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High Performance Liquid Chromatography For The Simultaneous Estimation Of Anti-Ulcer Drugs In Pharmaceutical Dosage Form

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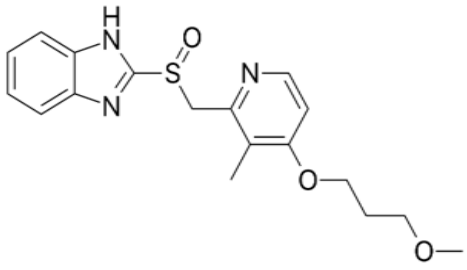
Abstract

A simple, rapid, precise, accurate and sensitive reverse phase liquid chromatographic method has been developed for the simultaneous determination of Mosapride and Rabeprazole in bulk and pharmaceutical dosage form dosage form. The chromatographic method was standardized using Waters ODS (C18) RP Column, 250 mm x 4.6 mm. 5µm I.D column with UV detection at 255nm, Methanol: Ammonium Acetate buffer (pH=6) = 75:25and other conditions optimized were: flow rate (1.0 ml/minute), wavelength (255 nm), Run time was maintained at 8 minutes. The proposed method was successfully applied to the simultaneous determination of Mosapride and Rabeprazole in bulk and pharmaceutical dosage form. Optimized retention time of Mosapride and Rabeprazole is 2.069 and 2. 488.The method was linear over the range of 10µg/ml for Mosapride and Rabeprazole. The recovery was in the range of 98% to 102%. Linearity range was found to be 0-30 µg/ml for Mosapride and 0-60 µg/ml for Rabeprazole. The correlation coefficient was found to be 0.995. LOD was found to be 0.05µg/ml and LOQ was found to be 0.15µg/ml for Mosapride & The LOD was found to be 0.09µg/ml and LOQ was found to be 0.27µg/ml for Rabeprazole. The results of the forced degradation studies indicated the specificity of the developed method that has been developed. Different analytical performance parameters such as precision, accuracy, limit of detection, limit of quantification and robustness were determined according to International Conference on Harmonization (ICH) guidelines

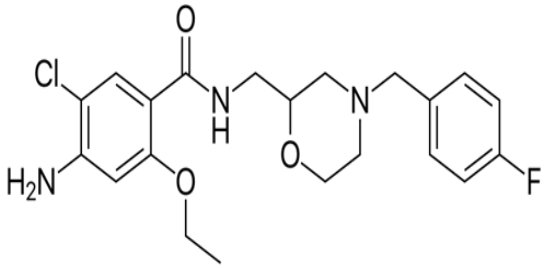
Keywords: Rabeprazole, Mosapride, Stability, Linearity, Accuracy.

Introduction

Rabeprazole sodium is chemically, Sodium;2-[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl] methylsulfinyl] benzimidazol-1-ide.It is a proton pump inhibitor and it is a prodrug. Rabeprazole sodium is converted to sulfonamide and decreases gastric acid secretion. It inhibits proton pumps activity and used in the therapy of gastroesophageal reflux and peptic ulcer disease.[1] Mosapride citrate is chemically, 2-hydroxypropane1,2,3-tricarboxylic acid; 4-amino-5-chloro-2-ethoxy-N- ({4-[(4 fluorophenyl) methyl] morpholin-2-yl}methyl) benzene-1-carboximidic acid. It is prokinetic drug. It is a 5-HT3 receptor antagonist. The metabolite of Mosapride produces 5-HT3 receptor antagonism and suppresses the inhibitory transmission in myenteric plexus. These all results in increased esophageal peristaltic activity, lower esophageal sphincter tone.so it is used in the treatment of gastroesophageal reflux disease.[2,3] Structure of Rabeprazole sodium and Mosapride citrate is given in figure 1 and 2.



(A)



(B)

Fig. 1 (A) Structure of Rabeprazole sodium (B) Structure of Mosapride citrate

Materials and Methods

Chemicals and Reagents

Rabeprazole sodium and Mosapride citrate were kindly provided as gift sample from Gufic Bioscience LtdNavsari and Pure and Cure Healthcare Pvt. LtdHaridwar. HPLC grade Methanol, Acetonitrile and Milli Q water and AR grade Hydrochloric acid, Sodium Hydroxide, Hydrogen Peroxide and were used.

Chromatographic Condition

HPLC with Empower2 Software with Isocratic with UV-Visible Detector (WATERS).Mosapride and Rabeprazole dilutions were prepared and the mobile phase was taken as Methanol : Ammonium acetate buffer pH.6 75:25 and column used-Develosil ODS RP C18, 5µm,15cmx4.6mm i.d. at wavelength at 255nm flowrate 1.0ml/min and runtime was 8 min

Method Development

The chromatographic method was standardized using Waters ODS (C18) RP Column, 250 mm x 4.6 mm. 5µm I.D column with UV detection at 255nm, Methanol: Ammonium Acetate buffer (pH=6) = 75:25and other conditions optimized were: flow rate (1.0 ml/minute), wavelength (255 nm), Run time was maintained at 8 minutes. The proposed method was successfully applied to the simultaneous determination of Mosapride and Rabeprazole in bulk and pharmaceutical dosage form.

Method Validation

Analytical validation parameters for this proposed method were determined according to ICH (Q2R1) guideline. 1

Linearity

The linearity was carried out at concentration range of 0-60µg/ml for Rabeprazole sodium and for Mosapride citrate the range was 0-30µg/ml.

Specificity

Specificity was performed by injecting diluent, placebo and sample solution to check the interference of excipients.

Accuracy

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of pure drug of Rabeprazole were taken and 3 replications of each has been injected to HPLC system

Precision

The precision of each method was ascertained separately from the peak areas & retention times obtained by actual determination of six replicates of a fixed amount of drug Mosapride & Rabeprazole (API)

Results and Discussion

The chromatographic method was standardized using Waters ODS (C18) RP Column, 250 mm x 4.6 mm. 5µm I.D column with UV detection at 255nm, Methanol: Ammonium Acetate buffer (pH=6) = 75:25and other conditions optimized were: flow rate (1.0 ml/minute), wavelength (255 nm), Run time was maintained at 8 minutes. The proposed method was successfully applied to the simultaneous determination of Mosapride and Rabeprazole in bulk and pharmaceutical dosage form.

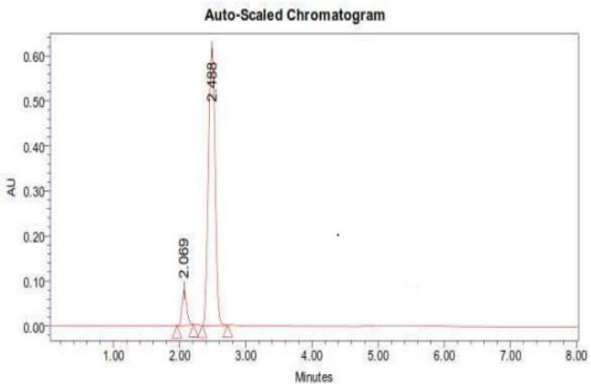


Fig.3 Chromatogram of Optimized condition

Optimized Chromatographic Conditions

Mobile Phase: Methanol: Ammonium Acetate buffer:
Flow rate: 1.0ml/min
Detection Wavelength : 255 nm
Injection Volume: 10µl
Runtime: 8 minutes

Linearity

Linearity spectra and graph is given in Figure 4 and 5.

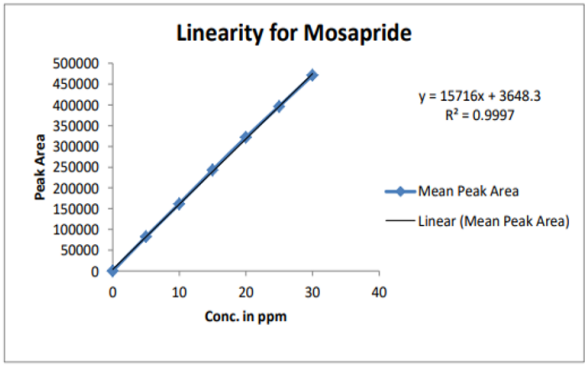


Figure 4: Standard curve for Mosapride

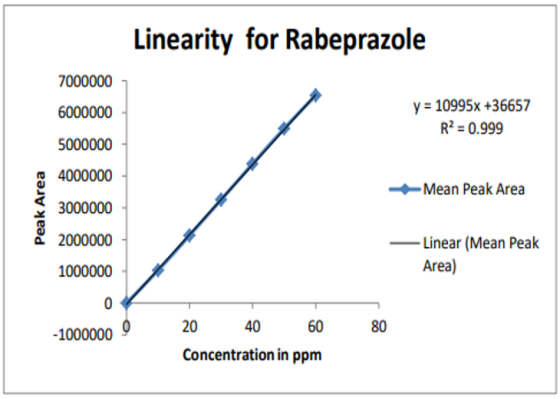


Figure 4: Standard curve for Rabeprazole

Precision and Accuracy

Repeatability and intraday, Interday precision for RP-HPLC method was measured in terms of RSD and it was found to be less than 2. Accuracy was found between the range of 98-102%. On the basis of accuracy and precision data we can conclude that method is accurate and precise. Results are shown in table 1 & 2

Sample ID	Concentration(□g/ml)			%Recovery of Pure drug	Statistical Analysis
	Conc.Found	Conc. Recovered	Peak Area		
S_1:80%	12	11.974	191834	99.783	Mean=99.769%
					S.D.=0.296248
S_2:80%		11.936	191235	99.466	
					% R.S.D.=0.296934
S_3:80%		12.007	192358	100.058	
S_4:100%	15	15.243	243212	101.62	Mean=100.8887%
S_5:100%		15.203	242581	101.353	S.D.=1.044048
					R.S.D.=1.034852
S_6:100%		14.954	238673	99.693	
S_7:120%	18	17.899	284962	99.438	Mean=100.9737%
					S.D.=1.331212
S_8:120%		18.324	291643	101.8	
					% R.S.D. =1.318376
S_9:120%		18.303	291312	101.683	

Table-3: Intra and Inter day precision and Accuracy of method Mosapride

Sample ID	Concentration(□g/ml)			%Recovery of Pure drug	Statistical Analysis
	Conc.Found	Conc. recovered	Peak Area		
S_1:80%	24	24.186	191834	100.775	Mean=100.779%
					S.D.=0.406015
S_2:80%		24.090	191235	100.375	
					% R.S.D.=0.402876
S_3:80%		24.285	192358	101.187	
S_4:100%	30	29.932	365768	99.773	Mean=99.45533%
					S.D.=0.293933
S_5:100%		29.820	364532	99.40	
					% R.S.D.=0.295542
S_6:100%		29.758	363851	99.193	
S_7:120%	36	35.696	429135	99.155	Mean=99.57733%
					S.D.=0.366784
S_8:120%		35.914	431534	99.761	
					% R.S.D. =0.368341
S_9:120%		35.934	431756	99.816	

Table-4: Intra and Inter day precision and Accuracy of method Rabeprazole

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The LOD was found to be 0.05µg/ml and LOQ was found to be 0.15µg/ml for Mosapride respectively which represents that sensitivity of the method is high. The LOD was found to be 0.09µg/ml and LOQ was found to be 0.27µg/ml for Rabeprazole respectively which represents that sensitivity of the method is high

System Suitability Parameter

S.No.	Parameter	Limit	Result
1	Resolution	Rs□2	2.97
2	Asymmetry	T□ 2	Mosapride=0.25 Rabeprazole=0.28

3	Theoretical plate	N□ 2000	Mosapride=2978 Rabeprazole=3067

Table 5: Data of System Suitability Parameter

Robustness

Robustness is defined as the capacity of that method to be unaffected by even small deliberate changes that occur in the method parameters. The evaluation of robustness of a method is done by varying the chromatographic parameters such as pH, temperature, flow rate, mobile phase proportions change, ionic strength etc., and determining any possible effect on the results obtained by that method

Table 6: Result of Method Robustness Test for Mosapride & Rabeprazole

Change in parameter	% RSD Mosapride		% RSD Rabeprazole
Flow (0.8 ml/min)	0.45		0.57
Flow (1.2 ml/min)	0.38		0.44
More organic	0.87		0.86
Less organic	0.76		0.75
Wavelength of Detection (242 nm& 271 nm)	0.99		1.03
Wavelength of detection (238 nm& 267 nm)	0.95		0.94

Degradation Studies

The results of the forced degradation studies indicated the specificity of the developed method that has been developed. Mosapride and Rabeprazole were stable only in acidic, basic and thermal stress conditions and photolytic stress conditions**.**

Table: 7 Results of Force Degradation Studies of Mosapride and Rabeprazole API

Stress condition	Time (hours)	Assay of active substance	Assay of degraded products	Mass Balance(%)
Acid Hydrolysis(0.1NHCl)	24Hrs.	99.2	0.2	100.00
Basic Hydrolysis(0.1NNaOH)	24Hrs.	98.5	1.5	100.00
Thermal Degradation(60^0C)	24Hrs.	99.5	0.5	100.00
UV(254nm)	24Hrs.	99.3	0.7	100.00
3%Hydrogenperoxide	24Hrs.	98.4	1.6	100.00

Conclusion

A sensitive & selective stability indicting RP-HPLC method has been developed & validated for the analysis of Mosapride and Rabeprazole in bulk and pharmaceutical dosage form. Based on peak purity results, obtained from the analysis of samples using described method, it can be concluded that the absence of co-eluting peak along with the main peak of Mosapride and Rabeprazole indicated that the developed method is specific for the simultaneous estimation of Mosapride and Rabeprazole in the bulk and pharmaceutical dosage forms. Further the proposed RP-HPLC method has excellent sensitivity, precision and reproducibility

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