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Research Article

SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF ESOMEPRAZOLE AND NAPROXEN IN BULK AND TABLET DOSAGE FORM

S. P. Mahaparale*[1], P. R. Mahaparale[1], I. D. Gonjari[2]

1. D. Y. Patil College of Pharmacy, Akurdi, Pune-411 044, Maharashtra, India.
2. Government College of Pharmacy, Vidyanagar, Karad- 410 115, Maharashtra, India.

***Corresponding Author: Email**: sonalimahaparale@gmail.com

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ABSTRACT

Esomeprzole and naproxen are available in tablet dosage form in the ratio 1:25. Two simple, accurate, precise and economic methods; simultaneous equation method and multicomponent method have been described for the simultaneous estimation of esomeprzole and naproxen in tablet dosage form. Absorption maxima of esomeprzole and naproxen in distilled water were found to be 301.0 nm and 262.0 nm respectively. Beer's law was obeyed in the concentration range 5-50 µg/ml for esomeprzole and 5-50 µg/ml for naproxen. The methods allow rapid analysis of binary pharmaceutical formulation with accuracy. Results of two methods were validated statistically and by recovery studies and were found to be satisfactory.

Keywords: Esomeprzole (ESO); naproxen (NAP); Ultraviolet spectrophotometry; Simultaneous equation method and Multi-component method.

INTRODUCTION

Esomeprazole magnesium trihydrate (esomeprazole) is used as antiulcerative in treatment of zollinger- Ellison syndrome. Chemically, Esomeprazole (ESO) is chemically bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1-H-benzimidazole-1-yl) magnesium trihydrate, a compound that inhibits gastric acid secretion. Esomeprazole is the S-isomer of omeprazole, the first single optical isomer proton pump inhibitor. It is cost effective in the treatment of gastric oesophageal reflux diseases. Naproxen (NAP) has non steroidal anti-inflammatory activity. Chemically it is d-2-(6-methoxy-2-napthyl) propionic acid. Esomeprazole (ESO) and Naproxen (NAP) are available in tablet dosage form in the ratio1:25. Esomeprazole is official in The Merck Index[1], Martindale, The Extra Pharmacopoeia[2] and I. P.[3] whereas Naproxen is official in The Merck Index[1], Martindale, The Extra Pharmacopoeia[2], I. P.[3], B. P.[4] and U.S.P.[5] Literature survey reveals that many analytical methods such as UV spectrophotometric[6,7], TLC[8], GC[9] and HPLC[10-20] methods are reported for determination of esomeprazole individually from pharmaceutical dosage form. However, analytical methods like UV spectrophotometry[21], HPLC[22, 23] and HPTLC[24] are reported for determination of naproxen. There are no reported UV spectrophotometric methods for simultaneous estimation of both drugs in combination. This paper represents two simple, rapid, accurate, precise, reproducible and economic UV spectrophotometric methods for simultaneous estimation of ESO and NAP in bulk and tablet dosage form.

MATERIALS AND METHODS

Instrument

A UV/ VIS double beam spectrophotometer, model 1700, with matched quartz cells corresponding to 1 cm pathlength and spectral bandwidth of 2 nm was used in the study.

Materials

Standard gift samples of esomeprzole (ESO) and naproxen (NAP) were procured from Glenmark Pharmaceuticals, Mumbai. Combined esomeprzole and naproxen tablets were purchased from local market.

Solvent used

Methanol AR grade and distilled water were used as solvents in the study.

Stock solutions

The stock solution (100µg/ml) of ESO and NAP were prepared separately by dissolving accurately about 10 mg of each drug in 25 ml methanol AR grade in 100 ml volumetric flask. The volume was adjusted up to the mark with distilled water.

Preparation of calibration curves

Working standard solutions of ESO and NAP were prepared separately from standard stock solution. These solutions were scanned in the spectrum mode from 400.0 nm to 200.0 nm. The maximum absorbance of ESO and NAP was found to be 301.0 nm and 262.0 nm, respectively. The linearity of ESO and NAP was found to be in the concentration ranges of 5-50 µg/ml and 5-50 µg/ml, respectively, at their respective maximas. The coefficients of correlation were found to be 0.9993 for ESO and 0.9995 for NAP, respectively.

METHOD I: Simultaneous equation method

The mixed standard solutions in Beer-Lambert's range for ESO and NAP in the ratio 1:1 from 10, 15 and 20 µg/ml of ESO and 10, 15 and 20 µg/ml of NAP were prepared by diluting appropriate volumes of standard stock solutions. The scanning was carried out in the range of 400.0 nm to 200.0 nm in spectrum mode and absorbances were measured at λ max of ESO i.e. 301.0 nm and λ max of NAP i.e 262.0 nm. The concentration of each drug present in mixed standard solution was calculated from the equations.

$$A_1 = 0.028\ C_x + 0.011\ C_y \quad (\text{at } \lambda\ 301.0)$$

$$A_2 = 0.015\ C_x + 0.013\ C_y \quad (\text{at } \lambda\ 262.0\ )$$

Where, C_x and C_y are concentration of ESO and NAP respectively. A_1 and A_2 are absorbances of sample at 301.0 nm and 262.0 nm respectively.

0.013 and 0.154 are absorptivity values of ESO at 301.0 nm and 262.0 nm respectively.

0.210 and 0.058 are absorptivity values of NAP at 301.0 nm and 262.0 nm respectively.

Method II: Multicomponent Method

The mixed standards in the Beer-Lambert's range for ESO and NAP in the ratio of 1:1 from 10, 15, 20, 25 and 30 µg/ml of ESO and 10, 15, 20, 25 and 30 µg/ml of NAP were prepared by diluting appropriate volumes of standard stock solutions. Two sampling wavelengths, 301.0 nm and 262.0 nm were selected for the estimation of ESO and NAP respectively. The data were fed to the instrument and all mixed standard solutions were scanned in the range of 400.0 nm to 200.0 nm (Fig.1). An overlain spectrum of mixed standards was used to determine the concentration of two drugs present in the tablet solutions. The instrument directly gave concentration of individual drug present in the mixed sample.

Analysis of tablet formulation

Each tablet strength (brand name Vimovo) contains 20 mg of ESO and 500 mg of NAP. Twenty tablets were weighed and average weight of tablet was determined and crushed to fine powder. The powder sample equivalent to 0.4 mg of ESO and 10 mg of NAP was weighed and transferred to 100 ml volumetric flask. Accurately weighed 9.6 mg of pure ESO was added to the above powder in the volumetric flask to obtain the required concentration of ESO. The total powder mixture obtained was equivalent to 10 mg of ESO and 10 mg of NAP. The powder mixture was dissolved in 25 ml of methanol AR grade and was kept in ultrasonicator for 45 min. Finally, the volume was made up to the mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. The filtrate was further diluted to obtain mixed sample solutions in Beer's-Lambert's range for each drug in the ratio of 1:1 having concentrations 10, 15 and 20 µg/ml of ESO and 10, 15 and 20 µg/ml of NAP, respectively. For method I, the absorbances of mixed sample solutions were measured at 301.0 nm (λ max of ESO) and 262.0 nm (λ max of NAP) selected for the estimation of ESO and NAP, respectively. These values were replaced in the

above mentioned equations and the concentrations of each drug were calculated.

For method II, sample solutions were subjected to analysis in the multicomponent mode of instrument. The concentration of ESO and NAP was determined by analysis of spectral data of the sample solutions with reference to the mixed standards at wavelengths 301.0 nm and 262.0 nm respectively. The tablet analysis obtained by proposed methods was validated by statistical evaluation (**Table 1**).

Table 1: Analysis of Tablet formulation

Method	Tablet sample	Label claim (mg/tablet)	Amount found* mg/tablet	% Label claim found*	% RSD
I	ESO	20	19.95	99.76	0.16
	NAP	500	499.20	99.84	0.09
II	ESO	20	19.90	99.80	0.07
	NAP	500	499.35	99.87	0.08

**Mean of six estimations*
ESO and NAP denote Esomeprazole and Naproxen respectively.

Table 2: Recovery Studies

Method	Level of % Recovery	% Recovery found*		± Standard Deviation		Standard Error	
		ESO	NAP	ESO	NAP	ESO	NAP
I	80	99.94	99.88	0.14	0.13	0.05	0.05
	100	99.84	99.81	0.09	0.08	0.03	0.03
	120	99.96	99.82	0.13	0.09	0.55	0.21
II	80	99.84	99.87	0.10	0.13	0.06	0.10
	100	99.89	99.82	0.12	0.07	0.11	0.03
	120	99.76	99.88	0.13	0.16	0.05	0.06

**Mean of six estimations*
ESO and NAP denote Esomeprazole and Naproxen respectively.

Validation of method[25, 26]

The method was validated in terms of linearity, accuracy, precision, specificity and reproducibility of sample applications.

a) Recovery study

To study validity and the reproducibility of the proposed method, recovery studies were carried out at 80 %, 100 % and 120 % level of label claim. The results of recovery studies are represented in **Table 2**.

b) Repeatability

Repeatability is given by inter and intra-day precision. Intra-day precision was determined by analyzing, two different concentration of drug for three times in the same day. Inter-day precision was determined by analyzing two different concentration of drug for three days in a week; results are represented in **Table 3**.

c) Ruggedness

Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot in different laboratories by different analyst, using similar operational and environmental conditions; the data is presented in Table 4.

RESULTS AND DISCUSSION

In Simultaneous equation method, absorption maxima of esomeprzole (ESO) and naproxen (NAP) in distilled water

Table 3: Results for Repeatability Studies

Method	Drug	Intraday		Interday	
		%Amount found*	% RSD	%Amount found*	%RSD
I	ESO	99.77	0.10	99.73	0.13
	NAP	99.80	0.21	99.82	0.17
II	ESO	99.95	0.20	99.83	0.20
	NAP	99.87	0.16	99.89	0.24

**Mean of six estimations*
ESO and NAP denote Esomeprazole and Naproxen respectively.

Table 4: Ruggedness Data

Method	Drug	Analyst I		Analyst II	
		%Amount found*	%RSD	%Amount found*	%RSD
I	ESO	99.83	0.18	99.73	0.17
	NAP	99.85	0.16	99.88	0.24
II	ESO	99.65	0.15	99.70	0.17
	NAP	99.93	0.18	99.93	0.20

**Mean of six estimations*
ESO and NAP denote Esomeprazole and Naproxen respectively.

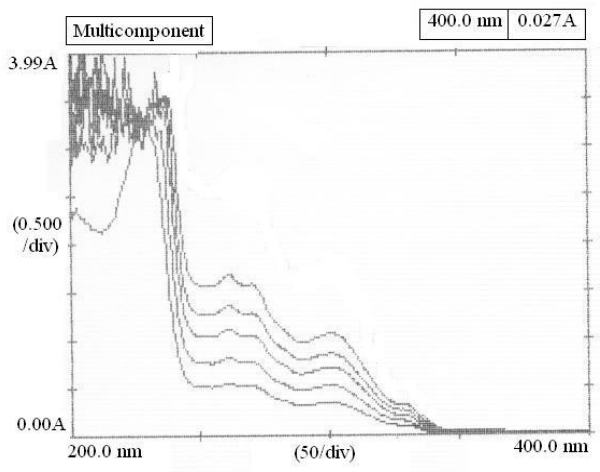

Fig. 1: Overlain spectrum of mixed standards of Esomeprazole and Naproxen.

were found to be 301.0 nm and 262.0 nm respectively. ESO and NAP follow linearity in the concentration range 5-50 g/ml and 5-50 g/ml respectively. This method is simple, accurate and reproducible.

The Multicomponent method is simple, rapid, easy and less time consuming because it does not require any manual calculations. However this method is specific for the instrument having multicomponent mode. It gives better results.

The tablets were analyzed and amount of drug determined by proposed methods; it was in good agreement with label claim. The proposed methods were validated as per ICH guidelines. Recovery studies, statistical validation, precision of method were carried out for both the methods. The value of standard deviation was satisfactorily low and the recovery was close to 100 % indicating the reproducibility and accuracy of the methods.

Hence all the developed methods were found to be simple, rapid, reproducible, precise and accurate for the routine simultaneous estimation of esomeprzole and naproxen in bulk and tablet dosage form.

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