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Research Article

METHOD DEVELOPMENT AND VALIDATION FOR THE DETERMINATION OF ESOMEPRAZOLE IN TABLET DOSAGE FORM BY RP-HPLC METHOD

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ABSTRACT:
A simple, precise, rapid, and accurate RP-HPLC method has been developed to determine esomeprazole magnesium trihydrate using chromatographic separation isocratically on C18 column (5 µm, 150mm x 4.60mm) and acetonitrile: water (HPLC grade) in the ratio of 50:50 (v/v) as the mobile phase, at a flow rate of 1ml/min. Detection was carried out at 289 nm. The retention times was found to be 5.6, the method was linear in the concentration range of 10-60µg/ml with R^2=0.997 respectively. The proposed method is successfully applied for the determination of drugs in commercial tablet preparation. The results of the analysis have been validated statistically and by recovery studies.
KEYWORDS: Esomeprazole magnesium trihydrate, isocratic, RP-HPLC.

INTRODUCTION:

Esomeprazole magnesium trihydrate is chemically bis(5-methoxy-2-[(S) -[(4- methoxy-3, 5-dimethyl-2- pyridinyl) methyl] sulfinyl]-1- H-benzimidazole-1-yl) magnesium trihydrate and it belongs to a class of proton pump inhibitor used in treatment of peptic ulcer disease[1,5]. Nafisur Rahman et al developed Spectrophotometric determination of esomeprazole magnesium in commercial tablets using 5-sulfosalicylic acid and n-bromo succinimide[2], M. C. Sharma et al estimated esomeprazole magnesium trihydrate in pharmaceutical formulations using indigo carmine reagent by UV-Vis spectrophotometric method[3] and S. Lakshmana Prabu et al performed simultaneous estimation of esomeprazole and domperidone by UV spectrophotometric method[4]. But there is no simple and easy method for the analysis of esomeprazole. Hence, it is necessary to develop a rapid, accurate and validated RP-HPLC method for the determination of Esomeprazole in tablet dosage form. The method proved to be simple model since it does not contain a buffer system. This paper describes the development and validation of reliable, simple, robust, time and money saving reversed phase HPLC method, using PDA detection, for the estimation of Esomeprazole in tablet dosage forms. The developed method validated according to ICH guidelines.

EXPERIMENTATION:

EQUIPMENT:

Chromatographic separation was performed on Waters HPLC system having PDA detector and Rheodyne injector with 20µl loop volume. Waters Empower software was applied for data collecting and processing.

REAGENTS AND CHEMICALS:

Acetonitrile and water of HPLC grade were procured from Merck Ltd. API of Esomeprazole received as a gift sample from Dr.Reddy's. The commercial sample ESOZ- 40mg (Glenmark) is purchased from the local market.

HPLC CONDITIONS:

A Thermo scientific C_{18} (25cm×4.6mm, 5µ) column was used as the stationary phase. A mixture of Acetonitrile and water in the ratio of (50:50v/v) was used as a mobile phase. It was filtered through 0.45µ membrane filter and degassed. The mobile phase was pumped at 1 ml/min. The eluents were monitored at 289nm.The injection volumes of sample and standard were 20µl.

STANDARD-PREPARATION:

Standard stock solutions were prepared by dissolving separately 20mg of the drug in 100 ml of diluents which was a mixture of acetonitrile and water in the ratio of 50:50 to get a concentration of 200 µg/ml. 2ml of stock was diluted to 10ml with the mobile phase to get concentration 40µg/ml.

ASSAY OF FORMULATION:

Twenty tablets were weighed and finely powdered. A synthetic mixture was prepared by taking powdered equivalent to 40 mg of esomeprazole in 100 ml diluents and then sonicated for 10 min. different concentrations of solution were prepared by a serial dilution technique as per standard and each dilution was analyzed. The drug was initially dissolved in acetonitrile and sonicated for 10 minutes. The volume was made up to 50ml with mobile phase. The solution was filtered using 0.2µm membrane filter. The aliquot was then suitably diluted to get final concentrations of 40 µg/ml of esomeprazole. Then 20µl of these solutions was injected in to the column, recorded and chromatogram was shown in Fig.1. Concentrations of esomeprazole in the tablet formulation were calculated by comparing area of the sample with that of standard. The percentage assay of the drug was calculated and presented in Table 1.

VALIDATION OF THE METHOD:

ACCURACY:

Recovery studies were carried out by applying the standard addition method. A known amount of standard esomeprazole corresponding to 50%, 100%, and 150% of the label claim was added to pre analyzed sample of tablet dosage form separately. The recovery studies were carried out three times, at each level of recovery. The data's of accuracy were shown in (Table 2)

PRECISION:

In the system precision studies, six replicate injections of the working standard solution prepared as per the proposed method and chromatograms were recorded. Standard deviation and relative standard deviation for the area was calculated and presented in (Table 3).

LINEARITY AND RANGE:

The developed method has been validated as per ICH guidelines. Every 20µl of the working standard solution of esomeprazole in the concentration range of 10-60 µg/ml (Fig 2) injected into the chromatographic system. The chromatograms were developed and the peak area was determined for each concentration of the drug solution. Calibration curves of esomeprazole were obtained by plotting the peak area ratio versus the applied concentrations. Linearity data's were shown in Table.4.

RUGGEDNESS AND ROBUSTNESS:

The ruggedness of the method was determined by carrying out the experiment on different instrument like Waters HPLC and Shimadzu HPLC by different operators using different columns of similar type like Phenomenex C_{18},Hypersil C_{18}.Robustness of the method was determined by making slight changes in the experimental conditions such as the composition of the mobile phase, pH of the mobile phase, and flow rate of the mobile phase and the chromatographic characteristics were evaluated.

TABLE 1: REPORT FOR ASSAY:

S.No	Drug	Amount present (mg/tab)	Amount found* (mg/tab)	% label claim*
1	esomeprazole	40	39.97	99.92%

TABLE 2: RECOVERY STUDIES OF ESOMEPRAZOLE

Concentration	Peak area	Amount Added µg/Ml	Amount Present µg/Ml	% Recovery	Mean % Recovery
50%	19249	20	19.94	99.83%	100.11%
	19431	20	20.08	100.4%	
	19278	20	19.98	100.1%	
100%	38543	40	40.20	99.5%	
	38472	40	40.001	100%	99.81%
	38490	40	40.019	99.95%	
150%	47460	60	59.73	100.4%	
	47696	60	59.94	100.1%	99.9%
	48013	60	60.45	99.2%	

TABLE 3: DATA FOR PRECISION:

Sampling	Area
1	38642
2	38548
3	38472
4	38562
5	38693
6	38428
Mean	38557
Standard Deviation	44.46
%RSD	0.11%

TABLE 4: DATA FOR LINEARITY:

Concentrations (ug/ml)	Area
10	11307
20	17982
30	29160
40	38480
50	48100
60	57722

FIG 1. CHROMATOGRAM OF THE SAMPLE:

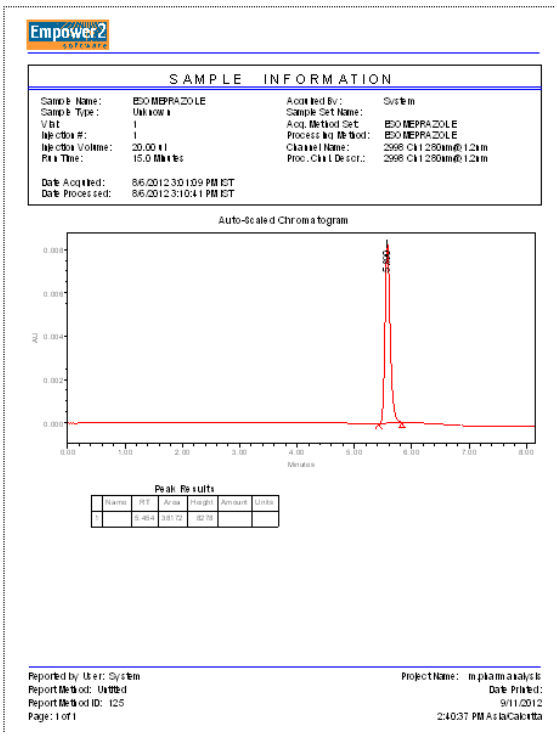
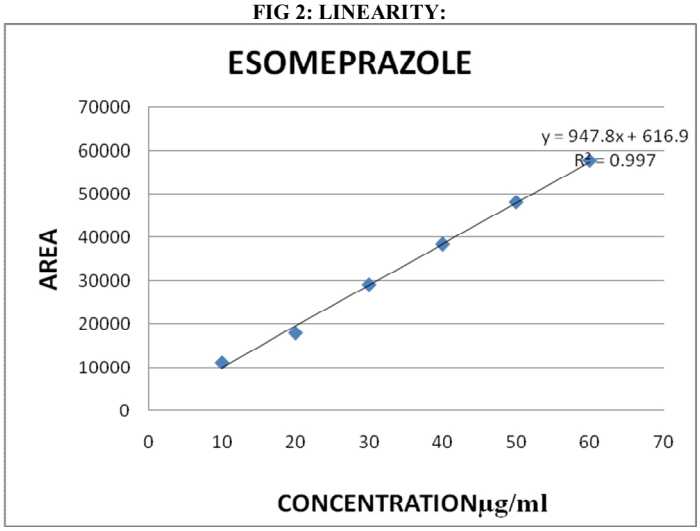


FIG 2: LINEARITY:



RESULTS AND DISCUSSION:

The proposed method was found to be simple and sensitive with linearity in the concentration range of esomeprazole between 10-60µg/ml. System suitability parameter indicates high column efficiency from the large number of theoretical plates (>2000). The degree of asymmetry was also evaluated using the tailing factor result 0.42, which did not exceed the critical value (1.5) indicating acceptable degree of peak asymmetry. The method was found to be accurate and precise as indicated by results of recovery studies and precision studies %RSD not more than 2%. There were no marked changes in the chromatograms which confirmed the ruggedness of the method. The standard deviation of % assay for sample was calculated for each parameter in robustness studies and relative standard deviation was found less than 2%. The low RSD value confirms the robustness of the method.

CONCLUSION:

The developed RP-HPLC method for the determination of esomeprazole can be used for routine analysis of this component in tablet dosage form.

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