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ESTIMATION OF NAPROXEN AND ESOMEPRAZOLE SIMULTANEOUSLY IN TABLET DOSAGE FORM BY RP-HPLC METHOD

M. Prasanthi Evangelin*, Amgotu Vamsi, Manohar Babu S

Assistant Professor, SIMS College of Pharmacy, SIMS Group of Institutions, Mangaldas Nagar, Guntur,-522001, Andhra Pradesh, India.

Abstract:

Estimation of Naproxen and Esomeprazole simultaneously in tablet dosage forms by RP-HPLC method. The analytical method was developed by studying different parameters. First of all, maximum absorbance was found to be at 332nm Naproxen for and 285nm for Esomeprazole. Common wavelength will be 272nm and the peaks purity was excellent. Injection volume was selected to be 20µl which gave a good peak area. The column used for study was Inertsil C_{18}, ODS chosen good peak shape. Ambient temperature was found to be suitable for the nature of drug solution. The flow rate was fixed at 1.0ml/min because of good peak area, satisfactory retention time and good resolution. Different ratios of mobile phase were studied, mobile phase with ratio of 45:55 Methanol: Buffer was fixed due to good symmetrical peaks and for good resolution. So this mobile phase was used for the proposed study. The present recovery was found to be 98.0-101.50 was linear and precise over the same range. Both system and method precision was found to be accurate and well within range. Detection limit was found to be 0.25 Naproxen and 0.52 for Esomeprazole. Linearity study was, correlation coefficient and curve fitting was found to be. The analytical method was found linearity over the range of 20-80ppm of the target concentration for both the drugs. The analytical passed both robustness and ruggedness tests. On both cases, relative standard deviation was well satisfactory.

Keywords: *Naproxen, Esomeprazole, RP-HPLC method*

Corresponding Author:

M. Prasanthi Evangelin,
Assistant Professor,
SIMS College of Pharmacy,
SIMS Group of Institutions,
Mangaldas Nagar,
Guntur,-522001,
Andhra Pradesh, India.

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1. INTRODUCTION:

Pharmaceutical Analysis plays a very vital role in the quality assurance and quality control of bulk drugs and their formulations. Pharmaceutical analysis is a specialized branch of analytical chemistry which involves separating, identifying and determining the relative amounts of components in a sample of matter. It is concerned with the chemical characterization of matter both quantitative and qualitative. In recent years, several analytical techniques have been evolved [1-3].

SPECTROPHOTOMETRIC METHODS [3-5]

Spectrophotometry is generally preferred especially by small-scale industries as the cost of the equipment is less and the maintenance problems are minimal. The method of analysis is based on measuring the absorption of a monochromatic light by colorless compounds in the near ultraviolet path of spectrum (200-380nm). The photometric methods of analysis are based on the Bouger-Lambert-Beer‟s law, which establishes the absorbance of a solution is directly proportional to the concentration of the analyte. The fundamental principle of operation of spectrophotometer covering UV region consists in that light of definite interval of wavelength passes through a cell with solvent and falls on to the photoelectric cell that transforms the radiant energy into electrical energy measured by a galvanometer.

The important applications are [6]

- Identification of many types of organic, inorganic molecules and ions.
- Quantitative determination of many biological, organic and inorganic species.
- Monitoring and identification of chromatographic of effluents.

MODES OF CHROMATOGRAPHY [7]

Modes of chromatography are defined essentially according to the nature of the interactions between the solute and the stationary phase, which may arise from hydrogen bonding, Vander walls forces, electrostatic forces or hydrophobic forces or basing on the size of the particles (e.g. Size exclusion chromatography).

Different modes of chromatography are as follows [8]

- Normal Phase Chromatography
- Reversed Phase Chromatography
- Reversed Phase – ion pair Chromatography
- Ion-Exchange Chromatography
- Size Exclusion Chromatography

Table-1- Classification of Chromatographic Methods

Stationary phase	Mobile phase	Method
Solid	Liquid	Adsorption column, thin-layer, ion exchange, High performance liquid chromatography.
Liquid	Liquid	Partition, column, thin-layer, HPLC, paper chromatography.
	Gas	Gas–Liquid Chromatography

The modern form of column chromatography has been called high performance, high pressure, and high-resolution and high-speed liquid chromatography.

High-Performance Liquid Chromatography (HPLC) is a special branch of column chromatography in which the mobile phase is forced through the column at high speed. As a result the analysis time is reduced by 1-2 orders of magnitude relative to classical column chromatography and the use of much smaller particles of the adsorbent or support becomes possible increasing the column efficiency substantially [9].

2. MATERIALS AND METHODS:

Naproxen and Esomeprazole, Methanol HPLC Grade, Buffer (KH2PO4) Hplc Grade

OPTIMIZED METHOD

Mobile Phase: Degassed Methanol and Buffer in the ratio of 60:40 V/V.

Preparation of(KH2PO4 0.1M) buffer: Weight 3.8954g of di-sodium hydrogen phosphate and 3.4023 of potassium dihydrogen phosphate in to a beaker containing 1000ml of distilled water and dissolve completely. Then ph is adjusted with orthophosphoric acid and then filtered through 0.45µm membrane filter.

Preparation of stock solution:

Reference solution: The solution was prepared by dissolving 20.0 mg of accurately weighed Naproxen and 25.0 mg Esomeprazole in Mobile phase, in two 100.0 mL volumetric flasks separately and sonicate for 20min. From the above solutions take 10.0 mL from each solution into a 50.0 mL volumetric flask

and then makeup with mobile phase and sonicate for 10min.

Preparation of working standard solution:

The stock solutions equivalent to 20ppm to 80ppm with respect to both drugs were prepared in combination of Naproxen and Esomeprazole above, sonicated and filtered through 0.45µ membrane.

Table 2: Optimized chromatographic conditions:

Parameters	Method
Stationary phase (column)	Inertsil -ODS C_{18}(250 x 4.6 mm, 5 µ)
Mobile Phase	Methanol : Buffer (45:55)
Flow rate (ml/min)	1.0 ml/min
Run time (minutes)	10 min
Column temperature (°C)	Ambient
Volume of injection loop (µl)	20
Drug RT (min)	3.532 for Esomeprazole and 2.955 for Naproxen
Detection wavelength (nm)	272nm

3. RESULTS AND DISCUSSION:

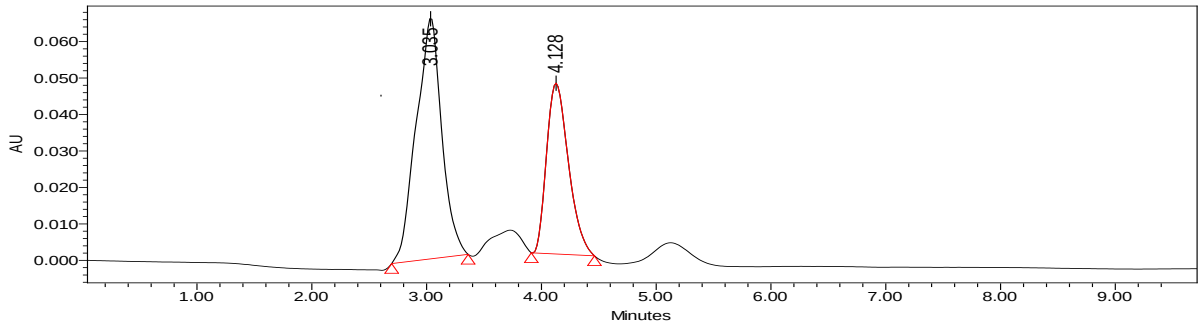


Fig1: Chromatogram of Trial 1

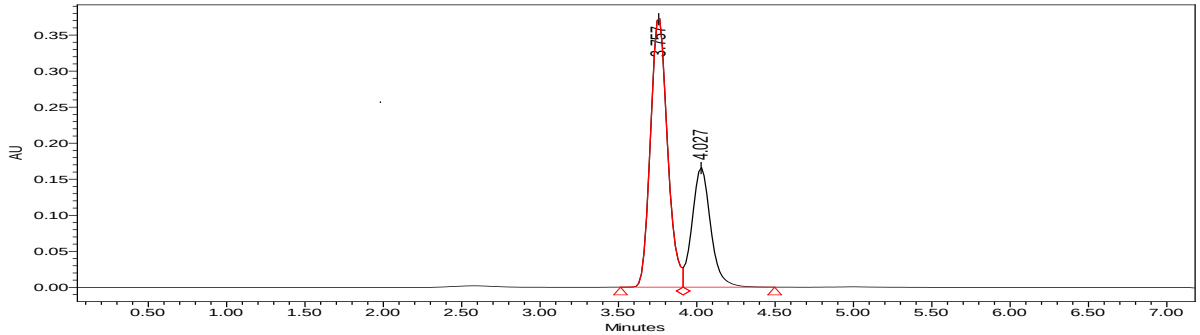


Fig 2: Chromatogram of Trial 2:

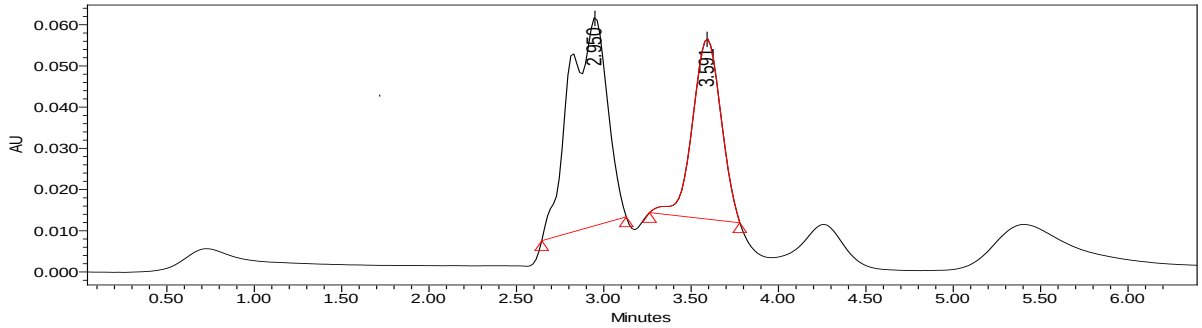


Fig 3: Chromatogram of Trial3

OPTIMIZED METHOD

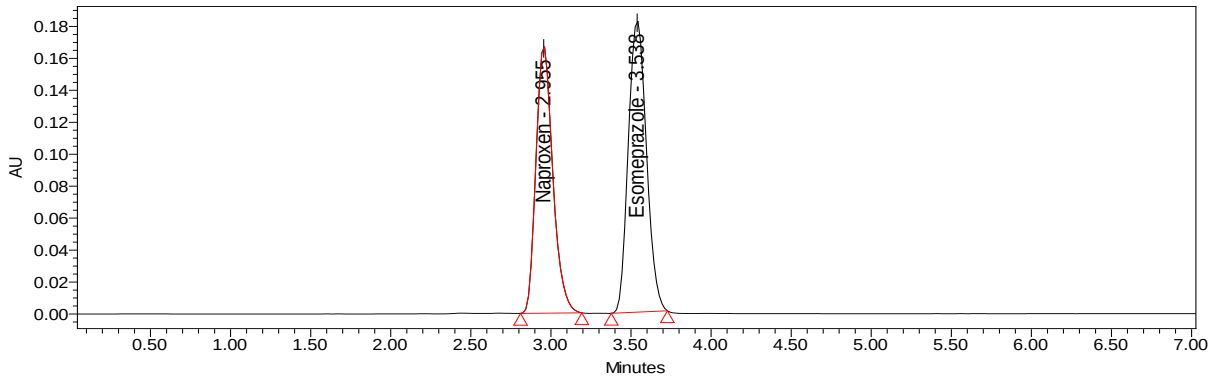


Fig 4: Chromatogram of standard

Inference: Got chromatogram at RT's of 2.955min to Naproxen and 3.538min to Esomeprazole

S.NO	Name of the peak	Retention time(min)
1	**Naproxen**	2.955
2	**Esomeprazole**	3.532

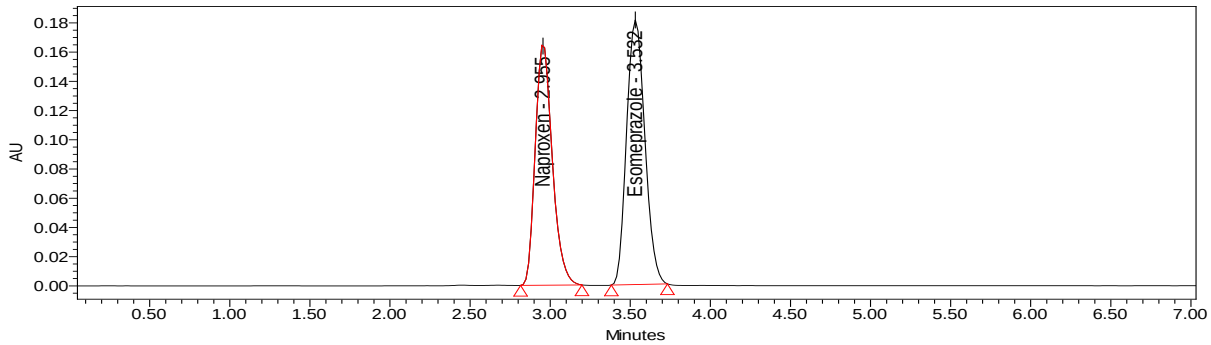


Fig5:Chromatogram of sample

Inference: Got same chromatogram with same RT values as of standard.

S.NO	Name of the peak	Retention time(min)
1	**Naproxen**	2.955
2	**Esomeprazole**	3.532

TABLE- 3(a): Data of System Suitability forNaproxen

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	2.869	1139272	5890.964069	1.238915
2	2.868	1140892	5915.423628	1.230637
3	2.872	1136301	5934.796986	1.240858
4	2.868	1141067	5976.253744	1.238995
5	2.872	1136024	5953.814152	1.241073
Mean	2.873218	1138711	5934.251	1.236496
SD	0.000837	57540.015	-------	-------
% RSD	0.028363	0.213538	-------	-------

TABLE-3(b): Data of System Suitability for Esomeprazole

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	2.955	2164732	6648.722084	1.119216
2	2.956	2161848	6673.911816	1.142210
3	2.955	2198427	6630.743655	1.167058
4	2.954	2231236	6778.292084	1.140170
5	2.954	2254490	6687.924039	1.132946
Mean	2.955318	2202147	6683.919	1.14032
SD	0.000837	40693.03	-------	-------
% RSD	0.026462	1.84788	-------	-------

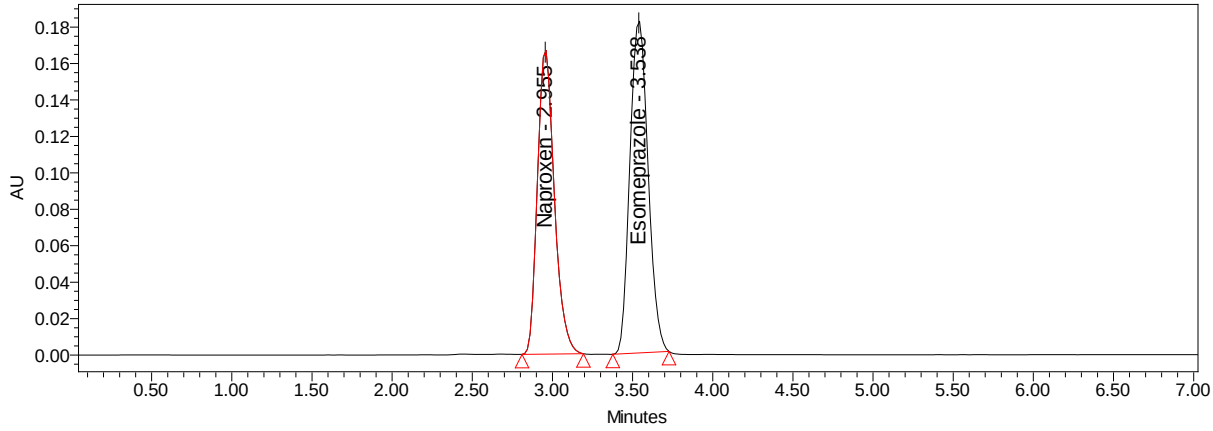


Fig: 6 Chromatograms of system suitability

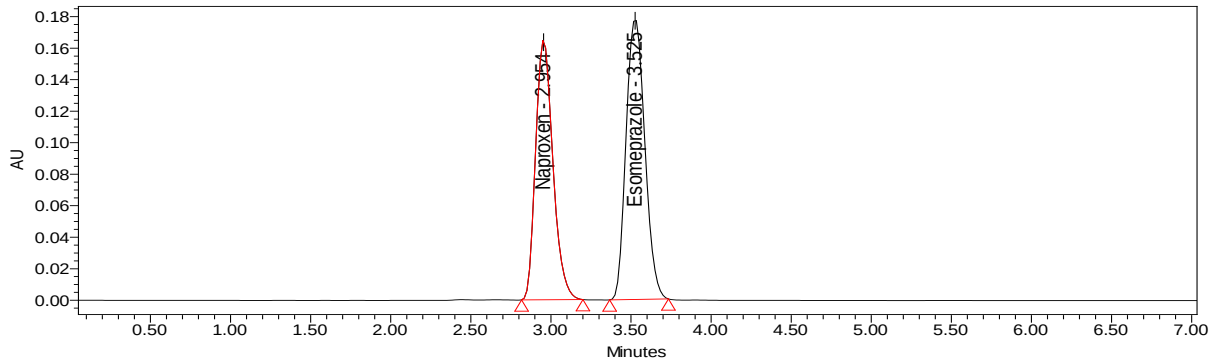


Fig 7: Chromatogram of standard Specificity

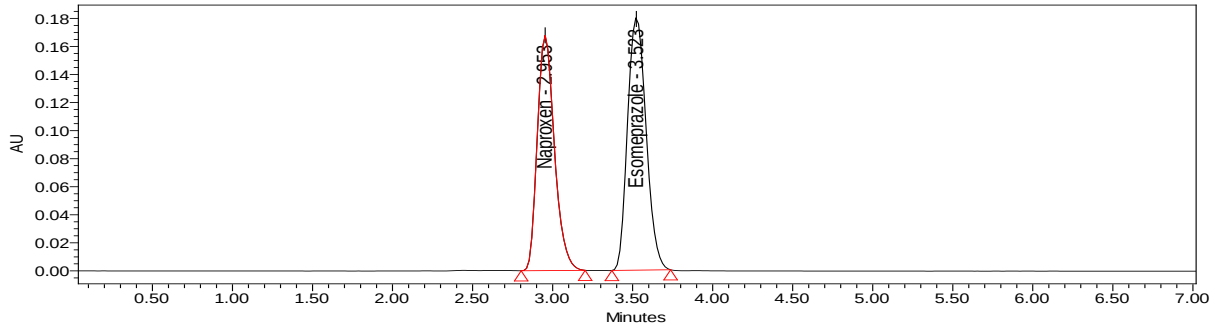


Fig 8: Chromatogram of sample Specificity

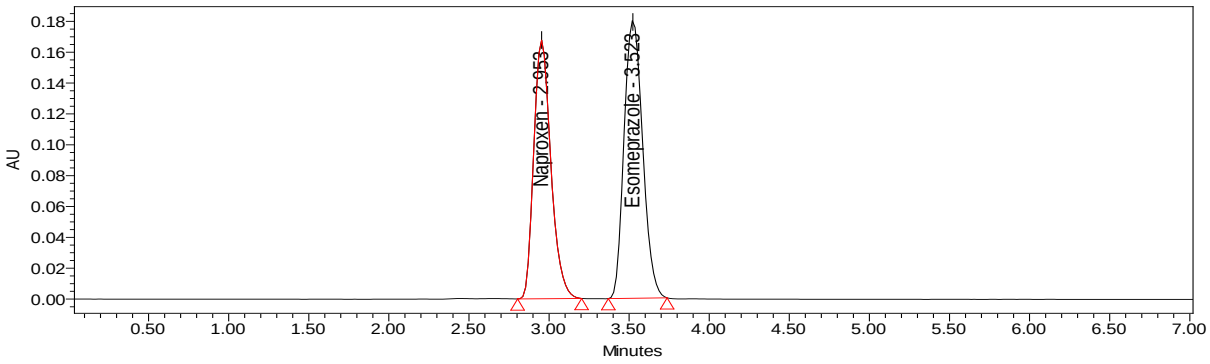


Fig:9 Chromatogram for system precision

TABLE-4(i): Data of Repeatability (System precision) for Naproxen

	Injection	**Peak Areas of** Naproxen	**%Assay**
Concentration 40ppm	1	1146923	99.65
	2	1143596	99.08
	3	1158293	99.98
	4	1147283	100.04
	5	1152490	100.16
Statistical Analysis	**Mean**	1149717	99.78
	SD	5754.015	0.435569
	% RSD	0.500472	0.43652

TABLE-4(ii): Data of Repeatability (System precision) for Esomeprazole

	Injection	**Peak Areas of Esomeprazole**	**%Assay**
Concentration 40ppm	1	2164732	98.66
	2	2161848	99.30
	3	2198427	101.53
	4	2231236	100.53
	5	2254490	99.98
Statistical Analysis	**Mean**	2202147	100.00
	SD	40693.03	1.107678
	% RSD	1.84788	1.10

TABLE-5(i): Data of Repeatability (Method precision) forNaproxen

	Injection	**Peak Areas of Naproxen**	**%Assay**
Concentration 40ppm	1	1152293	99.55
	2	1146923	99.88
	3	1147283	99.40
	4	1152490	99.56
	5	1139272	99.85
	6	1147283	99.40
Statistical Analysis	**Mean**	1147591	99.67
	SD	4815.615	0.250093
	% RSD	0.419628	0.250913

TABLE-5(ii): Data of Repeatability (Method precision) for Esomeprazole

	Injection	**Peak Areas of Esomeprazole**	**%Assay**
Concentration 40ppm	1	2245703	99.55
	2	2291408	99.88
	3	2278639	99.40
	4	2239286	100.30
	5	2267407	100.53
	6	2278639	99.28
Statistical Analysis	**Mean**	2266847	99.82333
	SD	20436.91	0.505754
	% RSD	0.901557	0.506649

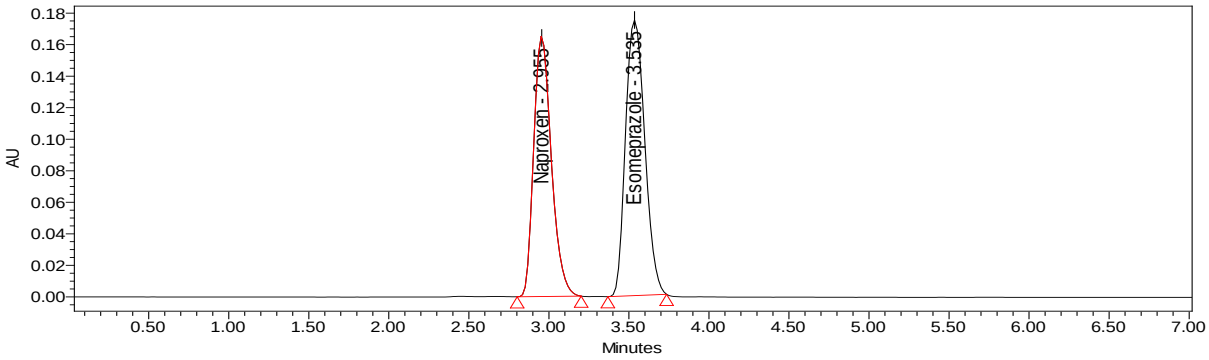


Fig 10: Chromatograms of Repeatability

TABLE-6 (i) Data of Intermediate precision (Analyst 2) forNaproxen

	Injection	**Peak Areas of Naproxen**	**%Assay**
Concentration 40ppm	1	1139272	98.80
	2	1140892	99.54
	3	1136601	99.98
	4	1141067	100.02
	5	1136024	101.08
	6	1140892	99.54
Statistical Analysis	**Mean**	1139125	99.82
	SD	2281.417	0.755001
	% RSD	0.200278	0.756312

TABLE-6 (ii)Data of Intermediate precision (Analyst 2) for Esomeprazole

	Injection	**Peak Areas of Esomeprazole**	**%Assay**
Concentration 40ppm	1	2278639	99.99
	2	224732	99.66
	3	2267407	101.53
	4	2254490	99.98
	5	2231236	99.97
	6	2267407	101.10
Statistical Analysis	**Mean**	2260652	100.37
	SD	16338.36	0.753536
	% RSD	0.722728	0.75

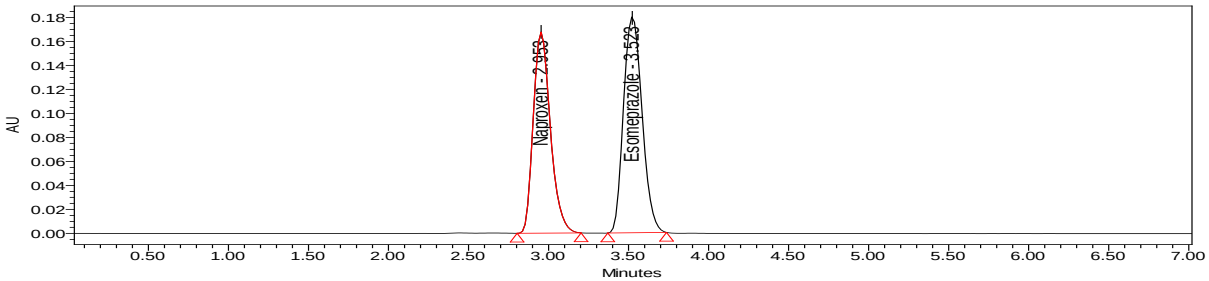


Fig 11: Chromatograms of Intermediate precision

TABLE-7 (i)Data of Accuracy for Naproxen

Concentration % of spiked level	**Amount added (ppm)**	**Amount found (ppm)**	**% Recovery**	**Statistical Analysis of % Recovery**	
50% Injection 1	20	19.85	99.25	**MEAN**	99.88
50% Injection 2	20	19.96	99.80		
50 %Injection 3	20	20.12	100.6	**%RSD**	0.67
100 % Injection 1	40	39.74	99.35	**MEAN**	99.81
100 % Injection 2	40	40.08	100.2		
100% Injection 3	40	40.24	100.6	**%RSD**	0.399
150% Injection 1	60	59.04	98.40	**MEAN**	99.19
150% Injection 2	60	59.62	99.36		
150% Injection 3	60	59.89	99.81	**%RSD**	0.72

TABLE-7 (ii)Data of Accuracy for Esomeprazole

Concentration % of spiked level	Amount added (ppm)	Amount found (ppm)	% Recovery	Statistical Analysis of % Recovery	
50% Injection 1	20	19.86	99.30	**MEAN**	99.46
50% Injection 2	20	19.98	99.90		
50% Injection 3	20	19.84	99.20	**%RSD**	0.38
100 % Injection 1	40	39.54	98.85	**MEAN**	99.76
100 % Injection 2	40	39.82	99.55		
100% Injection 3	40	39.96	99.9	**%RSD**	0.189
150% Injection 1	60	59.92	99.86	**MEAN**	100.0067
150% Injection 2	60	60.08	100.13		
150% Injection 3	60	60.02	100.03	**%RSD**	0.136

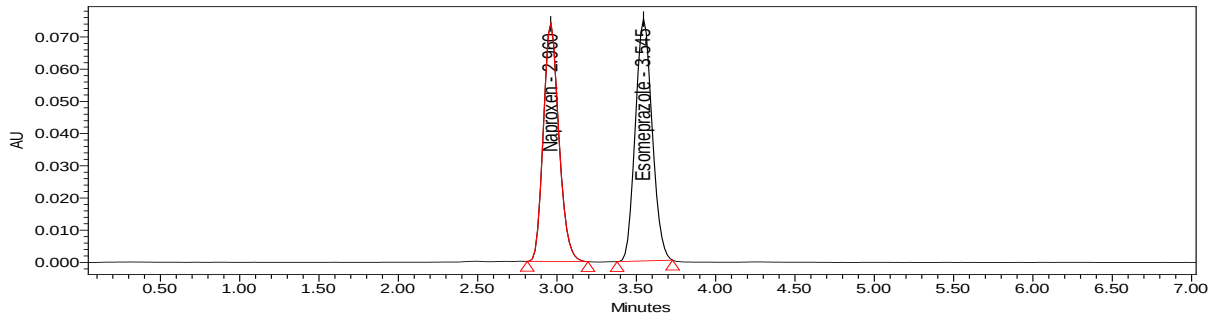


Fig.12: Chromatograms for accuracy (50%)

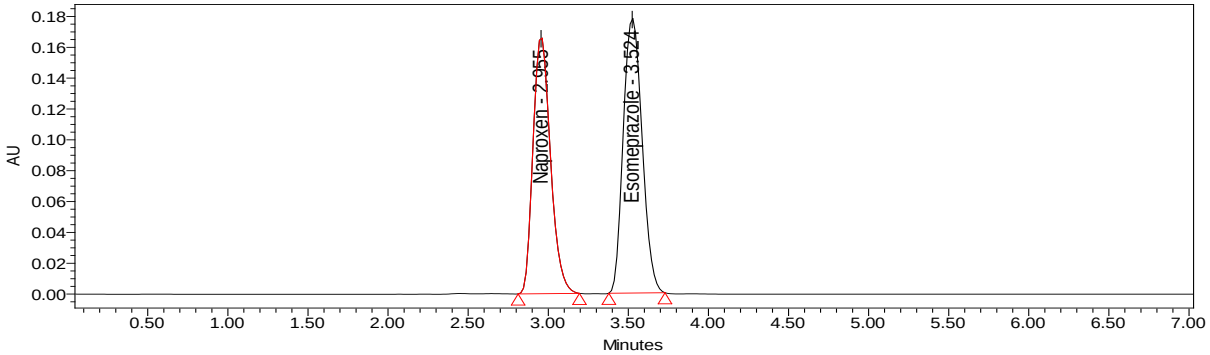


Fig 13: Chromatograms for accuracy (100%)

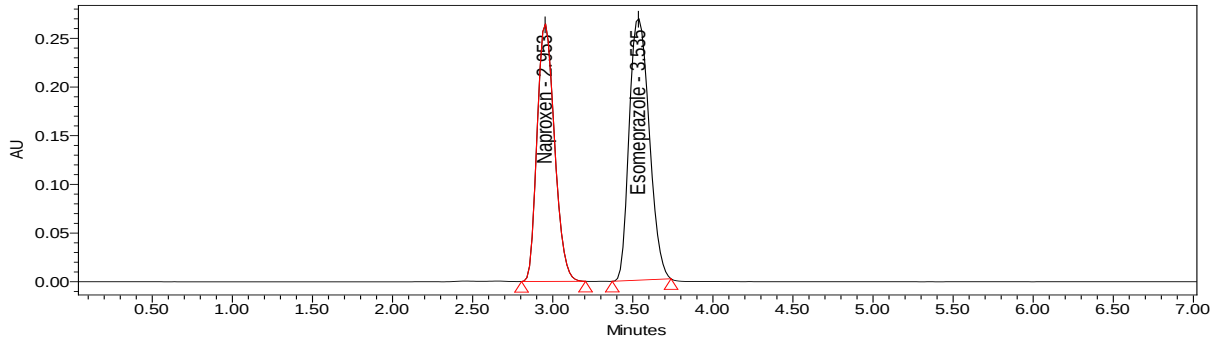


Fig 14: chromatograms For Accuracy (150%)

TABLE8 (i) Data of Linearity (Naproxen)

Concentration (ppm)	**Average Area**	**Statistical Analysis**	
0	0	Slope	31282
20	523467	y-Intercept	11218
30	829544	Correlation Coefficient	0.999
40	1139272		
50	1448018		
60	1728926		
70	2089505		
80	2407574		

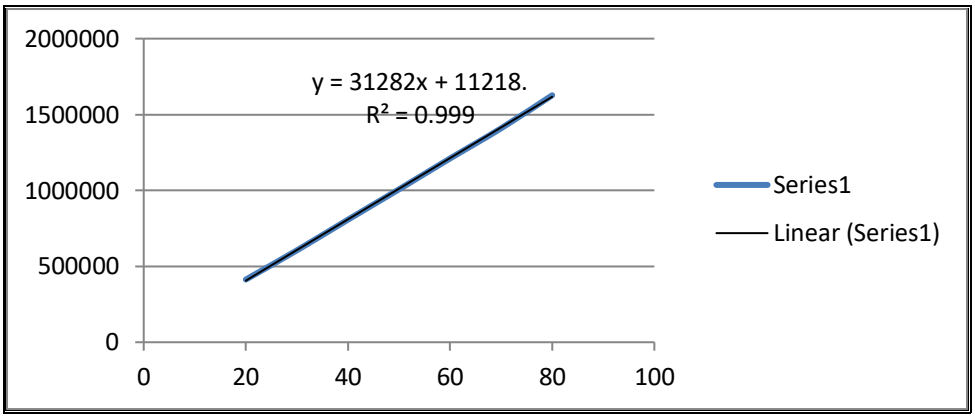


Fig: 9(a) Linearity Plot (Concentration Vs Response) of**Naproxen**

(ii) Data of Linearity (Esomeprazole)

Concentration (ppm)	**Average Area**	**Statistical Analysis**	
0	0	Slope	10310
20	560960	y-Intercept	540.63
30	1602034	Correlation Coefficient	0.999
40	2164732		
50	3171457		
60	4138838		
70	5276830		
80	6523097		

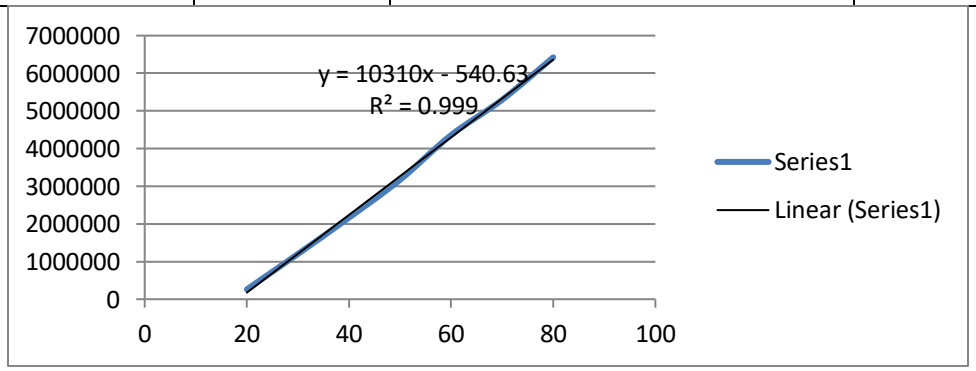


Fig: 15(b) Linearity Plot (Concentration Vs Response) **of Esomeprazole**

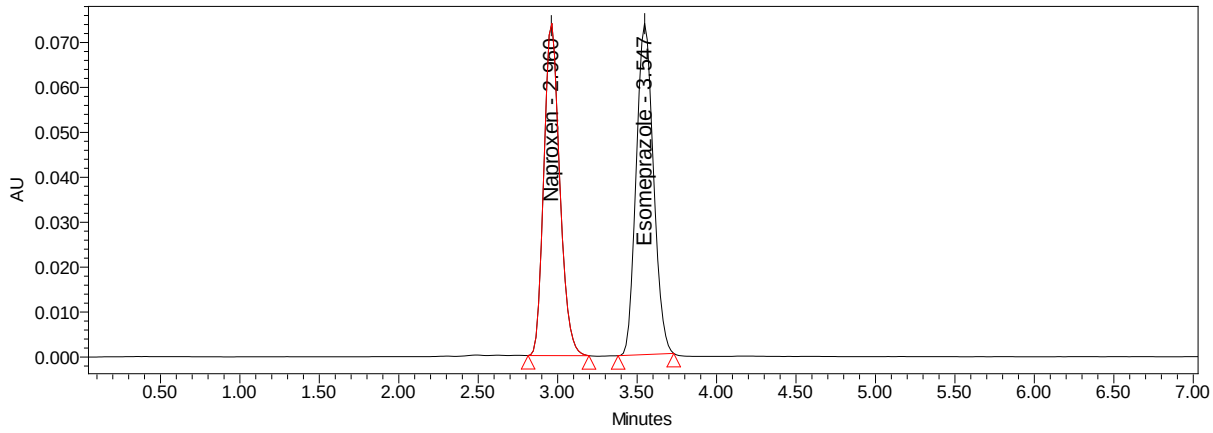


Fig 16: Chromatograms for 20 ppm:

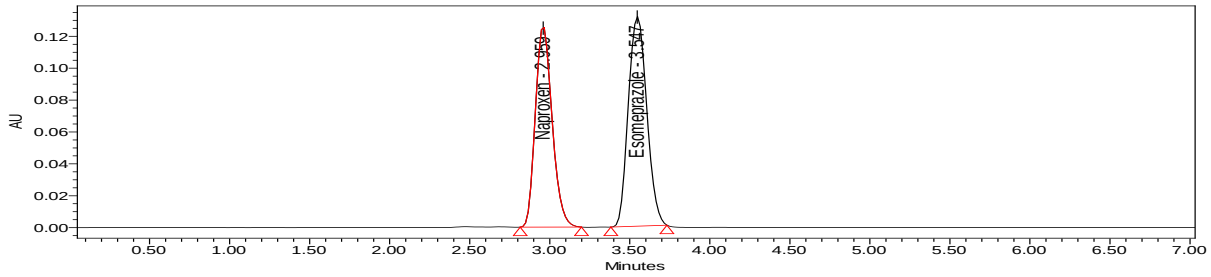


Fig 17: chromatograms for30ppm

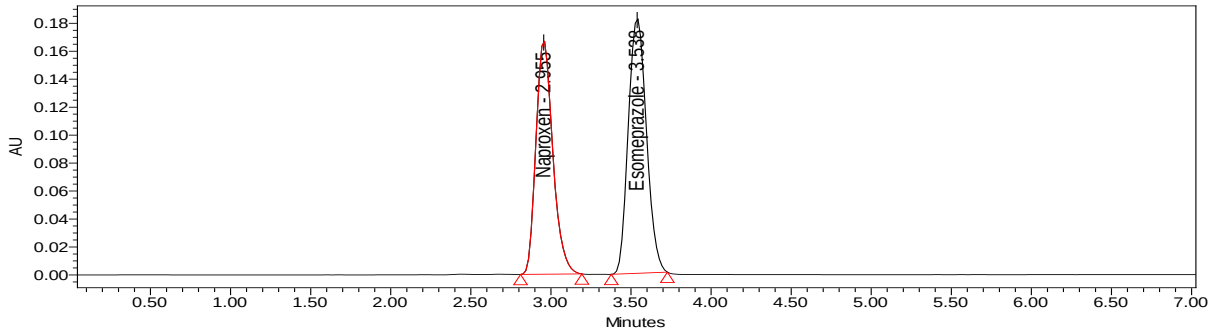


Fig 18: chromatograms for 40 ppm

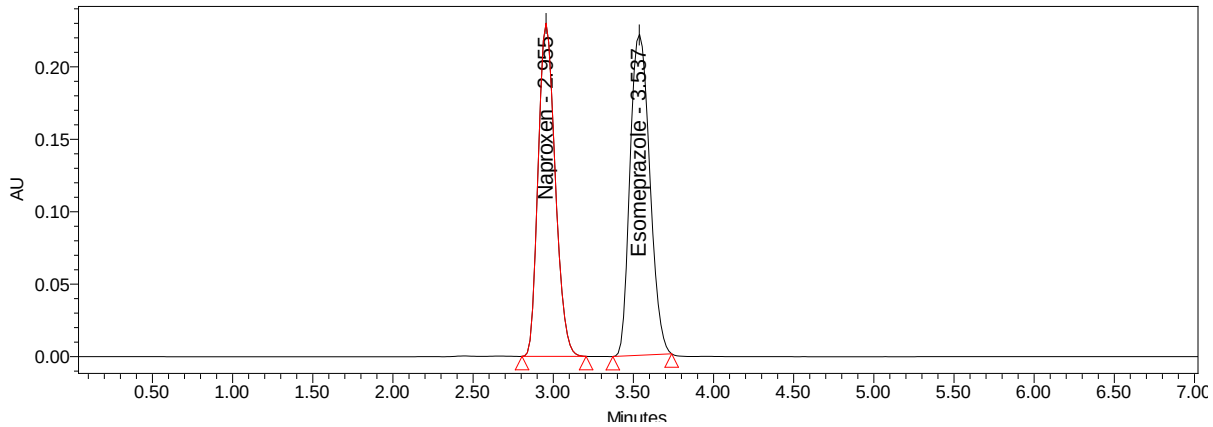


Fig 19: Chromatograms for 50 ppm

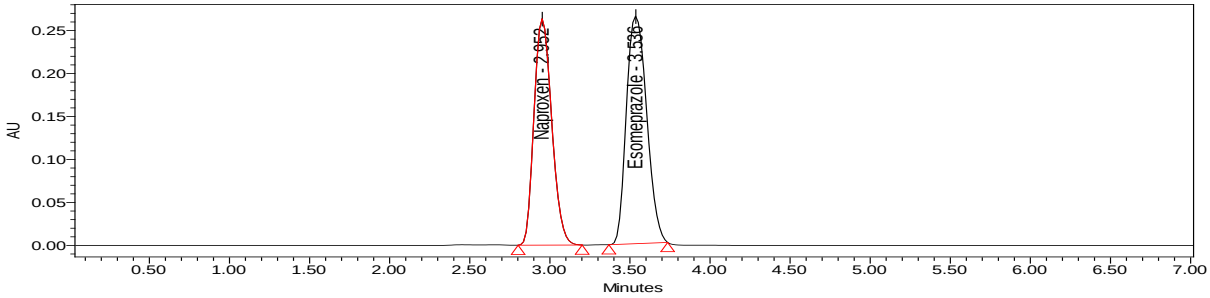


Fig 20: Chromatograms for 60 ppm

TABLE-10 (i)Data of system to system variability (Naproxen)

System-2

S.NO:	Peak area	Assay % of Naproxen
1	1146923	99.65
2	1143596	99.08
3	1158293	99.98
4	1147283	100.04
5	1152490	100.16
6	1158293	99.98
Mean	1151146	99.78
%RSD	0.540725	0.43652

TABLE-10 (ii) Data of system to system variability (Esomeprazole)

System-2

S.NO:	Peak area	Assay % of Esomeprazole
1	2161848	98.65
2	2198427	98.63
3	2231236	98.86
4	2254490	98.52
5	2245703	98.63
6	2238426	98.55
Mean	2221693	98.64
%RSD	1.578192	0.12

Chromatograms of system to system variability

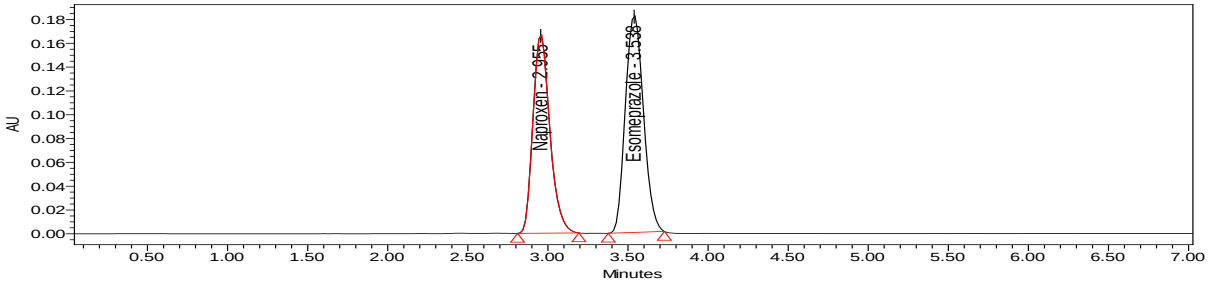


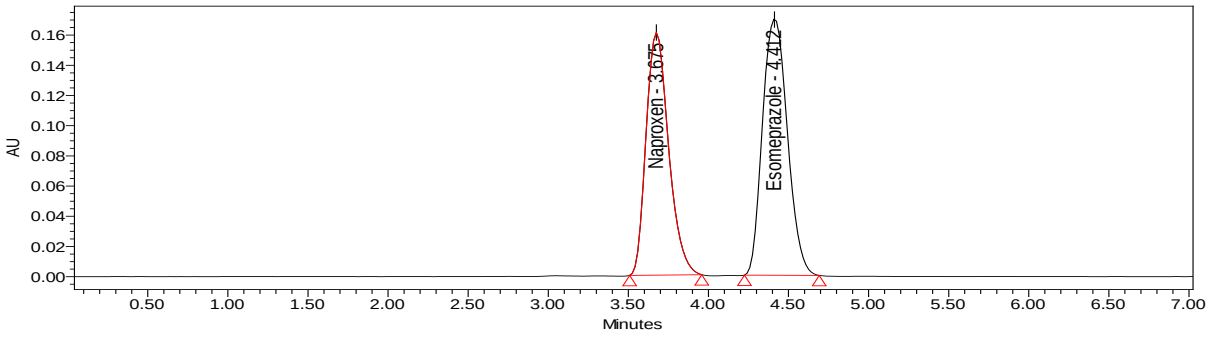
TABLE: 11(i) Data for Effect of variation in flow rate (Naproxen):

Flow 0.8 ml	Std Area	Tailing factor	Flow 1.0 ml	Std Area	Tailing factor	Flow 1.2 ml	Std Area	Tailing factor
	1139272	1.238915		1146923	1.251658		1152293	1.262464
	1140892	1.230637		1143596	1.245435		1146923	1.251658
	1136301	1.240858		1158293	1.262464		1147283	1..237018
	1141067	1.238995		1147283	1.237018		1152490	1.239010
	1136024	1.241073		1152490	1.239010		1139272	1.238915
Avg	1138711	1.236496	**Avg**	1149717	1.247117	**Avg**	1148852	1.245813
SD	2431.578	0.005254	**SD**	5754.015	0.010328	**SD**	7076.841	0.010984
%RSD	0.213538	0.424907	**%RSD**	0.500472	0.008282	**%RSD**	0.615992	0.00881712

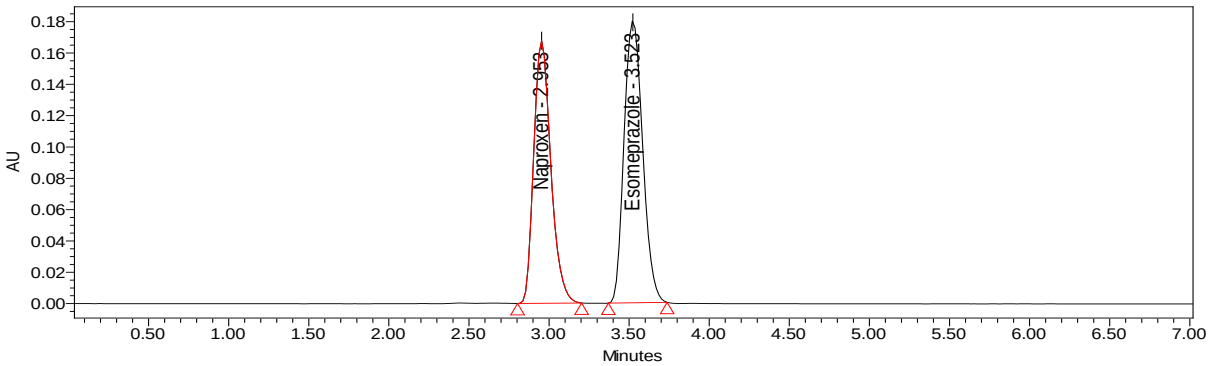
TABLE: 11(ii) Data for Effect of variation in flow rate (Esomeprazole)

Flow 0.8 ml	Std Area	Tailing factor	Flow 1.0 ml	Std Area	Tailing factor	Flow 1.2 ml	Std Area	Tailing factor
	2245703	1.119216		2278639	1.114878		2161848	1.115372
	2291408	1.142210		2164732	1.114354		2198427	1.119385
	2278639	1.167058		2367407	1.113805		2231236	1.112055
	2239286	1.140170		2254490	1.118590		2254490	1.114561
	2267407	1.132946		2231236	1.119986		2245703	1.114621
Avg	4231159	1.14032	**Avg**	2266847	1.116323	**Avg**	2221693	1.115199
SD	27435.85	0.017452	**SD**	20436.91	0.002778	**SD**	55808.37	0.002654
%RSD	0.648424	1.530435	**%RSD**	0.901557	0.248825	**%RSD**	1.345138	0.237999

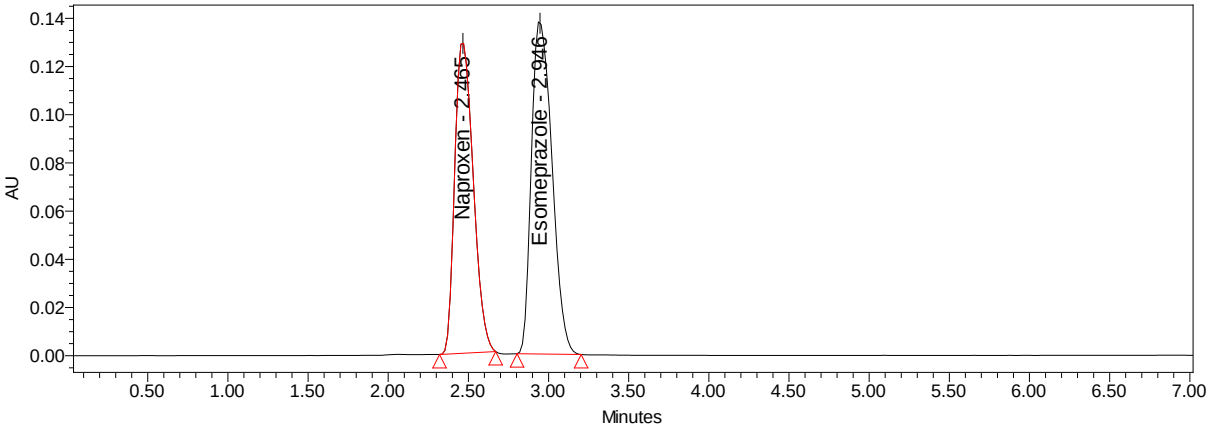
a) Effect of variation of flow rate (for 0.8 ml/min flow)



chromatograms for 1ml/min



Chromatograms for 1.2ml/min



4. SUMMARY AND CONCLUSION:

The analytical method was developed by studying different parameters. First of all, maximum absorbance was found to be at 332nm Naproxen for and 285nm for Esomeprazole. Common wavelength will be 272nm and the peaks purity was excellent. Injection volume was selected to be 20µl which gave a good peak area. The column used for study was Inertsil C_{18}, ODS chosen good peak shape. Ambient temperature was found to be suitable for the nature of drug solution. The flow rate was fixed at 1.0ml/min because of good peak area, satisfactory retention time and good resolution. Different ratios of mobile phase were studied, mobile phase with ratio of 45:55 Methanol : Buffer was fixed due to good symmetrical peaks and for good resolution. So this mobile phase was used for the proposed study.

The present recovery was found to be 98.0-101.50 was linear and precise over the same range. Both system and method precision was found to be accurate and well within range. Detection limit was found to be 0.25 Naproxen and 0.52 for Esomeprazole. Linearity study was, correlation coefficient and curve fitting was found to be. The analytical method was found linearity over the range of 20-80ppm of the target concentration for both the drugs. The analytical passed both robustness and ruggedness tests. On both cases, relative standard deviation was well satisfactory.

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