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Simultaneous estimation of Rabeprazole and Mosapride by RP-HPLC method in tablet dosage form

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ABSTRACT

A simple, selective, accurate high Performance Liquid Chromatographic (HPLC) method was developed and validated for the analysis of Rabeprazole and Mosapride in Tablet dosage form. Chromatographic separation achieved isocratically on Inertsil C18, ODS column using mobile phase Acetonitrile 100%, with flow rate of 1.0ml/min with UV detection at 276nm. The retention time of Rabeprazole and Mosapride are 2.951 and 4.195 respectively. The developed method was validated in terms of accuracy, precision, linearity, limit of detection, limit of quantitation. This study aimed at developing and validating an HPLC method, being simple, accurate and selective, and the proposed method can be used for the estimation of these drugs in combined dosage forms.

Keywords: Simultaneous estimation, Rabeprazole, Mosapride, RP-HPLC, tablet dosage forms.

INTRODUCTION

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole proton pump inhibitors) that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+/K^+ATPase (hydrogen-potassium adenosine triphosphatase) at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, rabeprazole has been characterized as a gastric proton-pump inhibitor. Rabeprazole blocks the final step of gastric acid secretion. In gastric parietal cells, rabeprazole is protonated, accumulates, and is transformed to an active sulfenamide. When studied in vitro, rabeprazole is chemically activated at pH 1.2 with a half-life of 78 seconds.

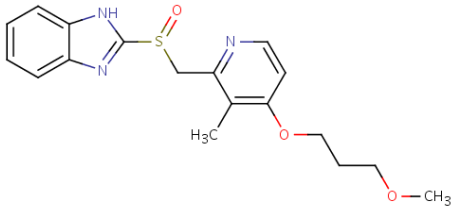

Fig 1. Stucture of Rabeprazole

Rabeprazole is an antiulcer drug in the class of proton pump inhibitors. It is a prodrug – in the acid environment of the parietal cells it turns into active sulphenamide form. Rabeprazole inhibits the H+, K+ATPase of the coating gastric cells and dose-dependent oppresses basal and stimulated gastric acid secretion.

Mosapride acts through the stimulation of the serotonin 5-HT_4 receptors which increases acetylcholine release in the enteric nervous system (specifically the myenteric plexus). This results in increased tone and amplitude of gastric (especially antral) contractions, relaxation of the pyloric sphincter and the duodenal bulb, and increased peristalsis of the duodenum and jejunum resulting in accelerated gastric emptying and intestinal transit.

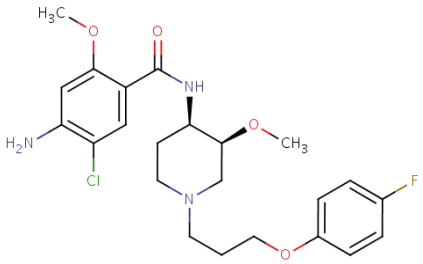

Fig 2. Stucture of Mosapride

It acts through the stimulation of the serotonin 5-HT_4 receptors which increases acetylcholine release in the enteric nervous system (specifically the myenteric plexus). This results in increased tone and amplitude of gastric (especially antral) contractions, relaxation of the pyloric sphincter and the duodenal bulb, and increased peristalsis of the duodenum and jejunum resulting in accelerated gastric emptying and intestinal transit [1-3]

MATERIALS AND METHODS

HPLC grade Sodium dihydrogen phosphate (NaH2PO4), disodium hydrogen phosphate Na2HPO4), acetonitrile- procured from Merck, India. High pure water was prepared by using Millipore Milli Q plus purification system

Table 1: Optimized chromatographic conditions

Parameters	Method
Stationary phase (column)	Inertsil -ODS C_{18}(250 x 4.6 mm, 5 µ)
Mobile Phase	Methanol : Acetonitrile (60:40)
Flow rate (ml/min)	1.0 ml/min
Run time (minutes)	8min
Column temperature (°C)	Ambient

Volume of injection loop (µl)	20
Detection wavelength (nm)	254nm
Drug RT (min)	2.9min for Rabeprazole and 4.1 for Mosapride.

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The stock solution was prepared by dissolving 20.0 mg of accurately weighed Rabeprazole and 25.0 mg Mosapride 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 [4-7].

RESULT AND DISCUSSION

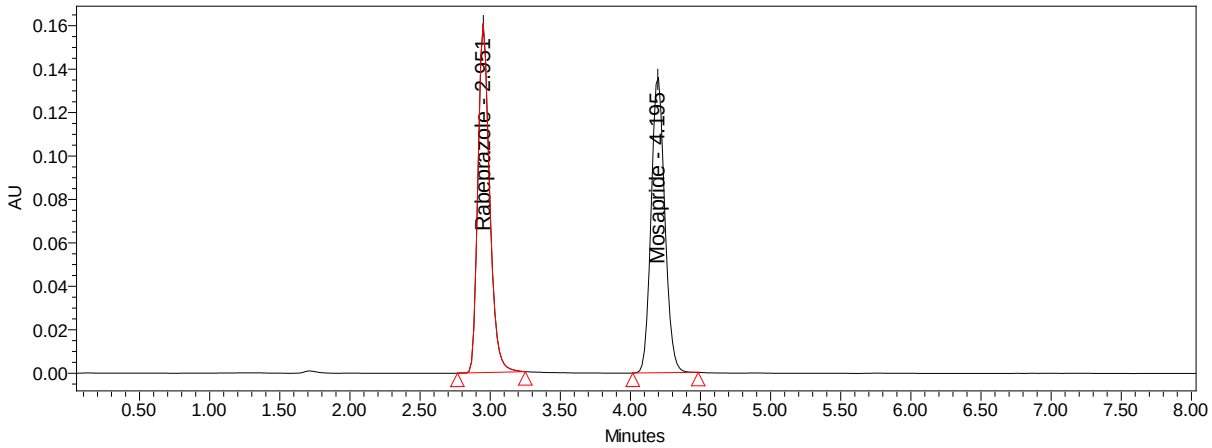

Fig 3: Chromatogram of standard

Table 2: Chromatogram at RT's Rabeprazole and Mosapride

S.No	Name of the peak	Retention time(min)
1	**Rabeprazole**	2.951
2	**Mosapride**	4.195

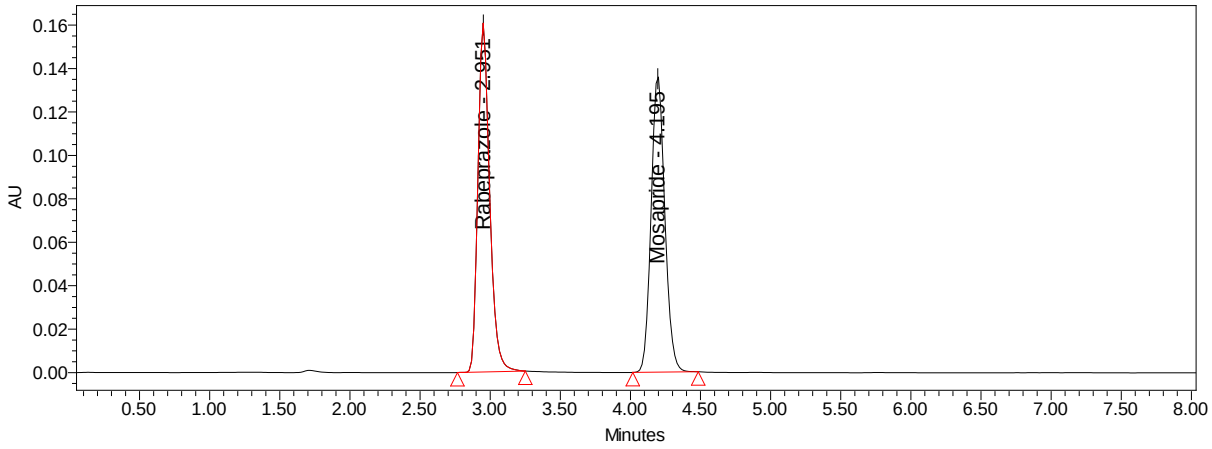

Fig 4:Chromatogram of sample

Table 3: Chromatogram with same RT values as of standard

S.No	Name of the peak	Retention time(min)
1	**Rabeprazole**	2.951
2	**Mosapride**	4.195

Table 4: Data of System Suitability forRabeprazole

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	2.951	1139272	5890.964069	1.238915
2	2.950	1140892	5915.423628	1.230637
3	2.948	1136301	5934.796986	1.240858
4	2.949	1141067	5976.253744	1.238995
5	2.949	1136024	5953.814152	1.241073
Mean	2.9498	1138711	5934.251	1.236496
SD	0.000837	57540.015	-------	-------
% RSD	0.028363	0.213538	-------	-------

Table 5: Data of System Suitability for Mosapride

Injection	RT	Peak Area	USP Plate count	USP Tailing
1	4.195	797564	8676.113795	1.099100
2	4.193	795138	8803.641669	1.103929
3	4.189	795685	8616.937115	1.111477
4	4.189	800569	8820.182543	1.117660
5	4.188	797049	8735.115629	1.119004
Mean	4.1912	797201	8730.398	1.110234
SD	0.002683	2124.413	-------	-------
% RSD	0.064022	0.266484	-------	-------

SPECIFICITY:

Validation Data

Table 6: Data of System Suitability for Rabeprazole

Injection	RT	Peak Area	USP Plate count	USP Tailing
Mean	2.9498	1138711	5934.251	1.236496
SD	0.000837	57540.015	-------	-------
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Injection	RT	Peak Area	USP Plate count	USP Tailing
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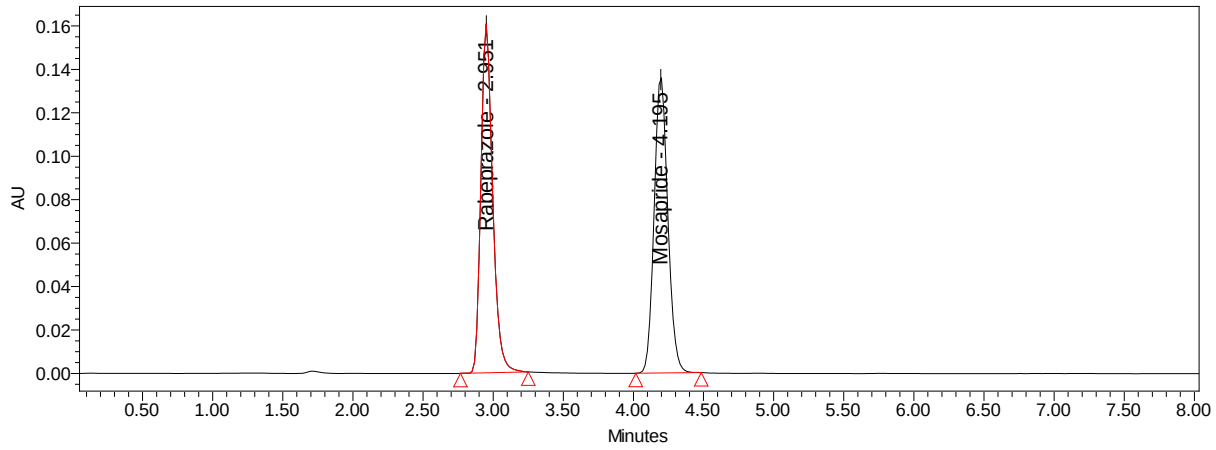

Fig 5: Chromatograms of system suitability (standards 1-5)

Inference: System suitability Chromatogram for standard – 1

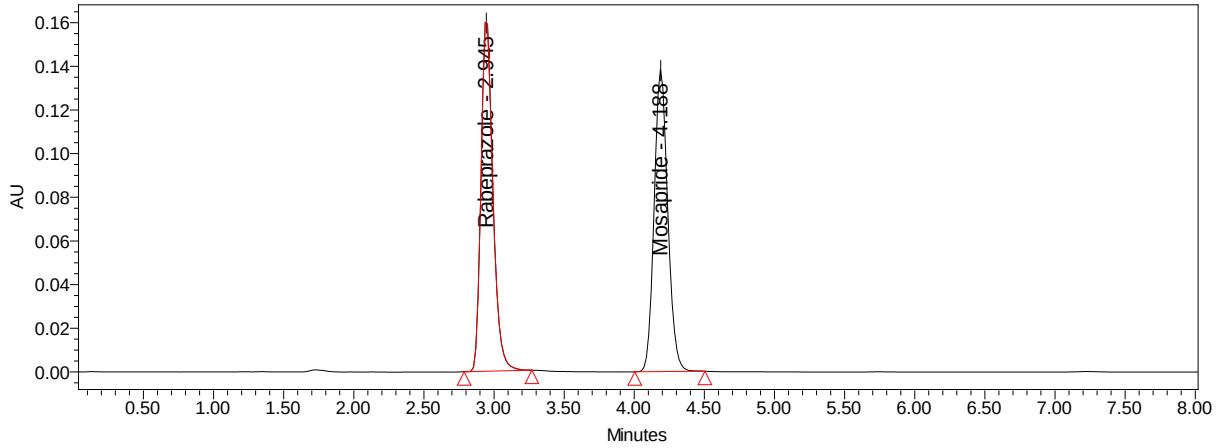

Fig 6: Chromatogram of standard

Inference: Got a peak for standard at an Rt of 2.945min forRabeprazole and 4.188min for Mosapride

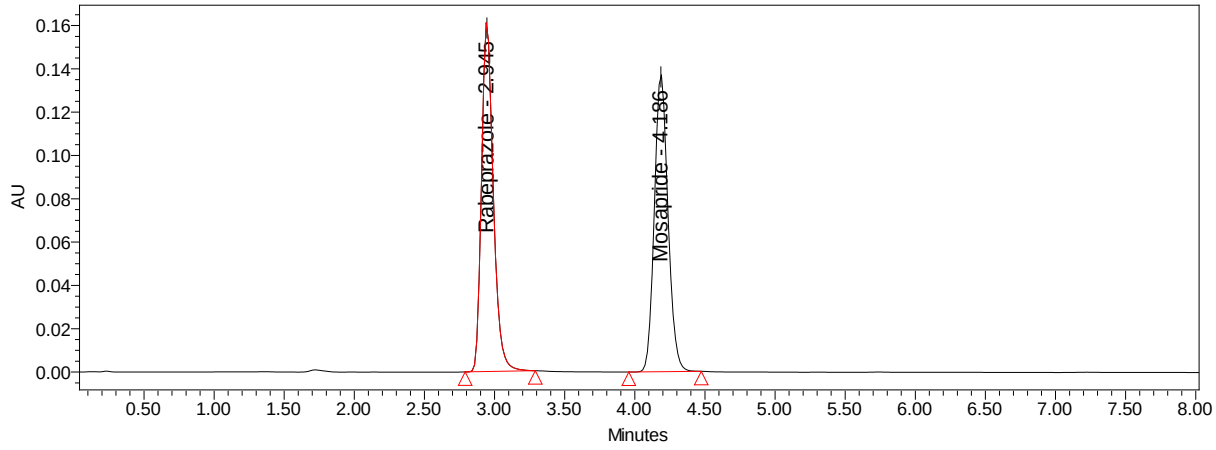

Fig 7: Chromatogram of sample

Inference: Got a peak for sample at an Rt of 2.945min for Rabeprazole and 4.186min for Mosapride

PRECISION

System precision

Table 7: Data of Repeatability (System precision) for Rabeprazole

	Injection	Peak Areas of Rabeprazole	%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 8: Data of Repeatability (System precision) for Mosapride

	Injection	Peak Areas of Mosapride	%Assay
Concentration 40ppm	1	801690	98.84
	2	797631	99.69
	3	805783	100.05
	4	801496	101.11
	5	806432	100.96
Statistical Analysis	**Mean**	802606.4	100.13
	SD	3590.034	0.937203
	% RSD	0.447297	0.935987

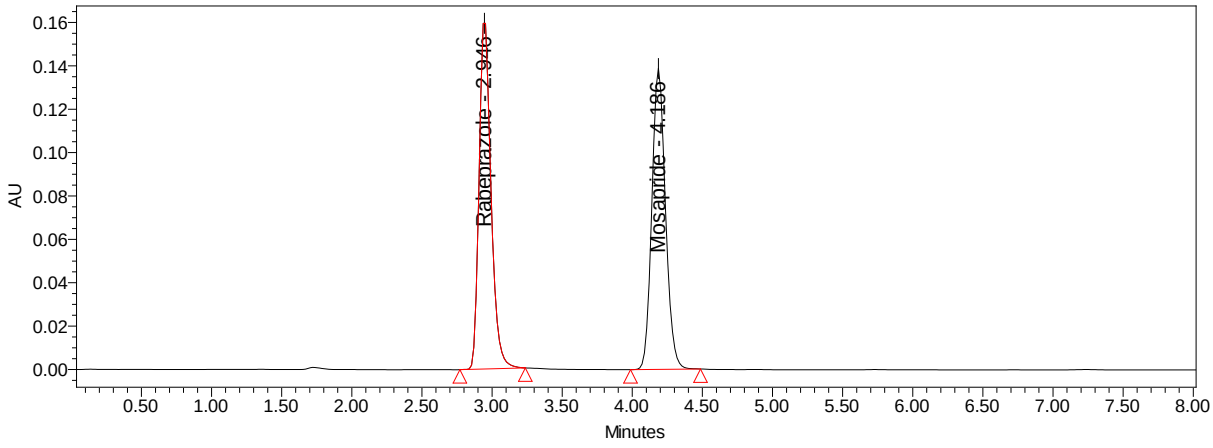

Fig 8: Chromatograms of system precision

Inference: Chromatogram for system precision (standard - 1)

Intermediate precision

Table 9: Data of Intermediate precision (Analyst 2) for Rabeprazole

	Injection	Peak Areas of Rabeprazole	%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: Data of Intermediate precision (Analyst 2) for Mosapride

	Injection	Peak Areas of Mosapride	%Assay
Concentration 40ppm	1	797564	99.85
	2	795138	99.68
	3	795685	100.08
	4	800569	100.01
	5	797049	99.52
	6	795685	100.08
Statistical Analysis	**Mean**	796948.3	100.37
	SD	1998.386	0.337086
	% RSD	0.250755	0.337299

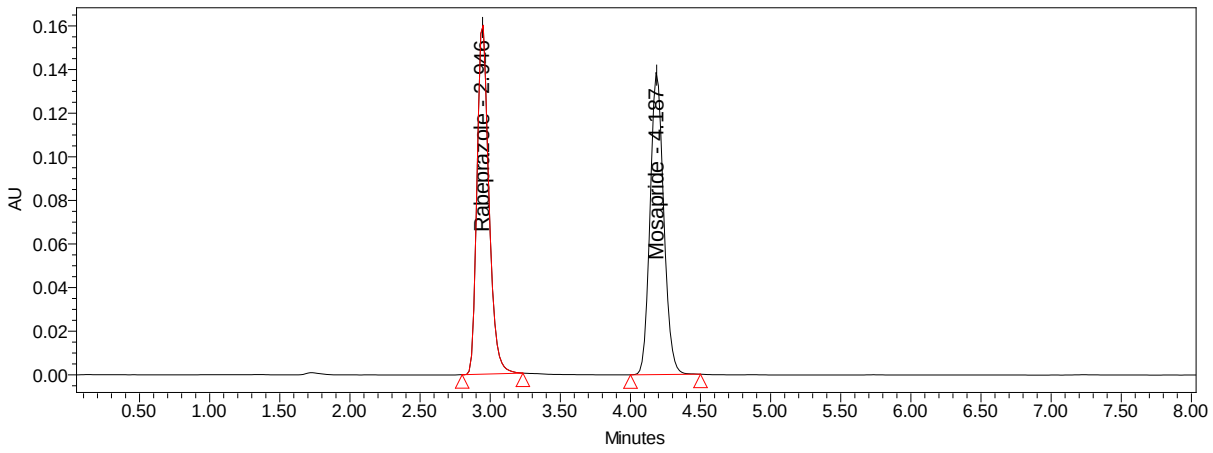

Fig 9: Chromatograms of Intermediate precision

Inference: Chromatogram for Intermediate Precision

Accuracy (recovery)

Table 10: Data of Accuracy for Rabeprazole

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 11: Data of Accuracy for Mosapride

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

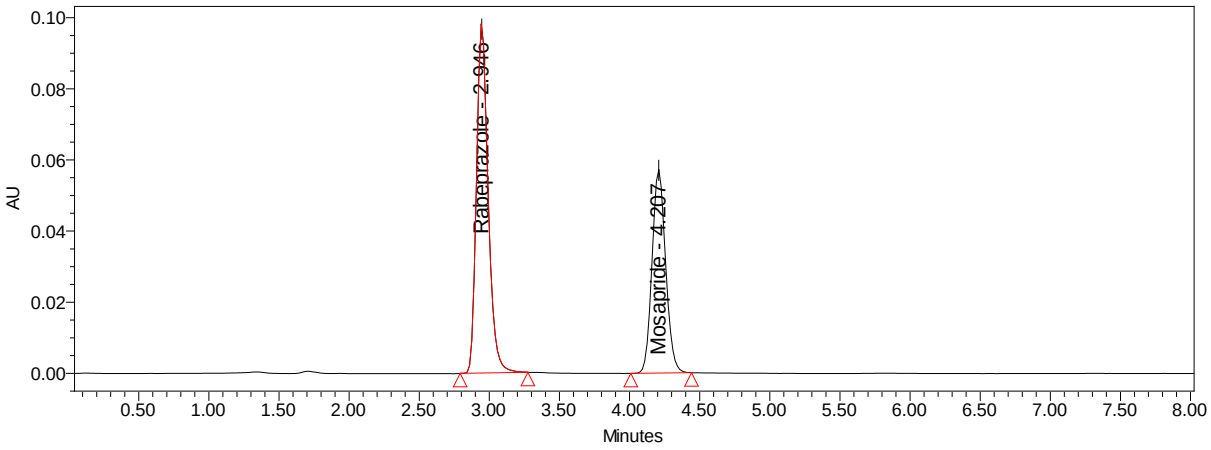

Fig 10: Chromatograms for accuracy (50%)

Inference: Chromatogram for standard 1

Linearity

Table 12: Data of Linearity (Rabeprazole)

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		

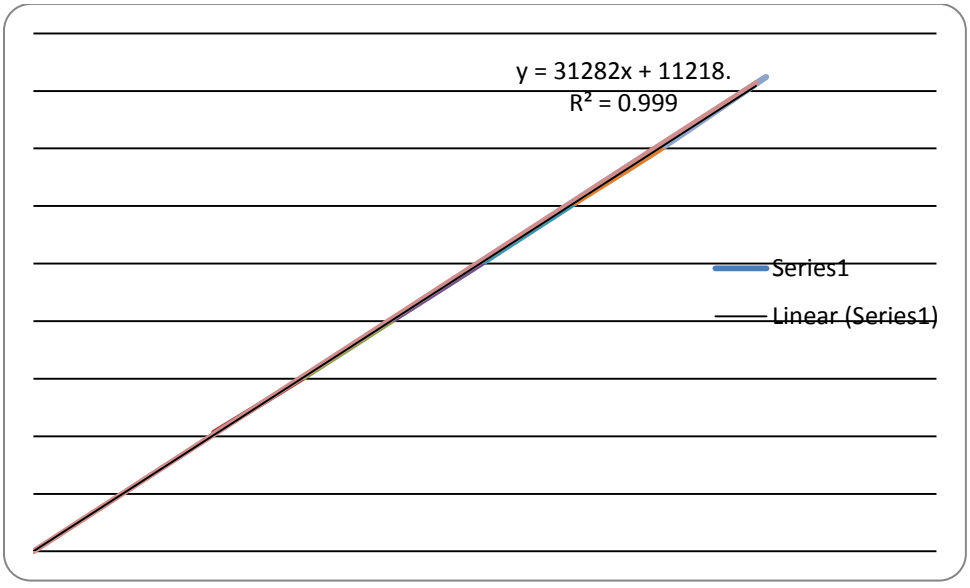

Fig 11: Linearity Plot (Concentration Vs Response) of Rabeprazole

Table 13: Data of Linearity (Mosapride)

Concentration (ppm)	Average Area	Statistical Analysis	
0	0	Slope	20193
20	412977	y-Intercept	1902
30	605369	Correlation Coefficient	0.999
40	807564		
50	1007428		
60	1210925		
70	1409560		
80	1627087		

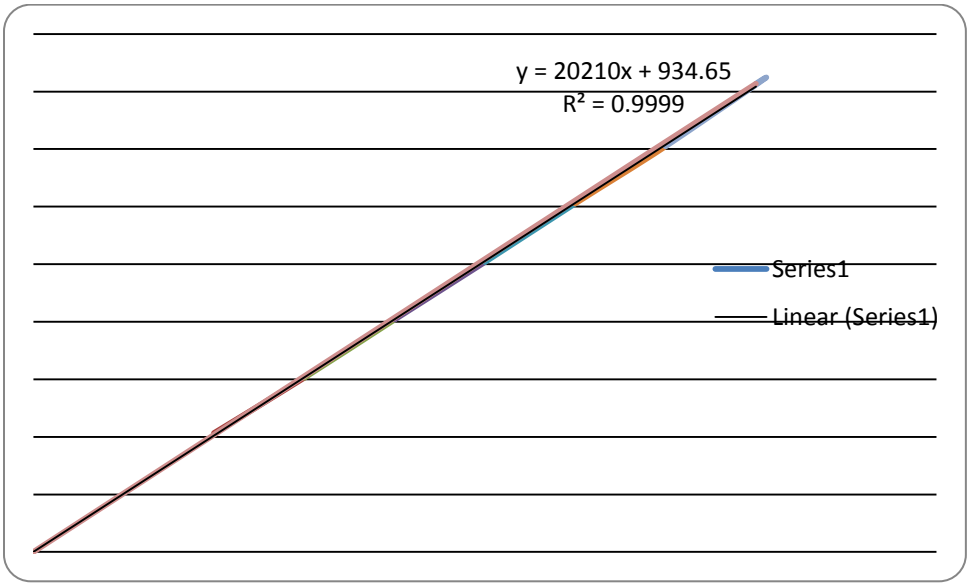

Fig 12: Linearity Plot (Concentration Vs Response) of Mosapride

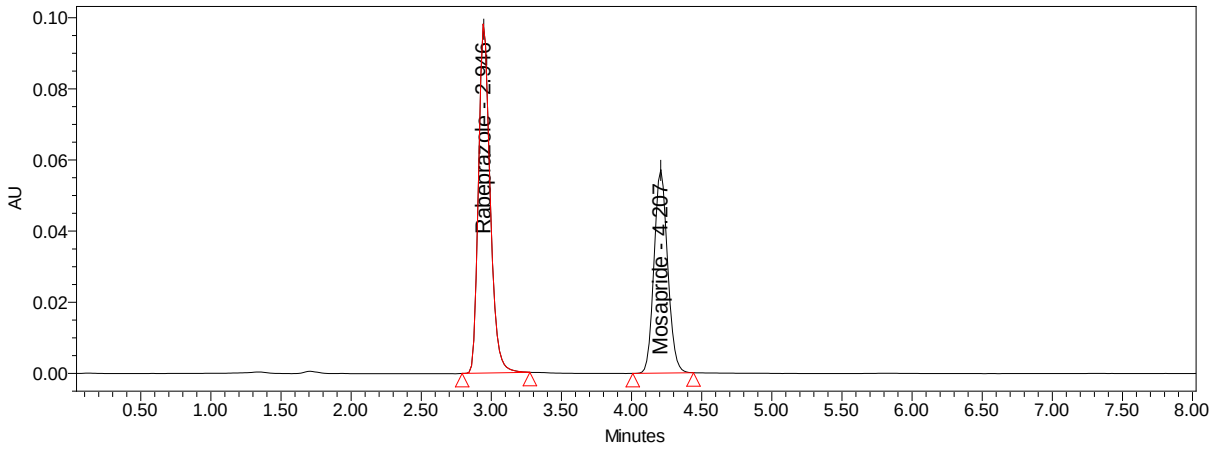

Fig 13: Chromatograms for 20 ppm

Inference: Chromatogram for 20 ppm standard 1

Ruggedness

Table 14: Data of system to system variability (Rabeprazole)- System-2

S.No.	Peak area	Assay % of Rabeprazole
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 15: Data of system to system variability (Mosapride)- System-2

S.No	Peak area	Assay % of Mosapride
1	801690	98.84
2	797631	99.69
3	805783	100.05
4	801496	101.11
5	806432	100.96
6	800569	100.01
Mean	802266.8	100.11
%RSD	0.413454	0.838768

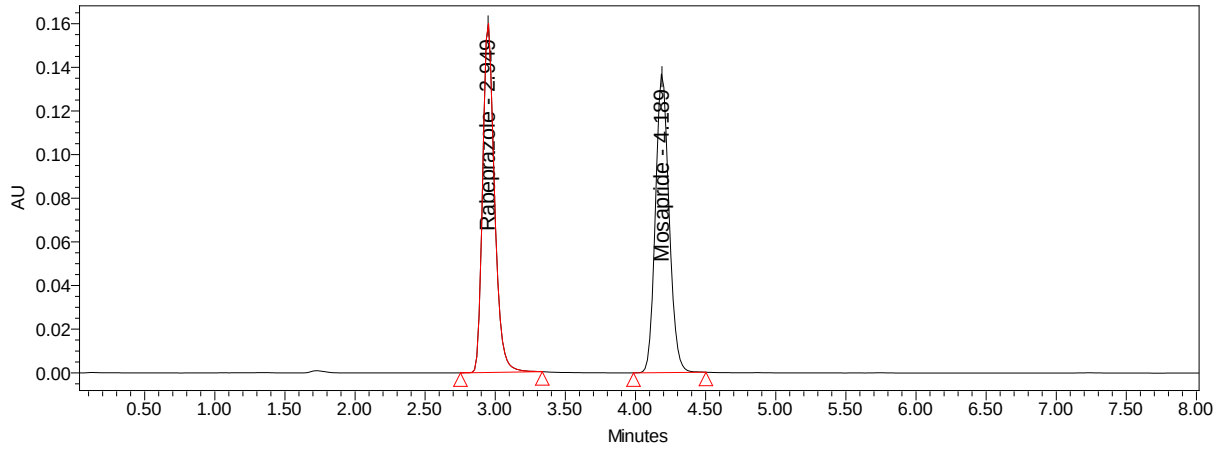

Fig 14: Chromatograms of system to system variability

Inference: Chromatogram of system to system variability std- 1

Table 16: Data for Effect of variation in flow rate (Rabeprazole):

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 17: Data for Effect of variation in flow rate (Mosapride)

Flow 0.8 ml	**Std Area**	**Tailing factor**	**Flow 1.0 ml**	**Std Area**	**Tailing factor**	**Flow 1.2 ml**	**Std Area**	**Tailing factor**
	797564	1.099100		801690	1.122813		805783	1.121321
	795138	1.103929		797631	1.112181		801690	1.122813
	795685	1.111477		805783	1.121321		801496	1.124805
	800569	1.117660		801496	1.124805		806432	1.123373
	797049	1.119004		806432	1.123373		797564	1.099100
Avg	797201	1.110234	**Avg**	802606.4	1.120899	**Avg**	801593	1.118282
SD	2124.413	0.008622	**SD**	3590.034	0.00503	**SD**	3613.298	0.047969
%RSD	0.500472	0.77655	**%RSD**	0.447297	0.004488	**%RSD**	0.450203	0.965376

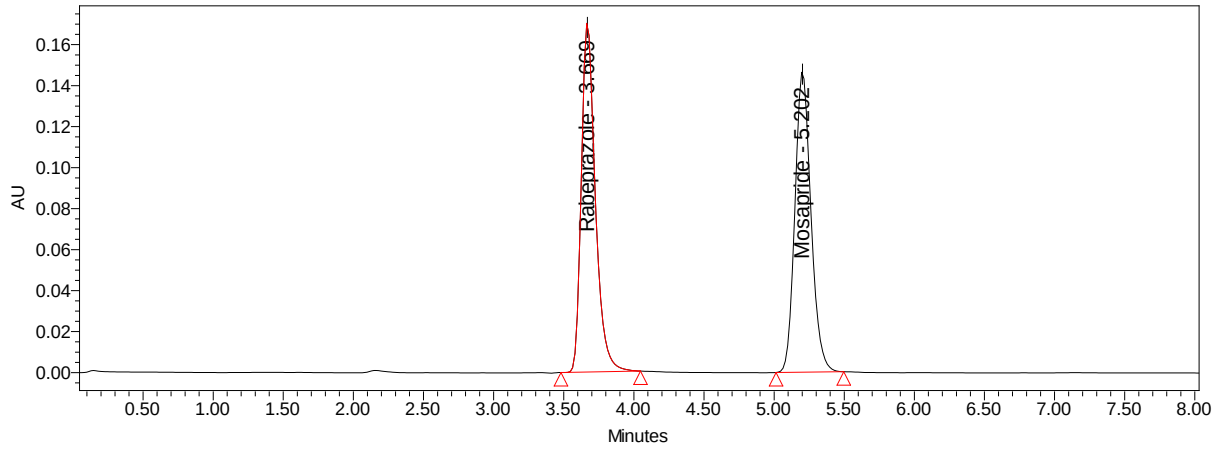

Fig 15: Chromatograms of robustness

Inference: Chromatogram for robustness standard - 1

CONCLUSION

In the present study it was observed that the 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 2.9 Rabeprazole and 4.1 for Mosapride. 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 and precised.

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