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Validated RP-HPLC Method for the Estimation of Esomeprazole Enteric Coated Tablets

Alex D Chacko[1], Vembu P[2], Dhanalakshmi K[1*]

[1]*Department of Pharmaceutical Chemistry, Manonmaniam Sundaranar University, Tirunelveli-627 012, India*
[2]*Bafna Pharmaceuticals Ltd., Chennai, India*

ABSTRACT

A simple, efficient and reproducible RP-HPLC method for determination of Esomeprazole in enteric coated tablet pharmaceutical dosage has been developed. The Separation was carried out on Zorbax SB C18 column (250 × 4.6 mm, 5 µm) column using buffer 6.8 g of potassium dihydrogen orthophosphate and 0.9 g of sodium hydroxide (NaOH) in 1000 ml of water (adjusted to pH 6.8 with 0.2 M NaOH). Buffer: Acetonitrile in the ratio of 40:60 v/v as diluent. The flow rate was 1.0 ml/min and effluent was detected at 280 nm. The retention times of esomeprazole was 3.2 min and the linearity ranges were found to be 50-150 µg/ml (r^2=0.9990). The percentage relative standard deviation for accuracy and precision was found to be less than 2%. Hence, the method was effectively used for the regular analysis of esomeprazole in enteric coated tablet dosage form.

Keywords: Esomeprazole, Enteric coated tablet, Method development, RP-HPLC, Validation

INTRODUCTION

Esomeprazole chemically is bis (5-methoxy-2-[(s)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole-1-yl) magnesium trihydrate. $(C_{17}H_{18}N_3O_3S)_2Mgx3H_2O$. Esomeprazole magnesium trihydrate is a classic example of proton pump inhibitors and is approved by FDA for the treatment of symptomatic Gastroesophageal Reflux Disease (GERD), short-term treatment and maintenance of erosive esophagitis. It is an S-isomer of omeprazole and the first proton pump inhibitor to be developed as an optical isomer [1]. The drug has an improved pharmacokinetic profile, ensuring an improved systemic exposure and fewer inter individual variability compared with omeprazole, and more effective suppression of gastric acid production compared with other proton pump inhibitors. Its bioavailability is 89% and plasma elimination half-life is 1.5 h [2]. The stability of esomeprazole magnesium trihydrate decreases with a corresponding decrease in the pH of the media. Hence, the exposure of the drug to the acidic contents of the stomach would lead to significant degradation of the drug and would result in reduced bioavailability [1]. Few attempts have been made to deliver this drug by per oral route in the form of enteric coated granules, solid dispersion, suspension and matrix tablets [3-5]. A number of enteric coating polymers are available and capable of protecting the drug core from the aggressive environments of the stomach [6-9]. Being soluble at higher pH values, these polymers dissolve in the intestine and release the core for ready action. The polymers which said above include all the several synthetic polymers like Polymethacrylates (Eudragits), Cellulose Acetate Phthalate (CAP), Hydroxy Propyl Methyl Cellulose Phthalate (HPMCP).

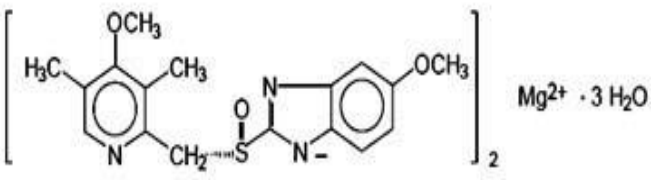

Figure 1: Chemical structure of esomeprazole magnesium trihydrate

Literature survey reveals that Esomeprazole is estimate in tablet dosage form individually or in combination with naproxen, diclofinac sodium, levosulpiride, aspirin etc. It is also estimated in human plasma, in pellet form, in micro pellet formulation, in capsule dosage form and in bulk drugs and it is estimated and validated in tablet dosage form by HPLC, UV-Spectrophotometry, RP-HPLC by using different mobile phase ratio, column temperature etc. So the present work is aimed to develop a simple feasible and sensitive RP-HPLC method for the qualitative Esomeprazole magnesium trihydrate in enteric coated tablet dosage form. This proposed method was validated in accordance with International Conference on Harmonization (ICH) guidelines [10].

MATERIALS AND METHODS

Methodology

Esmeran 20 mg tablets containing esomeprazole magnesium trihydrate was estimated by RP-HPLC using a mobile phase of mixture 60 volume acetonitrile and 40 volume of buffer of pH 6.8 and UV detector at 280 nm. The sample was compared to that of standard solution of known concentration.

Chromatographic conditions

Apparatus	HPLC
Column	Zorbax-SB C18, 250 × 4.6 mm, 5 µm
Flow Rate	1.0 ml/min
Detector	UV, 280 nm
Injection Volume	20 µl
Mobile Phase	ACN: Buffer (60:40)
pH	6.8

Preparation of buffer

Weigh accurately 6.8 g of potassium dihydrogen orthophosphate and 0.9 g of NaOH in 1000 ml of water; adjust pH 6.8 with 0.2 M NaOH.

Preparation of mobile phase

Prepare a mixture of 60 volume of acetonitrile and 40 volume of buffer, degas the mobile phase. Mobile phase is used as diluent.

Preparation of standard solution

Accurately weigh and transfer about 40 mg of esomeprazole working standard into a 200 ml volumetric flask. Add 70 ml of diluents sonicate to dissolve with intermediate shaking, dilute to volume with diluents. Filter the solution through 0.45 µ filter.

Preparation of sample

Weigh accurately 20 tablets and take average weight, crush the tablets and take the powder equivalent to 40 mg of esomeprazole into a 200 ml volumetric flask and add 70 ml of diluent, sonicate for about 30 min. Cool the sample solution make up to the volume with diluent. Filter the solution through 0.45 µ filter.

Calculations

Amount of esomeprazole was calculated using the formula:

$$\frac{AT}{AS}\times\frac{WS}{200}\times\frac{200}{WT}\times\frac{P}{100}\times\frac{690.84}{713.12}\times\frac{100}{LC}\times\text{Average weight}$$

Where, AT: Area of esomeprazole peak in sample preparation, AS: Average area of esomeprazole peak in standard preparation, WS: Weight of esomeprazole magnesium working standard in mg, WT: Weight of sample in mg, P: % purity of esomeprazole working standard on as such basis, LC: Label claim.

RESULTS AND DISCUSSION

System suitability

System suitability is an important parameter to perform the quality of the chromatographic system. The parameters are peak area and retention time which was calculated for the standard drug solutions and mentioned in Tables 1 and 2. Six injections of standard drug solution of esomeprazole were given to the system. The mean area, standard deviation and %RSD were calculated for the standard drug solution and it is shown in Table 1. It was observed that all the values are within the limits.

Table 1: System suitability for esomeprazole

S. No.	Standard	Concentration (µg/ml)	Area
1.	Standard -1	20	5761935
2.	Standard -2	20	5783992
3.	Standard -3	20	5803373
4.	Standard -4	20	5775334
5.	Standard -5	20	5764570
6.	Standard -6	20	5763878
Mean			5775514
Standard deviation			16047
%RSD			0.28

Table 2: System suitability parameters for esomeprazole

S. No.	System suitability parameters	Esomeprazole
1.	Retention time	3.22 min
2.	Peak area response	5775514

Specificity

In the specificity of the HPLC method complete separation of esomeprazole was noticed in presence of excipients. In addition there was no any interference at the retention time of placebo solution. In analysis the of peak purity with PDA, clarity of the angle was always less than purity threshold for the analyte. This shows that the peaks of analyte were pure and excipients in the formulation does not interfere the analyte. The results were shown in Table 3.

Table 3: Specificity for esomeprazole

S. No.	Name	No. of injections	Area
1.	Blank	1	Nil
2.	Placebo	1	Nil
3.	Standard_1	1	5588616
4.	Standard_2	1	5585984
5.	Standard_3	1	5586818
6.	Standard_4	1	5592170
7.	Standard_5	1	5590565
8.	Standard_6	1	5589151
9.	Sample_1	1	5588256
10.	Sample_2	1	5603801

Precision

The precision is defined as the closeness of agreement between a series of measurements obtained from multiple sampling of the homogenous sample under the prescribed conditions.

Repeatability

Repeatability is one of method in the precision which is done under the same operating conditions over a small period of time. One aspect of this is instrumental precision. A second one is sometimes termed intra-assay precision and involves several measurements of the same sample by the same analyst under the same conditions. Repeatability data for standard and sample esomeprazole were shown in Table 4. This indicated that the method was highly precise.

Table 4: Precision -repeatability for standard and sample esomeprazole

S. No.	Name	Area	Mean	Standard deviation	%RSD
1.	Standard -1	5793281	5806741	17528	0.30
2.	Standard -2	5795056			
3.	Standard -3	5796529			
4.	Standard -4	5797148			
5.	Standard -5	5831663			
6.	Standard -6	5826767			
7.	Sample -1	5876137	5838338	35439	0.61
8.	Sample -2	5784456			
9.	Sample -3	5879928			
10.	Sample -4	5829809			
11.	Sample -5	5829151			

Intermediate precision

Examines the precision between laboratories and is often determined in collaborative studies. Reproducibility data for Standard Esomeprazole and Sample were shown in Table 5. This indicated that method was highly precise.

Table 5: Precision-intermediate precision for standard and sample esomeprazole

S. No.	Name	Area	Mean	Standard deviation	%RSD
1	Standard -1	5793281	5806741	17528	0.30
2	Standard -2	5795056			
3	Standard -3	5796529			
4	Standard -4	5797148			
5	Standard -5	5831663			
6	Standard -6	5826767			
7	Sample -1	5845891	5823614	30822	0.53
8	Sample -2	5819548			
9	Sample -3	5871792			
10	Sample -4	5797933			
11	Sample -5	5788631			

Accuracy

Accuracy was done by standard addition method. The known quantity of standard esomeprazole was added to pre-analysed samples at a target level of 50%-150% and it was subjected to HPLC individually. The report of amount recovered was shown in Table 6. It was observed that the mean percentage recoveries were found to be within the limits, which demonstrates that the method was highly accurate.

Table 6: Accuracy for recovery solutions of esomeprazole

S. No.	Target level (%)	Area	Mean area	Amount recovered (mg/ml)	Recovery (%)
1.	50	3003738	2992384	19.87	99.35
2.	50	2980406			
3.	50	2993007			
4.	75	4358425	4364332	30.11	100.36
5.	75	4337907			
6.	75	4396663			
7.	100	5865261	5814726	40.47	101.17
8.	100	5779200			
9.	100	5799716			
10.	125	7241256	7240373	49.98	99.96
11.	125	7235297			
12.	125	7244565			
13.	150	8764755	8782579	59.91	99.85
14.	150	8776480			
15.	150	8806502			
Mean					**100.13**
Standard deviation					**0.1724**
%RSD					**0.17**

Linearity

The Linearity of this method was determined using five different concentrations from 50%-150% of Esomeprazole and it was shown in Table 7. The graph has been plotted using peak area against each sample respective concentration of esomeprazole which is found to be linear (Figures 1 and 2) in the range of 50%-150% of operating concentrations. Beer's law was found to be obeyed over this concentration range. The linearity was evaluated by using least square method for linear regression analysis. The regression equations were found to be Y=29111.2439x and correlation coefficient of the standard curves were found to be 0.9990 respectively. It observed that correlation coefficient and regression analysis are within the limits.

Table 7: Linearity response for standard linearity preparations of esomeprazole

S. No.	Linearity level	Concentration (µg/ml)ppm	Volume of stock solution (ml)	Volume made up to (ml)	Area
1.	50	100	2.0	20	3012722
2.	75	150	3.0	20	4311871
3.	100	200	4.0	20	5769835
4.	125	250	5.0	20	7242727
5.	150	300	6.0	20	8791094

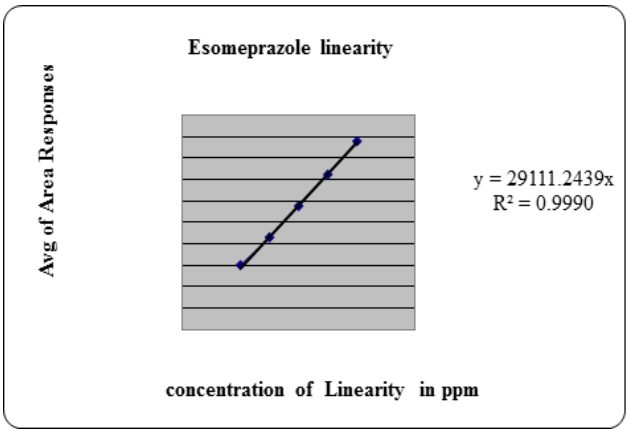

Figure 2: Linearity of response for esomeprazole enteric coated tablet

CONCLUSION

The proposed study describes new and simple RP-HPLC method for the estimation of esomeprazole in enteric coated tabled dosage form. The method was validated as per ICH guidelines and found to be simple, sensitive, accurate and precise. Therefore, the presented work can be effectively used for the routine analysis of estimation of esomeprazole in combined dosage form without interference.

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