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A VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE IN BULK AND COMMERCIAL DOSAGE FORM

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ABSTRACT

A simple, sensitive, accurate, precise, reproducible and cost-effective UV spectrophotometric method has been developed for the quantitative determination of Esomeprazole magnesium trihydrate in bulk and pharmaceutical formulation. The UV spectrum was scanned between 200 to 400 nm and the λ max of Esomeprazole trihydrate using methanol as the solvent was found to be 237 nm. The beer's law range was obeyed in the concentration range of 5-30 µg/mL with correlation coefficient (R^2 = 0.995). The percentage of recovery was found to be in the range of 99%-102%. The % RSD was found to be LT 2%, which indicates that the method is precise. The LOD and LOQ values were found to be 0.034µg/mL and 0.103µg/mL. The proposed method was found to be simple, accurate, and reproducible with the acceptable recovery of analyte which can be directly used for the analysis of Esomeprazole magnesium trihydrate in the bulk and pharmaceutical dosage form.

INTRODUCTION

Esomeprazole chemically is [5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]- 1H-benzimidazole-1-yl) magnesium trihydrate Figure (1). Its molecular formula is $(C_{17}H_{18}N_3O_3S)_2$ Mg.$3H_2O$ with a molecular weight of 767.2g/mol. The half-life of the magnesium salt is about 19 hours at 25^0C and about 8 hours at 37^0C [1]. Esomeprazole (S- omeprazole) is the single optical S-enantiomer of omeprazole, the first drug of the class of proton pump inhibitors [2]. Literature review reveals different methods including UV-Visible (3-4) and derivatives (5-7), differentialscanningcalorimetry [8], HPLC [9] andcapillary electrophoresis [10]. Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of its simplicity, specificity, and low cost. This study Presents a new spectrophotometric method for the determination of esomeprazole magnesium trihydrate in bulk and pharmaceutical formulations. Accordingly, the objective of this study was to develop and validate the UV-spectrophotometric method for the estimation of Esomeprazole magnesium trihydrate in bulk and pharmaceutical formulation as per ICH guidelines [11]. Esomeprazole magnesium hydrate was approved by Europe in 2000 and the US in 2001 with a brand name NEXIUM.

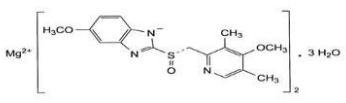

Figure 1: Chemical structure of Esomeprazole magnesium trihydrate

MATERIALS AND METHODS

Instruments and Materials

Esomeprazole magnesium trihydrate was received as a gift sample from Hetero Pharmaceuticals, (Hyderabad, India) with a percentage purity of 99.8%. All the solvents and chemicals like Methanol, Ethanol, etc used were of analytical grade and purchased from Merck, Mumbai, India. Esomeprazole magnesium trihydrate capsules of 40mg Nexiumwere purchased from the local market. LAB INDIA (T60) double beam UV/Visible spectrophotometer and ELITE analytical balance were used.

Preparation of standard stock solution: Accurately weighed 0.10 g of Esomeprazole magnesium trihydrate was transferred to a 100 ml volumetric flask, dissolved in 20 ml methanol by shaking manually for 10 min. The volume was adjusted with the same solvent up to the mark to give the final strength of 1000 µg/ml.

Preparation of working standard solution: From the above standard stock solution, 10 ml was transferred to a 100 ml volumetric flask and made up to the mark with methanol to get a concentration of 100µg/ml.

Absorbance maxima: The solution (100µg/ml) was scanned in UV spectrophotometer in the range of 200-400nm using methanol as blank and the absorbance maxima were found to be at 237nm (λmax).

Calibration curve: Aliquots ranging from 5-10 µg/ml solutions were prepared by using methanol as a solvent. The samples were then analyzed at a λmax of 237 nm to get respective absorbances. The calibration curve was plotted by taking concentrations on the x-axis and absorbances on the y-axis.

Preparation of the sample solution: The proposed method was applied to analyze the commercially available Esomeprazole magnesium trihydrate capsules Nexium (40mg). 10 capsules are weighed and powdered. The amount of powder equivalent to 100 mg of Esomeprazole magnesium trihydrate was weighed accurately and transferred into a 100 ml volumetric flask containing methanol and the volume was made up to 100 ml with methanol. The solution was subjected to filtration through Whattman filter paper #41. The filtrate was diluted suitably with methanol to get a final concentration of 20µg/ml concentration. This was subsequently analyzed using a Double beam UV spectrophotometer, using methanol as blank in the UV range of 200-400 nm. The spectrum was recorded at 237 nm.

METHOD VALIDATION

"Validation is defined as establishing documented evidence which provides a high degree of assurances that a specific process or equipment will consistently produce a product or result meeting its predetermined specifications and quality attributes. The method was validated for several parameters like linearity, accuracy, precision, ruggedness, robustness, and Limit of detection (LOD), Limit of quantification (LOQ) according to ICH guidelines [12].

Linearity: The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. For estimation of linearity at least 5 concentrations are required.

Accuracy: Accuracy can also be described as the closeness of agreement between the value that is adopted, either as a conventional, true, or accepted reference value, and the value found. Accuracy is assessed by using 9 determinations covering a minimum of 3 concentrations.

Precision: The closeness of agreement between the obtained values by analyzing the same sample multiple times under prescribed conditions. There are 3 levels of repeatability, intermediate precision, and reproducibility. Repeatability expresses the precision under the same operating conditions over a short interval of time. It is also termed as intra-assay precision. Intermediate precision express within laboratory variations: different days: different analysts, different equipment, etc. Reproducibility is assessed by means of an inter-laboratory. It is also known as inter-day

precision. Precision is expressed in, terms of % Relative Standard Deviation

% RSD =Standarddeviation x 100

Robustness: Robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters.

Ruggedness: The ruggedness of an analytical method is the degree of reproducibility of test results obtained by the analysis of the same samples under a variety of conditions, such as different laboratories, different analysts, different instruments, reagents, etc.

Sensitivity: The Sensitivity of measurements of Esomeprazole magnesium trihydrate by the use of the proposed method was estimated in the terms of limit of detection (LOD) and limit of quantification (LOQ) of the drug.

Limit of detection: The detection limit of an analytical method is the lowest amount of analyte in a sample that can be detected but not necessarily quantitated, under the stated experimental conditions.

$$LOD = 3.3 \times \sigma/S$$

Limit of quantification: The quantification limit of an analytical method is the lowest amount of analyte in a sample that can be determined, with acceptable precision and accuracy under the stated experimental conditions.

$$LOQ = 10 \times \sigma/S$$

Specificity: Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present.

Linearity study: To establish the linearity of the proposed method, various aliquots of the standard solution of the drug were prepared from the stock solution and analyzed. The drug showed linearity in the range of 5, 10, 15, 20, 25, and 30µg/ml, respectively. The solutions were scanned at 237nm and the absorbance was recorded [Table 1]. From this calibration curve was obtained by plotting absorbance versus concentration of Esomeprazole magnesium trihydrate and the linearity was represented in figure 3. The correlation coefficient was found to be (r^2= 0.995).

Precision: The precision of the method was studied as intraday and inter-day variations. An intraday precision study was carried out by preparing drug solutions of the same concentration 20µg/ml and analyzed it at three different times in a day (Morning, afternoon, and evening) and the absorbances was recorded [Table 3]. The same procedure was followed for six times in five different days todetermine the same concentration 20µg/ml were prepared and analyzed as inter-day precision. The results were reported as %RSD [Table 4].

Accuracy: The accuracy of the method was determined by spiking at different concentrations, i.e., 80, 100 and 120% in which the amount of marketed formulation Nexium was kept constant (20µg/ml) and the amount of the pure drug was varied, that is 16µg, 20µg, 24µg for 80, 100, and 120% respectively. The solutions were prepared in triplicate and the results of recovery studies are reported in [Table 5] which showed that the % amount found was between 99.1 and 101.1 % with % RSD LT 2%.

Robustness: The robustness of the method was carried out by analyzing the sample at different wavelengths to determine the robustness of the method and the respective absorbance was measured as shown in [Table 6].

Ruggedness: The ruggedness of the developed method was carried out by analyzing the sample using two different laboratories or different analysts and respective absorbance was measured as shown in [Table 7].

Limit of detection and limit of quantification: Limit of detection (LOD) and Limit of quantification (LOQ) of the drug was calculated by using equations according to ICH guidelines. The results are shown in [Table 8].

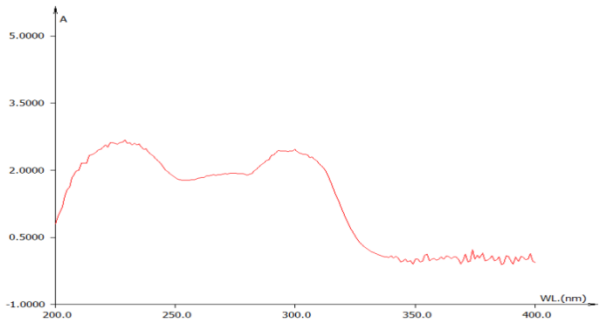

Figure 2: Absorbance spectra of Esomeprazole magnesium trihydrate

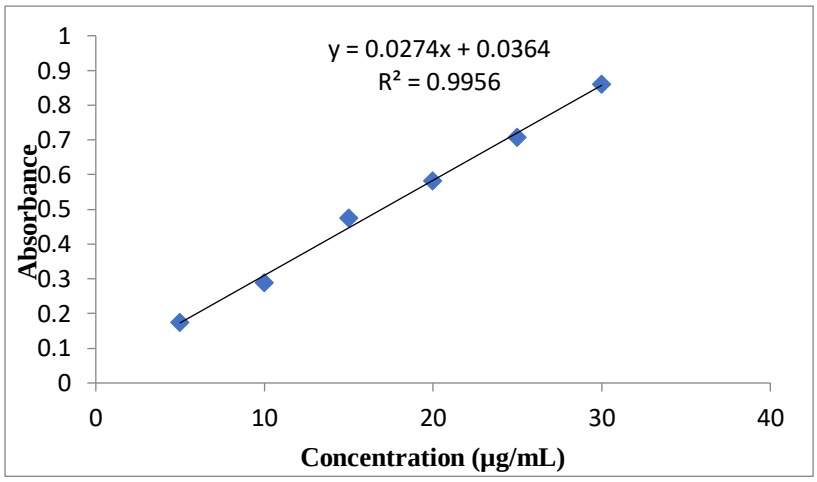

Figure 3: Calibration graph of Esomeprazole magnesium trihydrate

Table 1: Linearity study of Esomeprazole magnesium trihydrate

S. No.	Concentration (µg/mL)	Absorbance
1	5	0.1750
2	10	0.2895
3	15	0.4759
4	20	0.5828
5	25	0.7079
6	30	0.8603

Table 2: Repeatability data

S. No	Concentration (µg/ml)	Absorbance
1	20	0.5732
2	20	0.5753
3	20	0.5829
4	20	0.5808
5	20	0.5789
6	20	0.5786
Mean		0.5782
%RSD		0.6131%

Table 3: Intra-day Precision

Concentration (µg/ml)	Absorbance			%RSD
	1	2	3	
20	0.6113	0.6763	0.2996	0.5233

Table 4: Inter-day precision

Concentration (µg/ml)	Absorbance				%RSD
	Day 1	Day 2	Day 3	Day 4	
20	0.6053	0.6022	0.2018	0.1847	0.3985

Table 5: Accuracy data

% Level of Addition	Tablet Amount	Amount added	Amount Found	% Recovery	%Mean Recovery
80	20	16	15.9	99.7	100.2
100	20	20	20.1	100.5	
120	20	24	24.1	100.5	

Table 6: Robustness data

Concentration (µg/ml)	λ1 (236nm)	λ2 (237nm)	λ3 (238nm)
20	0.6039	0.5742	0.5705
20	0.5992	0.5753	0.5732
20	0.5979	0.5829	0.5743
20	0.6075	0.5808	0.5758
20	0.6065	0.5789	0.5736
20	0.6049	0.5786	0.5779
%RSD	**0.6494**	**0.5656**	**0.43572**

Table 7: Ruggedness data

Concentration (µg/ml)	Analyst 1	Analyst 2
20	0.5732	0.5949
20	0.5753	0.5936
20	0.5829	0.5923
20	0.5808	0.5930
20	0.5789	0.5931
20	0.5786	0.5916
%RSD	**0.6131**	**0.1905**

Table 8: LOD & LOQ

LOD	LOQ
0.034 µg/ml	0.103 µg/ml

Table 9: Validation parameter results for Esomeprazole

Parameters	Results
Absorption maxima (nm)	237 nm
Linearity range (µg/mL)	5-10
Regression equation	y=0.027x+0.024
Correlation coefficient	R^2= 0.995
LOD (µg/mL)	0.034
LOQ (µg/mL)	0.103

Accuracy (%Recovery)	99.7-100.5
Precision (%RSD)	LT 2%
Sandell's sensitivity (µg/cm2/0.001 absorbance units)	0.0336

Assay of Esomeprazole Capsules: For the analysis, 10 capsules of Esomeprazole were weighed and finely powdered. An accurately weighed quantity of powder equivalent to 100mg was taken in a 100ml volumetric flask. Few ml of methanol was added and sonicated for 15 minutes and then filtered through Whattman filter paper (No.41) and the volume was adjusted with solvent. From that, further dilution was made to get a final concentration of 20µg/ml.

RESULTS AND DISCUSSION

The method was developed and validated as per ICH guidelines. The method was validated in terms of linearity, precision, accuracy, robustness, ruggedness, LOD, and LOQ. Beers law was obeyed in the concentration range of 5-30 µg/ml, and the regression equation was found to be y=0.027x+0.024 with a correlation coefficient of r^2=0.995. The intraday and inter-day of the method were carried out and the % RSD was found to be less than 2 which indicate the proposed method is precise. The accuracy of the method was assessed by recovery studies at different levels i.e. 80%, 100%, and 120% and was found to be accurate. The proposed spectrophotometric method shows that the developed method was robust and rugged. The LOD and LOQ values indicate that the method is more sensitive. Determination of Esomeprazole in capsule formulation showed content of Esomeprazole was very close to the label amount. The % RSD values in all parameters were within the acceptable limits LT 2%). All the characteristics of the method are represented in the [Table 9].

CONCLUSION

The developed UV-spectrophotometric method is quiet simple, accurate, precise, reproducible, and sensitive. The UV method has been validated for the estimation of Esomeprazole magnesium trihydrate in bulk as well as the Pharmaceutical dosage form. The proposed method can be used for routine analysis of Esomeprazole magnesium trihydrate in bulk as well as a pharmaceutical formulation.

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