.24 for 285nm and 0.23 for 287nm. These values confirm the intra and inter day precision of the method. All parameters of these proposed method is validated and results were shown in table 1. In addition to method II requires an inbuilt programme for solving matrix equations. The concentration of each component in sample was obtained by analysis of the spectral data of sample solution with reference to that of the five mixed standards. Interference among the components can be reduced using five mixed standards and two sampling wavelengths. The sample solution containing RA and DMP was analyzed successfully at the sampling wavelength 285 nm and 287 nm with recovery 100.12 ± 0.27 and 100.08 ± 0.36 respectively. Market tablet formulation (Rioz DMP) procured from a local pharmacy was analyzed using the methods developed in this investigation and results were shown in table 2, table 4 and table 5.

4. CONCLUSION

The proposed methods were successfully developed for simultaneous estimation of RA and DMP from their combined dosage form and found to be simple, precise, accurate, sensitive, and selective. It does not suffer from the interference of excipients. The methods were also extended to analyze the marketed formulations and results obtained are good agreement with label claim.

Table: 1 Validation parameters for simultaneous equation method.

Parameter	*RA	*DMP
Absorbance maxima	285 nm	287nm
Linearity range	5 – 30 µg/ml	5 – 30 µg/ml
Slope	0.0381	0.0276
Intercept	- 0.0004	+ 0.0023
Correlation coefficient	0.9996	0.9985
LOD	0.089µg/ml	0.123 µg/ml
LOQ	0.298 µg/ml	0.44 µg/ml
Precision (% RSD)		
Interday	0.19	0.18
Intraday	0.24	0.23
Accuracy (% recovery)	99.90 ± 0.74	99.0 ± 1.58

RA - Rabeprazole sodium
DMP - Domperidone Maleate
* - Average of five determinations

Table: 2 Analysis of market formulation by simultaneous equation method

Drug Brand (Rioz DMP)	Label claim (mg)	% Recovery	%RSD
*RA	20	99.29 ± 0.22	0.22
*DMP	10	99.54 ± 0.29	0.29

RA - Rabeprazole sodium
DMP - Domperidone Maleate
* - Average of five determinations

Table: 3 Analysis of market formulation by multicomponent mode

Brand	Label claimed		Obtained amount		% Recovery	
(Rioz DMP)	*C_X	*C_Y	*C_X	*C_Y	*C_X	*C_Y
Sample	10	5	9.92	4.90	99.20	98.00
80% addition of labeled claimed	17.92	8.90	17.99	8.94	100.39	100.44
100% addition of labeled claimed	19.92	9.90	19.89	9.91	99.84	100.10
120% addition of labeled claimed	21.92	10.90	21.95	10.87	100.13	99.72
Mean	-	-	-	-	100.12	100.08
STDEV	-	-	-	-	0.28	0.36
% RSD	-	-	-	-	0.27	0.36

C_X - Rabeprazole sodium
C_Y - Domperidone Maleate
* - Average of five determinations

Figure 1 Simple spectrum of RA

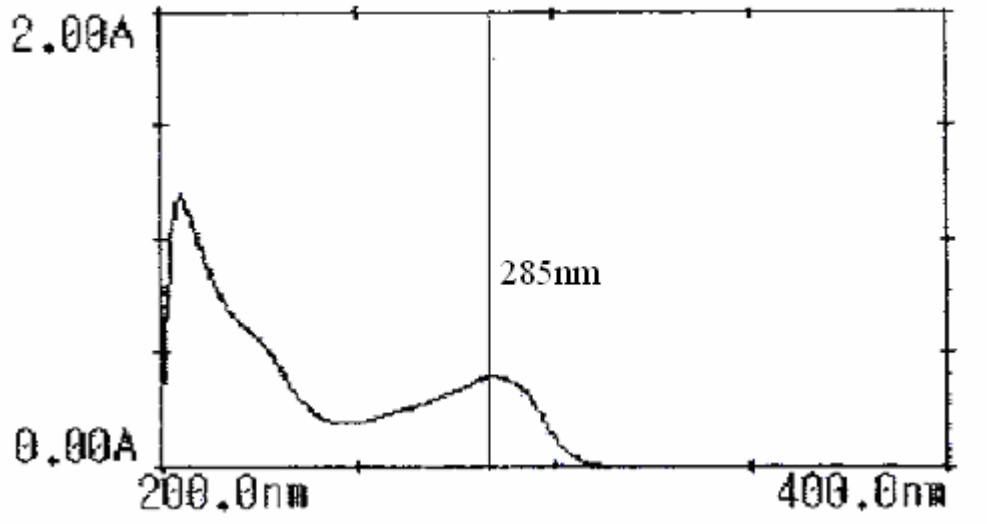
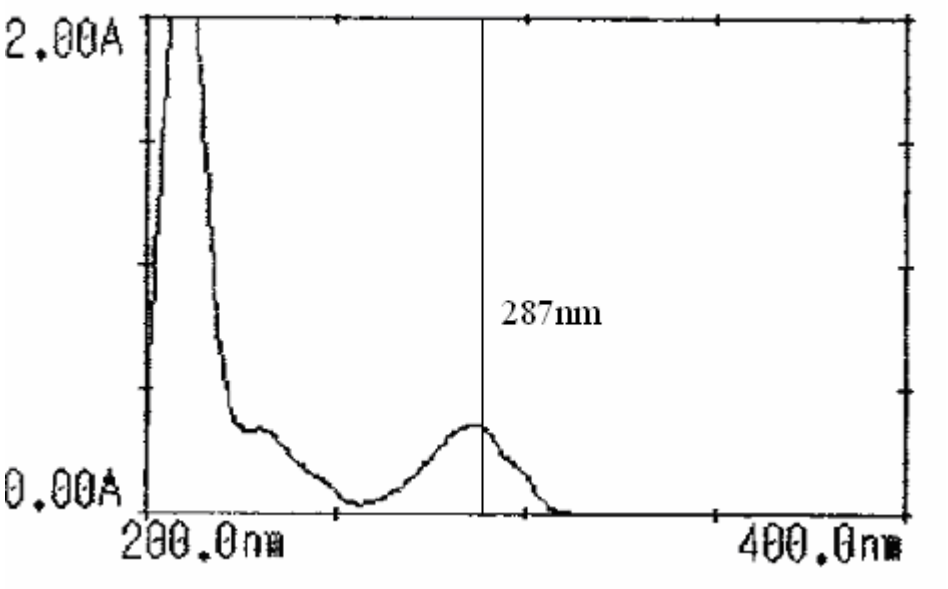


Figure 2 Simple spectrum of DMP



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