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Simultaneous determination of Domperidone and Esomeprazole magnesium in Pharmaceutical Capsule Formulation by Derivative Spectrophotometric Method

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Abstract: Simple, accurate and precise first derivative zero crossing spectrophotometric method has been developed for simultaneous determination of domperidon and esomeprazole magnesium in pure and commercial formulation without any prior separation or purification. The linearity range was found to be 3-12 µg ml^{-1} for both the drugs. The value of limit of detection and limit of quantification was 0.1674 µg ml^{-1} and 0.558 µg ml^{-1} for domperidone and 0.0454 µg ml^{-1} and 0.151 µg ml^{-1} for esomeprazole magnesium respectively. The method was satisfactorily validated in terms of accuracy and precision. The results of the study showed that the proposed spectrophotometric method is useful for the routine determination of domperidone and esomeprazole magnesium in its combined pharmaceutical dosage form.
Keywords: First derivative zero crossing spectrophotometry; domperidone, esomeprazole magnesium.

INTRODUCTION

Domperidone[1] (DOM) chemically,[5- chloro-1-[1,3-(2,3-dihydro-2-oxo-1H-benzmidazole- 1yl) propyl)-4piperdinyl-1,3 dihydro -2Hbenzimidazole- 2-one] is a dopamine antagonist. Esomeprazole magnesium trihydrate[2] (EMZ) is chemically bis(5-methoxy-2-[(S)-[(4-methoxy-3,5- dimethyl - 2 -pyridinyl)methyl]sulfinyl] - 1-H - enzimidazole - 1 -yl) magnesium trihydrate , a compound that inhibits gastric acid secretion . Esomeprazole is cost effective in the treatment of gastric oesophageal reflux diseases. It is S-isomer of omeprazole and is the first single optical isomer proton pump inhibitor. It provides better acid control than current racemic proton pump inhibitors and has a favorable pharmacokinetic profile relative to omeprazole[3]. Simultaneous equation method and chromatographic methods have been reported for simultaneous determination of DOM and EMZ[4,5]. In the present investigation, first derivative zero crossing spectrophotometry is proposed for simultaneous determination of DOM and EMZ.

MATERIALS AND METHODS

Spectrophotometric measurements were made on Agilent 8453 double beam UV-spectrophotometer with a fix slit width of 1 nm.

Reagents

Methanol (AR grade) was obtained from S. D. fine chemicals Ltd. (India). Standard bulk drug sample of DOM and EMZ was obtained as gift sample from Lincoln pharmaceutical Ltd. (India) and Unichem

Lab. Ltd (India) respectively. The pharmaceutical dosage form used in this study was procured from local market.

Procedure

First Derivative Zero Crossing Spectrophotometry

Preparation of calibration curve

Standard stock solution of DOM and EMZ were made by dissolving 25 mg of each drug in 50 ml of methanol individually. Suitable aliquots of these stock solutions were taken to prepare standard solutions containing 3-12 µg ml^{-1} of each of DOM and EMZ in 10 ml volumetric flask and the volume was made with methanol. The absorption spectra of the each solution were recorded in the range of 200 nm to 400 nm and were stored in the memory of computer. The 1st derivatives of stored spectra of individual drug were stressed after smoothing these at $\Delta\lambda = 4$ interval and multiplying the entire spectra with a constant factor 10. The amplitudes of standard DOM solutions at 276.72 nm were plotted against the respective concentrations of DOM. Similarly the amplitudes of standard EMZ solutions at 290 nm were plotted against the respective concentrations of EMZ.

Analysis of capsule formulation

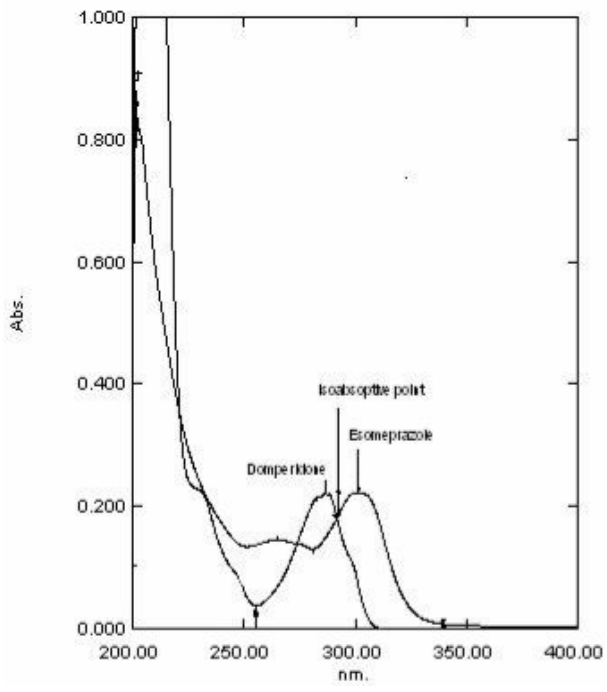
Twenty capsules were weighted accurately and the content were emptied. A quantity of powder equivalent to 30 mg DOM and 20 mg EMZ was weighed and transferred to 50 ml volumetric flask containing about 30 ml methanol. The mixture was ultrasonicated for 20 min. The solution was filtered using 0.45µ filter paper and volume was made up to the mark with methanol. After suitable dilution the solution was tested by the procedure as described in preparation of calibration curve.

METHOD VALIDATION

Accuracy

For studying the accuracy of the proposed methods and for checking the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This was performed at three different levels
(50,100 and 150%) by addition of known amount of DOM and EMZ to a pre-analysed sample of commercial tablets. The amount of standard recovered were calculated in terms of mean recovery with the upper and lower limits of percentage standard deviation.

Fig.1 Overlaid spectra of DOM and EMZ



Precision

Intra-day precision and inter-day precision for the developed methods were measured in terms of % RSD. The experiments were repeated five times in a day for intra-day precision and on three different days for inter day precision. The concentration value for both intra-day and inter-day precision were calculated separately and percentage relative standard deviation were calculated. Finally, the mean of % R.S.D (% R.S.D= [S/X]100, where S is standard deviation and X is mean of the sample analyzed) was calculated.

Limit of detection and limit of quantification

Limit of detection (LOD) and limit of quantification (LOQ) were calculated according to 3 s/m and 10 s/m criterions, respectively, where s is the standard deviation of the absorbance (n=10) of the sample and m is the slope of the corresponding calibration curve.

RESULTS AND DISCUSSION

The absorption spectra of the two drug compounds, DOM and EMZ overlapped closely as shown in **Fig 1. For this reason**, the determination of the above compounds was not possible by direct measurement of absorbance in zero-order spectra. On the other hand, derivative spectroscopy shows more resolution and makes it possible to analyze each drug in presence of one another as well as in presence of other excipients without any pretreatment.

In contrast to zero-order spectra, first derivative spectra showed more resolution in terms of zero crossing point. There is no contribution of DOM at 313 nm and there is no contribution of EMZ at 276 nm, hence 276 nm was considered to be the first derivative wavelength for DOM determination and 313 nm for EMZ determination. Thus one drug can be determined at the zero crossing point of another drug.

Table 1 Results of recovery study of DOM and EMZ

% Amount added to pre-analyzed sample	*% Recovery ± SD	
	DOM	EMZ
50%	101.81± 1.038	102.16± 1.736
150%	100.84± 0.415	98.50± 1.389
120%	99.49 ± 1.248	100.30± 0.668
Mean recovery	100.71 ±1.87	100.65 ± 1.26

Table 2 Results of validation parameters

Parameters	DOM	EMZ
Range	3-15µg ml^{-1}	3-15µg ml^{-1}
Slope	0.0028	0.0015
Intercept	0.00006	0.0002
Correlation coefficient (R^2)	0.9999	0.9997
Accuracy	100.71± 1.87	100.65± 1.26
Precision (% RSD)	1.484	1.284
LOD	0.1647µg ml^{-1}	0.0454µg ml^{-1}
LOQ	0.5580µg ml^{-1}	0.1674µg ml^{-1}

Table 3 Assay results of DOM and EMZ in combined commercial formulation

label claim		% obtained	
DOM	EMZ	DOM	EMZ
30 mg	20 mg	98.216 ± 0.465	99.022 ± 0.598

In this method, the standard and sample preparation required less time and no tedious extractions were involved. The results of recovery studies, 100.71 ± 1.87 % of DOM and 100.65± 1.26 % of EMZ, indicated high accuracy of the method (Table1). Results of validation parameters are depicted in Table 2. A good linear relationship (r =0.9999 for DOM and r = 0.9997 for EMZ) was observed within the concentration range of 3-12 mg/ml for both the drugs. Low values of standard deviation are indicative of the high precision of the method. The satisfactory assay results of DOM and EMZ combined tablet formulation, 100.27 ± 1.66 % for DOM and 99.97 ± 1.76 % for EMZ (Table 3), revealed the potential utility of the developed method in the tablet dosage form.

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