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Method Development and Validation For The Simultaneous Estimation of Esomeprazole and Levosulpiride By Using RPHPLC In Its Bulk And Pharmaceutical Dosage Form

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ABSTRACT

Esomeprazole is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing oferosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcerrecurrence. Esomeprazole and Levosulpiride selective dopamine D2antagonist with antipsychotic and antidepressant activity.Asimple,Accurate, precise method was developed for the simultaneous estimation of the Esomeprazole and Levosulpiride in Tablet dosage form. Retentiontime of Esomeprazole and Levosulpiride were found to be 2.2min and 4.0min. % RSD of the Esomeprazole and Levosulpiride were and found to be 0.97 and 0.50 respectively. % Recover was Obtained as 100.08% and 101.16% for Esomeprazole and Levosulpiride respectively. LOD, LOQ values were obtained from regression equations of Esomeprazole and Levosulpiride were 0.10ppm, 0.34ppm and 0.29ppm, 1.04ppm respectively. Regression equation of Esomeprazole is y = 10568x + 307.3 and of Levosulpiride is y = 11649.x+ 1207. Retention times are decreased and thatrun time was decreased so the method developed was simple and economical that can be adopted in regular Quality control test in Industries.

Keywords: Esomeprazole, Levosulpiride, method developement, Quality control test, Simultaneous Estimation.

INTRODUCTION

Most of the pharmaceutical industries, are manufacturing multiple drug formulation to meet the market demand. It is a well-known fact that a combination of drug has a wider range to treat ailment as compared to a single drug components. There are many method reported for simultaneous analysis of drug component of multiple component formulation. Almost all pharmacopoeial methods available for the analysis of such formulation are applicable only after prior separation of drug components. Hence making them tedious and time consuming. There is likely to be loss of accuracy and precision due to extraction or separation. In the pharmaceutical field, for assurance of the quality of drug formulation, it become necessary to develop analytical method which should have accuracy and precision. The accuracy and precision depend upon the relative and absolute errors. Errors will be less, if the method is simple. The method can be directly related to accuracy and precision. Therefore simplicity of method should be one of the prime consideration while developing the method of analysis[1-2].

Esomeprazole is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing of erosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcerrecurrence. Esomeprazole AndLevosulpiride selective dopamine D2antagonist with antipsychotic and antidepressant activity[3]. The main objective of the study is to develop a rapid, specific and

economic Method and Validation For The Simultaneous Estimation Of Esomeprazole And Levosulpiride By Using RPHPLC In Its Bulk And Pharmaceutical Dosage Form[4].

MATERIALS AND METHOD

Materials

The drug samples, Esomeprazole and Levosulpiride working standards were obtained as gift sample by CiplaPvt. Ltd, Kurkumbh, Pune, India. Potassium dihydrogenortho phosphate,Ortho phosphoric acid, Ammonium acetate, Acetonitrile were purchased from Merck HPLC grade Specialties Private Limited, Mumbai, India. Methanol, and water used were analytical grade.

Instrumentation

Analytical balance by Aicoset. HPLC instrument Series by Alliance e2695 EMPOWER-2, Columns by INERTSILODS3(250mm,4.6mm,5μ)SUNFIREC_{18}(250mm, 4.6mm,5μ) HYPERSILBDSC_{18}(100,4.6mm,5µ), Sonicator by SONICA 2200MH, pH meter by Metler Toledo, Vacuum filter by Model XI5522050 of Millipore.

Experiementals

Methods

Preparation of buffer (0.01NKH_2Po_4)

Accurately weighed 1.36gm of potassium dihydrogenOrtho phosphate in a1000mlofVolumetricflaskaddabout900mlofmilli-Qwateranddegasinasonicator and finally make up the volume with water and pH adjusted to 5.4 with dil.OPA

Standard Preparation

Accurately Weighed and transferred 15 mg of levosulpiride and 8 mg of Esomeprazole working Standards into a 10ml clean dry volumetric flask, add 3/4thvolume of diluent, sonicated for 5 minutes and make up to the final volume with diluents. 1ml from the above two stock solutions was taken into a 10ml volumetric flask and made up to 10ml.

Sample Preparation

5 tablets were weighed and powdered and transferred into a 50mL volumetricflask, 35mL of diluent added and sonicated for 25 min, further the volume made upwith diluent and filtered.From the filtered solution 0.2 ml was pipetted out into a 10mlvolumetricflask andmadeupto10ml with diluent.

Linearity

Linearity solutions are prepared such that 0.25ml, 0.5ml, 0.75ml, 1ml, 1.25ml, 1.5ml from the Stock solutions of Esomeprazole and Levosulpiride are taken in to 6differentvolumetricflasksanddilutedto10mlwithdiluentstoget20ppm,40 ppm. 60 ppm, 80 ppm, 100 ppm, 120 ppm of Esomeprazole and 37.5 ppm, 75 ppm, 112.5 ppm, 150 ppm, 187.5 ppm, 225 ppm of Levosulpiride.

Standard Preparation

AccuratelyWeighedandtransferred15mgoflevosulpirideand8 mgofEsomeprazole working Standards into a 10ml clean dry volumetric flask, add 3/4thvolume of diluent, sonicated for 5 minutes and make up to the final volume withdiluents. 1ml from the above two stock solutions was taken into a 10ml volumetricflaskand madeup to 10ml.

Sample Preparation

5 tablets were weighed and powdered and transferred into a 50mL volumetricflask, 35mL of diluent added and sonicated for 25 min, further the volume made up with diluent and filtered.From the filtered solution 0.2 ml was pipetted out into a 10 ml volumetric flask and made upto10ml with diluent.

Standard Preparation

Accurately Weighed and transferred 15 mg of levosulpiride and 8 mg of Esomeprazole working Standards into a 10ml clean dry volumetric flask, add 3/4thvolume of diluent, sonicated for 5 minutes and make up to the final volume with diluents. 1ml from the above two stock solutions was taken into a 10ml volumetricflaskand madeup to 10ml.

Sample preparation **50%:** 5 tablets were weighed and calculate the average weight of each tablet then 750 mg tablet powder was transferred into a 50 ml volumetric flask, 30 ml of diluent added and sonicated for 25 min, further the volume made up with diluent and filtered. From the filtered solution 0.2ml was pipetted out into a 10 ml volumetric flask and made up to 10ml with diluent.

100%: 5 tablets were weighed and calculate the average weight of each tablet then 1500mg tablet powder was transferred into a 50mL volumetric flask, 30ml of diluent added and sonicated for 25 min, further the volume made up with diluent and filtered. From the filtered solution 0.2ml was pipetted out into a 10 ml volumetric flask and made up to 10ml with diluent.

150%: 5 tablets were weighed and calculate the average weight of each tabletthen 2250mg tablet powder was transferred into a 50mL volumetric flask, 30mL of diluent added and sonicated for 25 min, further the volume made up with diluent andfiltered. From the filtered solution 0.2ml was pipetted out into a 10 ml volumetric flask and madeup to 10ml with diluent.

Method Development

Many trials were done by changing columns and Mobile phases and werereportedbelow.

Trial I

This trial was run through ods 250 column with mobile phase composition of 55:45 Buffer and Acetonitrile, Flow rate set at 1ml/min.

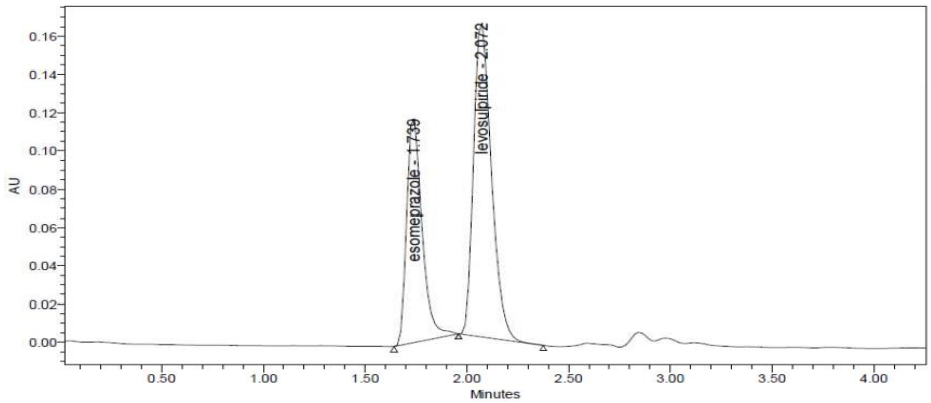

Fig 1: Trial chromatogram
Observation: resolution is not good

Trial II

This trial was run through ODS 250 mm column with mobile phase composition of 50:50 A water and Acetonitrile Flow rate set at 1 ml / min.

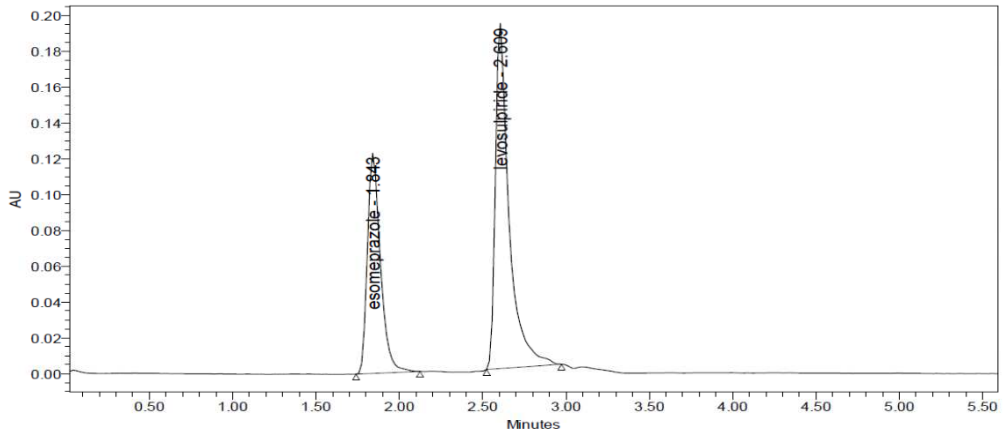

Fig2:TrialchromatogramObservation:
Esomeprazoleelutedin voidrange.

Trial III

This trial was run through ODS 250 mm column with mobile phase composition of 40:60 A water and Acetonitrile, Flow rate set at 1ml/min.

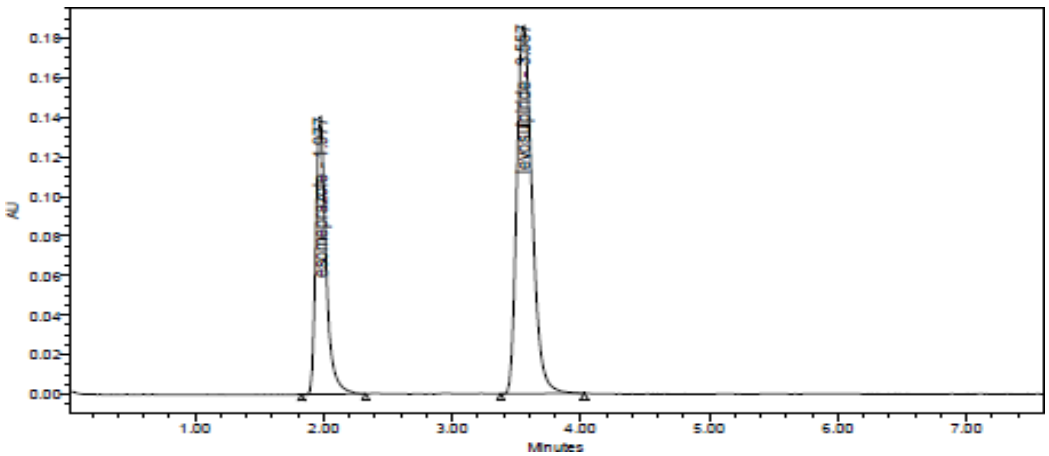

Fig 3: Trial chromatogram
Observation: Esomeprazole elute din void range.

Optimized Method : Drugs were eluted with good retention time, resolution; all the system suitable parameters like Plate count and Tailing factor were within the limits.
Mobile phase: Buffer and Acetonitrile taken in the ratio 32 B : 68A
Chromatographic conditions:
Flow rate **: 1**ml/min
Column **:** ODS 150mmx4.6mm,5□.
Detector wavelength : 290 nm
Column temperature : 30 ° C
Injection volume: 10□L
Run time **:** 7min
Diluent **:** water: methanol 50:50

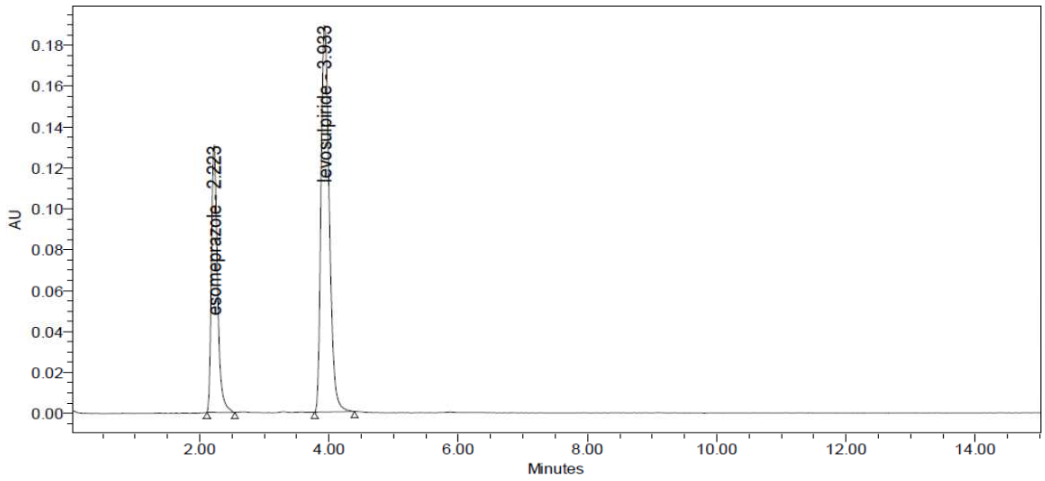

Fig 4: Optimized chromatogram of Esomeprazole and Levosulpiride

RESULTS AND DISCUSSIONS

System suitability

All the system suitability parameters are within range and satisfactoryasperICHguidelines.

Table1: System suitability studies of Esomeprazole and Levosulpiride method

Property			Esomeprazole	Levosulpiride
Retentiontime(tR)			2.21±0.3min	4.01±0.3min
Theoreticalplates(N)			2641 ±163.48	4414±163.48
Tailingfactor(T)	1.45 ±0.117	1.36±0.117		

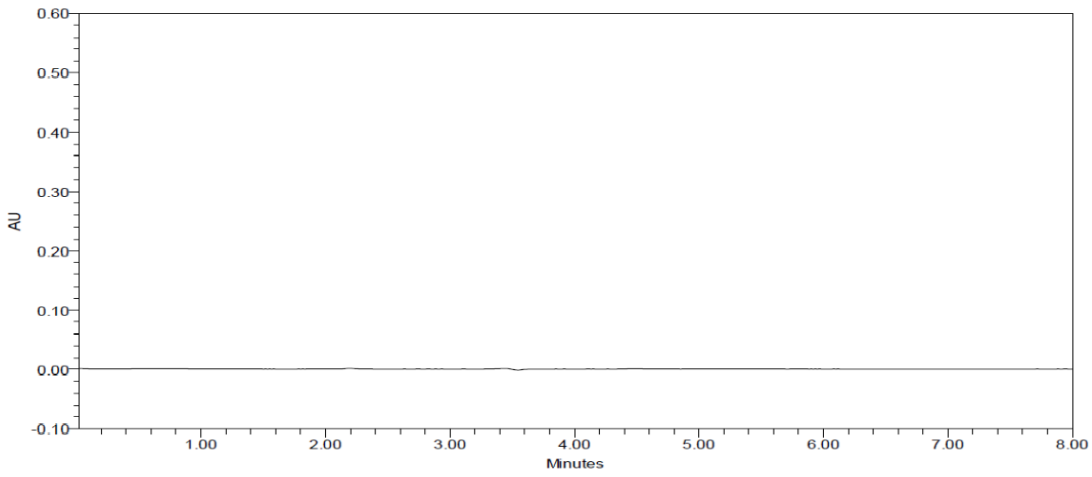

Fig 5: Chromatogramof blank

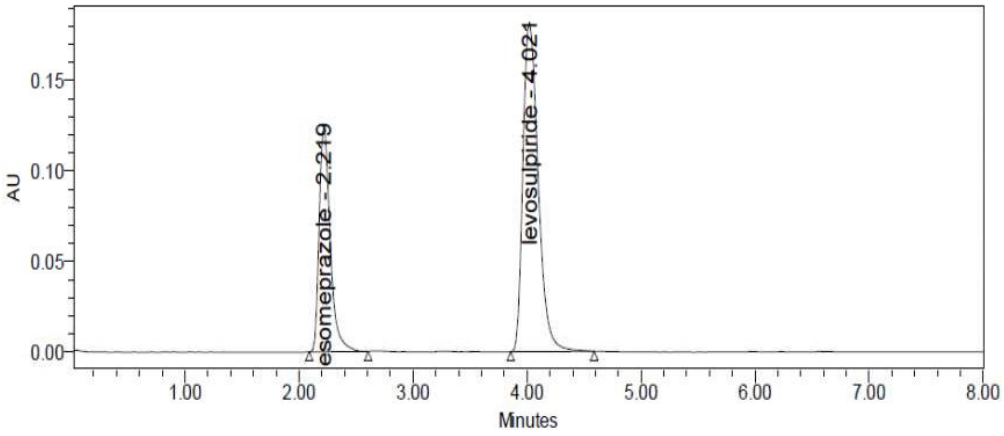

Fig 6: Typical chromategram of Esomeprazole and Levosulpiride

Linearity

Six Linear concentrations of Esomeprazole (20-120 ppm) and Levosulpiride (37.5 ppm to 225 ppm) are prepared and Injected. Regression equation of the the Esomeprazole and Levosulpiride are found to be, y = 10568x +307.3,y = 11649.x+120.7 and regression co-efficient was 0.999.

Table 2 : Calibration data of Esomeprazole and Levosulpiride method

S.No.	Concentration Esomeprazole(µg/ml)	Response	Concentration Levosulpiride(µg/ml)	Response
1	0	0	0	0
2	20	219743	37.5	436194
3	40	420301	75	891483
4	60	632028	112.5	1323196
5	80	839036	150	1697713
6	100	1049902	187.5	2202932
7	120	1279655	225	2630631

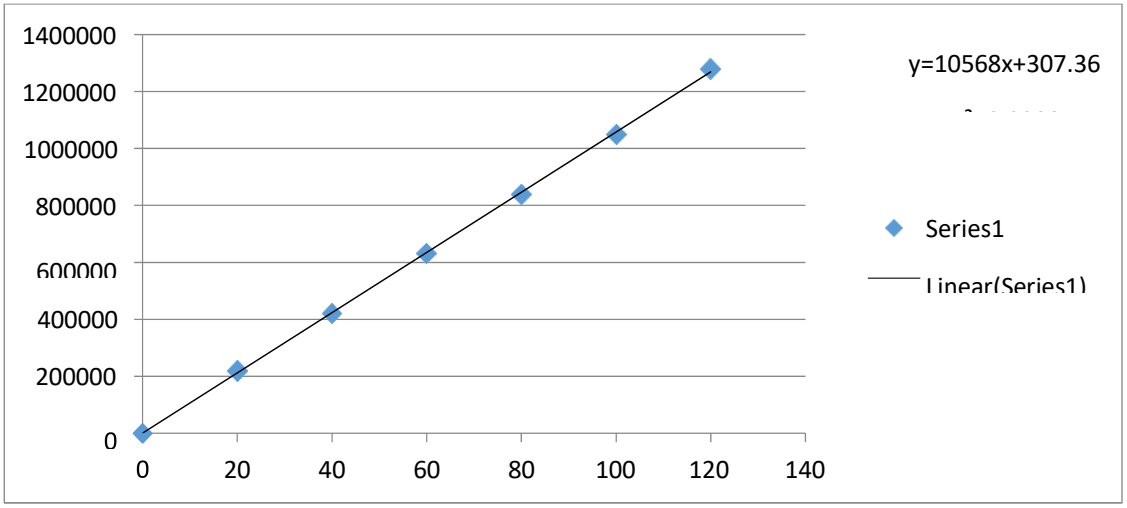

Fig 7: Calibration curve of Esomeprazole

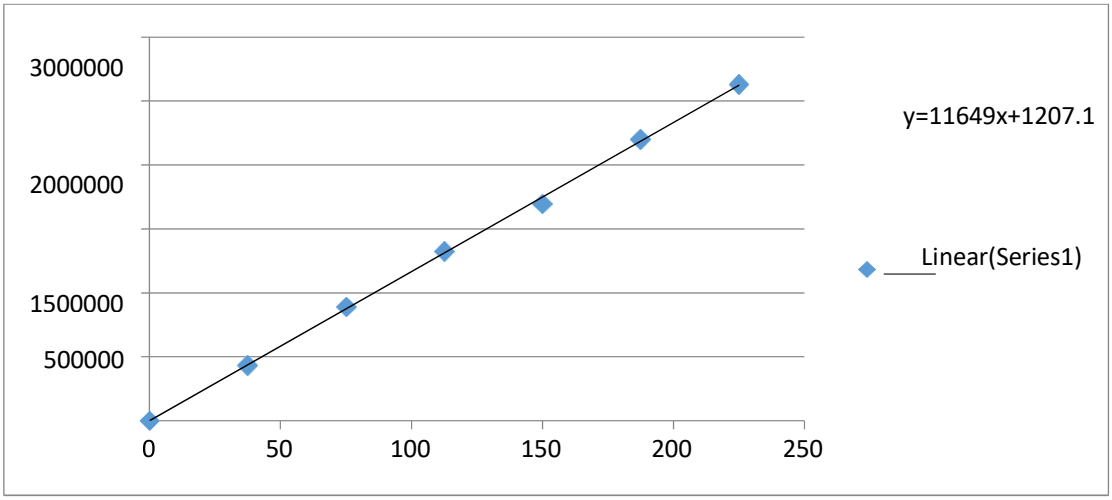

Fig 8: Calibration curve of Levosulpiride

Precision

Intraday precision (Repeatability)

Intraday Precision was performed and % RSD for Esomeprazole and Levosulpiride were found to be 1.3 % and 0.1 % respectively.

Table 3:Repeatability results for Esomeprazole and Levosulpiride.

Sr.No.	Esomeprazole	Levosulpiride
1	814986	1754081
2	825795	1754437
3	840851	1758333
4	819155	1752184
5	822084	1752359
6	839797	1754366
Mean	827111	1754293
Std.Dev.	10835.5	2217.2
%RSD	1.3	0.1

*Average of six determinations

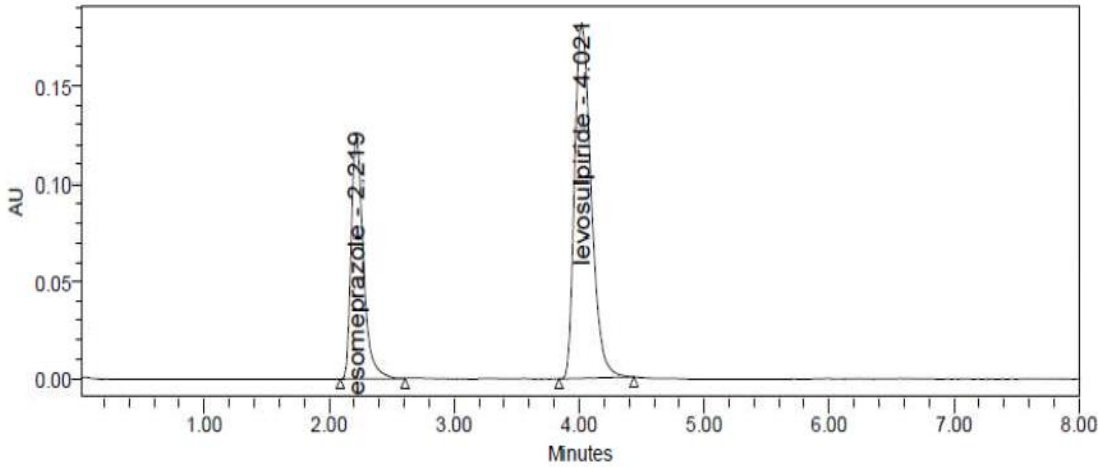

Fig 9: Repeatability Chromatogram of Esomeprazole and Levosulpiride method.

Interday precision

Interday precision was performed with 24 hrs time lag and the % RSD Obtained for Esomeprazole and Levosulpiride were 1.0 % and 0.5 %

Table 4 : Interday precision results for Esomeprazole and Levosulpiride

Sr.No.	Esomeprazole	Levosulpiride
1	834986	1743927
2	843663	1732187
3	830708	1728243
4	848290	1726706
5	832084	1720428
6	848665	1739622
Mean	839732.7	1731852
Std.Dev.	8135.6	8675.3
%RSD	1.0	0.5

LOD

The parameter LOD was determined by analysis of sample with known concentration of analyte and by establishing the minimum level at which the analyte can be reliably detected. LOD for Esomeprazole and Levosulpiride were found to be 0.10 and 1.04 respectively.

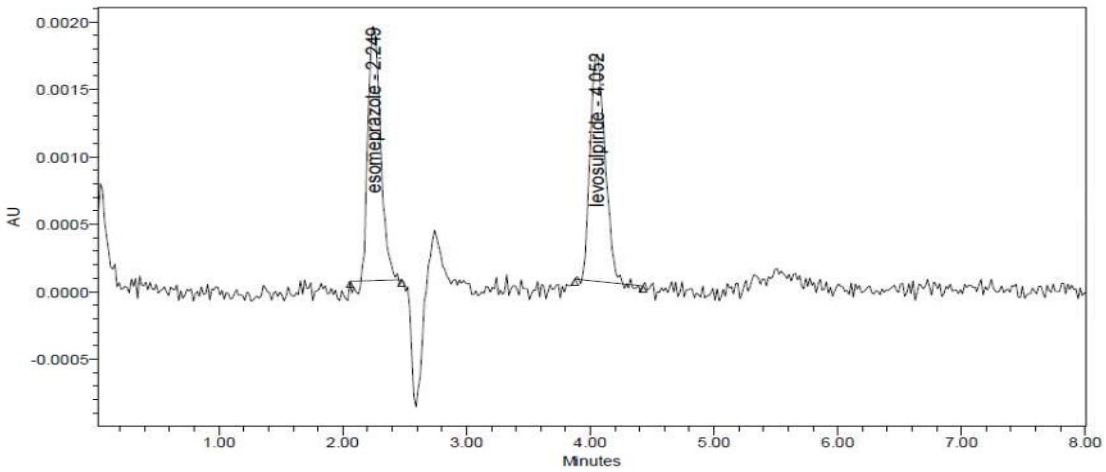

Fig 10: LOD Chromatogram of Esomeprazole and Levosulpiride method.

Robustness

Small deliberate changes in method like Flow rate, mobile phase ratio, and temperature are made but there were no recognized change in the result and are within range as per ICH Guidelines.

Table 5: Robustness data of Esomeprazole and Levosulpiride method.

S.NO	Robustnesscondition	Esomeprazole %RSD	Levosulpiride %RSD
1	Flowminus	0.4	1.0
2	FlowPlus	0.4	0.4
3	Mobilephaseminus	0.1	0.0
4	MobilephasePlus	0.1	0.1
5	Temperatureminus	0.2	0.5
6	TemperaturePlus	0.3	0.5

Assay

Standard preparations are made from the API and Sample Preparations arefrom Formulation. Both sample and standards are injected six homogeneous samples.

Drug in the formulation was estimated by taking the standard as the reference. The Average % Assay was calculated and found to be 100.08 % and 101.16 % for Esomeprazole and Levosulpiride respectively.

Table 6: Assay of Tablet

S.No.	Esomeprazole %Assay	Levosulpiride %Assay
1	99.51463	101.865
2	100.5488	101.1793
3	99.00477	100.9489
4	101.1002	100.8591
5	99.16876	100.4924
6	101.1449	101.6136
AVG	100.08	101.16
STDEV	0.97	0.51
%RSD	0.97	0.50

Summary (table)

Table 7: Summary Table

Parameters	Esomeprazole	Levosulpiride
Calibration range(mcg/ml)	20-120ppm	37.5-225ppm
Optimized wavelength	290nm	290nm
Retention time	2.2min	4.0min
Regression equation(Y*)	y=10568.x+307.3	y=11649.x+1207
Correlation coefficient(r^2)	0.999	0.999
Precision(%RSD*)	0.97	0.50
%Recovery	100.08%	101.16%
Limit of Detection(mcg/ml)	0.10ppm	0.34ppm
Limit of Quantitation(mcg/ml)	0.29ppm	1.04ppm

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CONCLUSION

A simple, Accurate, precise method was developed for the simultaneous estimation of the Esomeprazole and Levosulpiride in Tablet dosage form. Retentiontime of Esomeprazole and Levosulpiride were found to be 2.2min and 4.0min. % RSD of the Esomeprazole and Levosulpiride were and found to be 0.97 and 0.50 respectively. % Recover was Obtained as 100.08 % and 101.16 % for Esomeprazole and Levosulpiride respectively. LOD, LOQ values are obtained from regression equations of Esomeprazole and Levosulpiride were 0.10ppm, 0.34ppm and 0.29ppm, 1.04ppm respectively. Regression equation of Esomeprazole is y = 10568x + 307.3, and of Levosulpiride is y = 11649 .x + 1207. Retention times are decreased and that run time was decreased so the method developed was simple and economical that can be adopted in regular Qualitycontroltest inIndustries.

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