ORIGINAL RESEARCH

UV SPECTROPHOTOMETRIC ESTIMATION OF ESOMEPRAZOLE AND DOMPERIDONE IN TABLET DOSAGE FORM

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ABSTRACT:

Here an accurate, precise, sensitive and economical spectrophotometric methodwas developed and validated for simultaneous estimation of Esomeprazole and Domperidone tablet dosage form. The UV method employed was Simultaneous Equation Method. The method employs 304 nm as λ1 and 285 nm as λ2 for formation of equations. Esomeprazole and Domperidone obeys Beer's law in the concentration range 2-32 µg/ml (r^2=0.9939) and 5-60 µg/ml (r^2=0.9977).The mean recovery for Esomeprazole and Domperidone were found to be 99.12 and 99.43 % respectively. The developed method were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values. Thus the proposed methods were successfully applied for simultaneous determination of Esomeprazole and Domperidone routine industrial work.

KEY WORDS: Esomeprazole, Domperidone, Validation, Simultaneous Equation Method.

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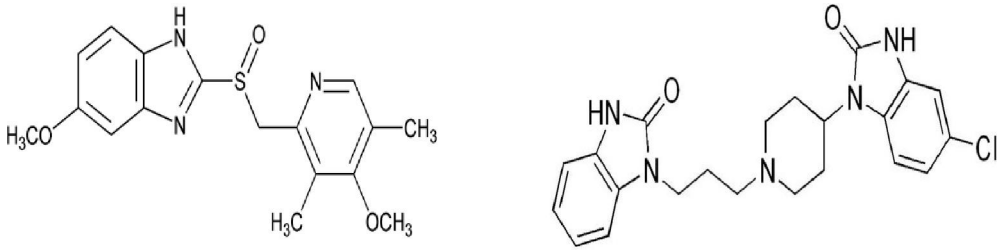
INTRODUCTION

Drugs play a vital role in the progress of human civilization by curing diseases. Analytical chemistry is divided into two branches qualitative and quantitative[1].Esomeprazole (ESO) is a chemically, (S)-(−)-5-Methoxy-2-[(4-methoxy-3,5-dimethylpyridin-2-yl)methylsulfinyl]-3H-benzoimidazole[2], Domperidone (DOM) is, 5-chloro-1-[-1-[3-(2,3-dihydro-2-oxo-1H-benzimadozol-1-yl)propyl]-4-piperidinyl]-1,3-dihydro-2H-benzimidazol-2-one[3]. ESO and DOM combination is used in treatment of gastrointestinal disorders. ESO is a proton pump inhibitor which reduces acid secretion through inhibition of ATPase enzyme in gastric parietal cells and prevents formation of gastric acid. DOM is an antidopaminergic drug and used to suppress nausea and vomiting. Several methods are available in the literature for the determination of ESO and DOM. Most of these methods are for the determination of ESO and DOM separately or in combination with other drug. Analytical methods reported for quantitative determination of ESO individually in pharmaceutical formulations or biological fluids are HPLC[4,5,6] and UV[7,8,9]. Analytical methods reported for quantitative determination of DOM individually in pharmaceutical formulations or biological fluids are HPLC[10,11,12,13].



Esomeprazole **Domperidone**

Figure 1 Chemical structure of Esomeprazole and Domperidone

EXPERIMENTAL

Chemicals and reagents

Esomeprazole and Domperidone were procured from Glenmark Pharmaceutical Labs. Pvt. Ltd. Commercial pharmaceutical preparation ESOZ D40, manufactured by Glenmark Pharmaceuticals Pvt. Ltd. containing 40 mg of ESO and 30 mg of DOM was collected from local market. Acetonitrile, methanol and water used were of analytical grade (Qualigens Fine Chemicals, Mumbai, India). A 0.45 µm nylon filter (Pall life Sciences, Mumbai, India) was used. All other chemicals and reagents used were analytical grade unless otherwise indicated.

Instrumentation:

The proposed work was carried out on a Shimadzu UV-visible spectrophotometer (model UV-1800 series), which possesses a double beam double detector configuration with a1 cm quartz matched cell. All weighing was done on electronic balance (Sansui-vibra DJ-150S-S). A Fast clean ultrasonicate cleaner (India) was used for degassing the mobile phase.

Selection of Solvents

On the basis of solubility study methanol was selected as the solvent for dissolving ESO and DOM.

Preparation of Standard Stock Solutions of ESO and DOM

ESO Stock Solution

An accurately weighed quantity of ESO (25 mg) was taken in 25 ml volumetric flask and dissolved in methanol (20 ml) with the help of ultrasonication for about 10 min. Then the volume was made up to the mark using methanol to get ESO standard stock solution (1 mg / ml).

ESO Working Standard Solution

ESO standard stock solution 5 ml was diluted to 25 ml using 72% v/v methanol to get working standard solution100 µg / ml.

DOM Stock Solution

An accurately weighed quantity of DOM (25 mg) was taken in 25 ml volumetric flask and dissolved in methanol (20 ml) with the help of ultrasonication for about 10 min. Then the volume was made up to the mark using methanol to get DOM standard stock solution (1 mg / ml).

DOM Working Standard Solution

DOM standard stock solution 5 ml was diluted to 50 ml using 72% v/v methanol to get working standard solution 100 µg / ml.

Determination of λ Max of Individual Component

An appropriate aliquot portion of ESO (0.2 ml) and DOM (0.1 ml) were transferred to two separate 10 ml volumetric flasks, the volume was made up to the mark using 72 %v/v methanol to obtain ESO (20 µg/ml) and DOM (10 µg/ml). Drug solutions were scanned separately between 200 nm to 400 nm. ESO shows λ max at 304 nm while DOM at 285 nm, respectively (Figure1).

Overlay Spectra of ESO and DOM

The overlain spectrum of both drugs was recorded (Fig.1) and two wavelengths 304.0 nm (λ max of ESO) and 285.2 nm (λ max of DOM) were selected for further study.

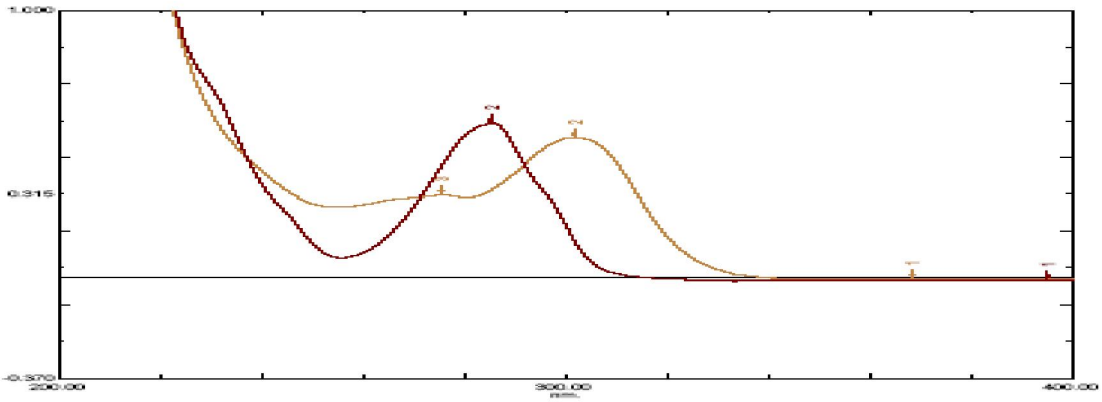


Fig.1: Overlay Spectra of ESO and DOM

Linearity Study for ESO

An accurately measured aliquot portion of working standard solution of ESO was transferred to seven separate 10 ml volumetric flasks. The volume was made up to the mark using 72% v/v methanol to obtain concentrations (2-32 µg/ml). Absorbance of these solutions was measured at 304 nm, (Table1) Calibration curve was plotted, absorbance Vs concentration as shown in (Fig. 2).

Linearity Study for DOM

Accurately measured aliquot portions of working standard solution of DOM were transferred to seven separate 10 ml volumetric flasks. The volume was made up to the mark using 72% v/v methanol to obtain concentrations (5-60 µg/ml). Absorbance of these solutions was measured at 285 nm, (Table 1). Calibration curve was plotted, absorbance Vs concentration as shown in (Fig. 3).

Table 1: Regression and Optical characteristics of ESO and DOM

Parameters	Value For ESO	Value For DOM
Beer's law limit (µg/ml)	2-32	5-60
Correlation Coefficient (r)	0.9939	0.9977
Regression equation		
Slope	0.0142	0.0128
Intercept	0.01749	0.0883

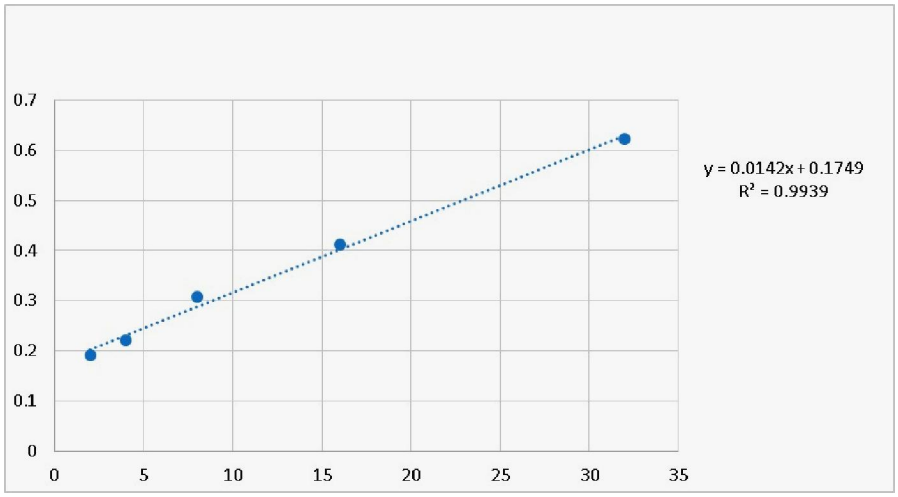


Fig. 2: Calibration Curve of ESO at 304 nm Wavelength

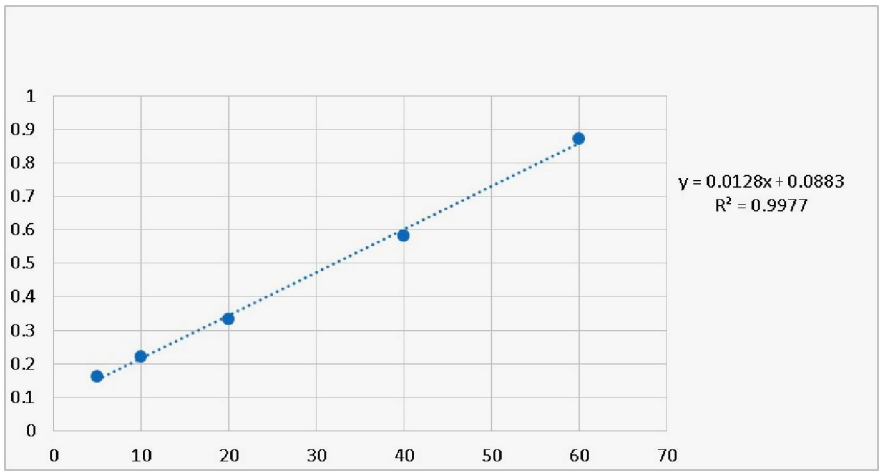


Fig. 3: Calibration Curve of DOM at 285 nm Wavelength

Estimation of Laboratory Mixture by Proposed Method

In order to see the feasibility of proposed method for simultaneous estimation of ESO and DOM in marketed pharmaceutical formulations, the method was first tried for estimation of drugs in standard laboratory mixture. Accurately weighed ESO (50 mg) and DOM (50 mg) were taken in 100 ml volumetric flask, dissolved in methanol (60 ml) with the help of ultrasonication for about 10 min and the volume was made up to mark using the same. Appropriate aliquot portion (1 ml) was transferred to 10 ml volumetric flask and further diluted using 72% v/v methanol to get ESO (50 µg/ ml) and DOM (50 µg/ ml). The absorbance was recorded at 304 nm and 285 nm against solvent as blank.

Amount of each drug was estimated using following equations,

$$C_x = \frac{A_2 \times ay_1 - A_1 \times ay_2}{ax_2\, ay_1 - ax_1\, ay_2}$$

$$Cy = \frac{A_1 \times ax_2 - A2 \times ax_1}{ax_2\, ay_1 - ax_1\, ay_2}$$

Where;

A1 and A2 are the absorbance of diluted mixture at λ_1 and λ_2

Cx and Cy are the concentration of X and Y respectively
ax1 and ax2 are absorptivities of X at λ_1 and λ_2 respectively
ay1 and ay2 are absorptivities of Y at λ_1 and λ_2 respectively
The results are reported in (Table 2).

Table 2: Results of Estimation of ESO and DOM Standard Laboratory Mixture.

Analyte	%Concentration estimated (Mean±S.D.)	%R.S.D.
ESO	99.43±0.1415	0.1412
DOM	99.04±0.4761	0.4768

*Average of five determinations; R.S.D. = Relative Standard Deviation

Application of the Proposed Method for Estimation of Drugs in Tablets

Twenty 'ESOZ D40' Tablets containing ESO (40 mg) and DOM (30 mg) were weighed and ground to fine powder. A quantity of sample equivalent to ESO (40 mg) and DOM (30 mg) was transferred into 100 ml volumetric flask containing methanol (60 ml), sonicated for 15 min and the volume was made up to the mark and filtered through Whatman filter paper (No. 45). This solution was (1 ml) transferred to 10 ml volumetric flaks, dissolved and volume was adjusted to the mark. The absorbance of the solutions was measured at 304 nm and 285 nm against blank. The concentrations of two drugs in sample were determined by using simultaneous equations.
The results are reported in the (Table 3).

Table 3: Results of Estimation of ESO and DOM in Tablets.

Analyte	Label claim (mg/tab)	% Label claim estimated (Mean ± S.D.)	%R.S.D.
ESO	40	99.94± 0.57212	0.57360
DOM	30	99.62± 0.64191	0.64992

*Average of five determinations; S.D. =Standard Deviation

Validation of Proposed Method

The Proposed method was validated as per the ICH guidelines.[14]

Accuracy [Recovery Study]

Accuracy of proposed method was ascertained on the basis of recovery study performed by standard addition method. A known amount of standard drug solutions were added to the tablet powder to make final concentrations in the range of 80%, 100% and 120% and re-analyzed it by the proposed method. The absorbance recorded and the % recoveries were calculated using formula.

% Recovery = [A - B/ C] X 100

Where,

A = Total amount of drug estimated

B = Amount of drug found on preanalysed basis

C = Amount of Pure drug added

The results are reported in (Table 4).

Table 4: Recovery Study.

Drug in mixture solution (µg/ml)		%Recovery ± S.D.	
ESO	**DOM**	**ESO**	**DOM**
30.02	20.01	99.10±0.173	99.72±0.143
40.10	30.00	99.61±0.369	99.36±0.463
50.05	39.98	99.32±0.525	99.12±0.656

S.D. =Standard Deviation

Precision

Precision was determined as intra-day and inter-day variations. Intra-day precision was determined by analyzing ESO (39, 40, and 41 µg/ml) and DOM (29, 30, and 31 µg/ml) for three times on the same day. Inter-day precision was determined by analyzing the same concentration of solutions for three different days over a period of week. The results are reported in (Table 5).

Table 5: Precision Study.

Precision	ESO	%R.S.D.	DOM	%R.S.D.
Interday, n = 3	99.25 ±0.8231	±0.8298	99.97 ± 0.3264	±0.3256
Intraday, n = 3	99.01 ±0.4552	±0.4591	99.20 ± 0.3251	±0.3271

RSD = Relative standard deviation

Ruggedness

Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot by two different analyst using same operational and environmental conditions. The results are reported in (Table 6).

Table 6: Ruggedness Study.

	ESO40 µg/ml		DOM 30 µg/ml	
	Amount Found in µg/ml Mean ± S.D. (n = 3)	% R.S.D.	Amount Found in µg/ml Mean ± S.D.(n = 3)	% R.S.D.
Analyst-I	40.17 ±0.75498	0.7587	30.41 ±0.45645	0.45104
Analyst-II	40.98 ±0.47892	0.4732	30.57 ±0.81658	0.81296
Day-I	40.91 ±0.82329	0.8245	30.32 ±0.19530	0.19659
Day-II	39.96 ±0.09470	0.2369	29.88 ±0.08911	0.7140

LOD: Limit of detection of ESO and DOM were found to be 0.06526 µg and 0.07313 µg respectively.
LOQ: Limit of Quantitation of ESO and DOM were found to be 0.08233 µg and 0.09769 µg respectively.

RESULTS AND DISCUSSION

A simultaneous UV Spectrophotometric Estimation method was developed for ESO and DOM. The method employs 304 nm as λ1 and 285 nm as λ2 for formation of equations. ESO and DOM obeys Beer's law in the concentration range 2-32 µg/ml (r^2=0.9939) and 5-60 µg/ml (r^2=0.9977). The mean recovery for ESO and DOM was found to be 99.12 and 99.43 % respectively. The developed method were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values.

CONCLUSION:

The proposed simultaneous UV Spectrophotometric Estimation method presented in this paper has advantages of simplicity, accuracy, precision and convenience for quantitation of ESO and DOM. The proposed method can be used for the quality control of ESO and DOM in typical laboratories.

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