Research Article

Simultaneous Determination of Famotidine and Omeprazole in Combined Formulation by RP-HPLC

Prasanth S.S*, Athulya K.K, Shibili Niyas K, Reeba K.R, Shibila N.T
Department of Pharmaceutical Analysis, Al Shifa College of Pharmacy, Kizhattur, Perinthalmanna, Malappuram, India
***Corresponding author's E-mail:** shibiliniyaskk94@gmail.com

Received: 18-01-2023; **Revised:** 24-03-2023; **Accepted:** 30-03-2023; **Published on:** 15-04-2023.

ABSTRACT

A simple and precise RP-HPLC method was developed and validated for the simultaneous estimation of famotidine and omeprazole in the tablet dosage form. The separation was carried out on C18 (CHROMOSIL,250 mm*4.6 mm id, 5 µ particle size) column using methanol: water (60:40 v/v) as mobile phase at a flow rate of 1.4 ml/min. The detection was carried out by using a photodiode array detector and a linear response was obtained at a range of 2-10 µg ml^{-1} for famotidine and a range of 4-20 µg ml^{-1} for omeprazole. The limit of detection and limit of quantification of famotidine was found to be 0.3022 & 0.916 µg ml^{-1}, respectively and omeprazole was found to be 0.231 & 0.7 µg ml^{-1}, respectively. The method was successfully validated as per ICH guidelines.

Keywords: Famotidine, omeprazole, RP-HPLC, ICH guidelines.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2023.v79i02.004

DOI link: http://dx.doi.org/10.47583/ijpsrr.2023.v79i02.004

INTRODUCTION

Omeprazole[1,2] is 5-methoxy-2-[(4-methoxy-3,5-dimethyl pyridin-2-yl)methylsulfinyl]-1H-benz imidazole and it suppresses gastric acid secretion by inhibiting the gastric H+/K+ ATPase at the secretory surface of the gastric parietal cell. Omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. After rapid disappearance from plasma, Omeprazole can be found within the gastric mucosa for a day or more [3]. Omeprazole is used to treat gastroesophageal reflux disease (GERD)[4], peptic ulcer, Zollinger- Ellison syndrome[5], and other conditions caused by excess stomach acid. It is also used to promote the healing of erosive esophagitis [6]. Famotidine[7,8] is an H2-receptor antagonist used in ulcers, chemically is 3-[[2-(diaminomethylideneamino)-1,3-thiazol-4-yl] methyl sulfanyl]-N'-sulfamoylpropanimid amide and the empirical formula is $C_8H_{15}N_7O_2S_3$ with molecular weight is 337.5. Famotidine is classified as a class III drug according to the Biopharmaceutics Classification System (BCS)[9] and is used in the treatment of gastroesophageal reflux disease and gastric ulceration.

The literature review indicates that some individual analytical methods are available for the estimation of famotidine and omeprazole. UV absorption spectrophotometric methods like the first and second derivative method[10] for the estimation of famotidine have been described, RP-HPLC method for the determination of omeprazole and several spectrophotometric methods have been used for these two drugs, however simultaneous estimation methods of famotidine and omeprazole is not found in the data. The present work describes a simple, precise, and accurate isocratic RP-HPLC method for the simultaneous estimation of famotidine and omeprazole in a single tablet dosage form.

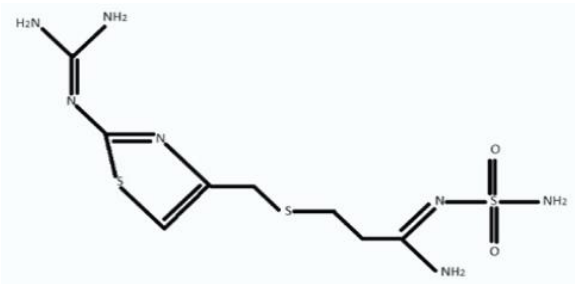


Figure 1: Structure of famotidine

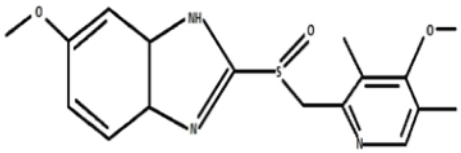


Figure 2: Structure of Omeprazole

MATERIALS AND METHODS

Chemicals

Famotidine and omeprazole were obtained from Yarrowchem products, Mumbai. Water (HPLC grade) ethanol and methanol (HPLC grade) were purchased from Research Lab fine Chem Industries, Mumbai.

Equipment

- Analysis was performed on a chromatographic system of Shimadzu UFLC equipped with two LC 20 AD pumps,

SPD-M 20 detector, and RP- C18 column[11] (CHROMOSIL, 250 mm*4.6 mm id, 5 µ particle size), Data acquisition was made by CLASS VP software.

- Analytical balance (Tandem TJ series)
- Calibrated volumetric flask and pipettes of borosilicate glass were used in the study.

Standard solutions and calibration graphs

Standard stock solutions of famotidine and omeprazole were prepared with ethanol. To study the linearity range, various dilutions were prepared from standard stock solutions, 2-10 µg/ml for famotidine and 4-20 µg/ml for omeprazole. Finally, the concentration versus peak area graph was plotted and both the analytes were found linear.

Sample solution

The sample solution was prepared by using methanol as solvent and the final concentrations were 12 µg/ml of famotidine & 6 µg/ml of omeprazole.

Method Validation

Method validation in accordance with ICH guidelines[12] is important to prove that the proposed method is valid for its intended purpose and it is done by considering the parameters like system suitability, linearity, precision, accuracy, LOD, LOQ, reproducibility, and robustness.

System suitability

Standard solutions of famotidine and omeprazole were analyzed 6 times to check the system's suitability, and parameters such as retention time, tailing factor, and theoretical plates are considered.

Linearity

Linearity of an analytical method is the linear detector response of the sample in proportionate concentration, calibration curve method was used for the determination of linearity, and linear correlations were obtained between peak area versus concentration of FAM and OME in the concentration ranges of 4-20 µg/ml and 2-10 µg/ml. linear regression[13] coefficients were calculated.

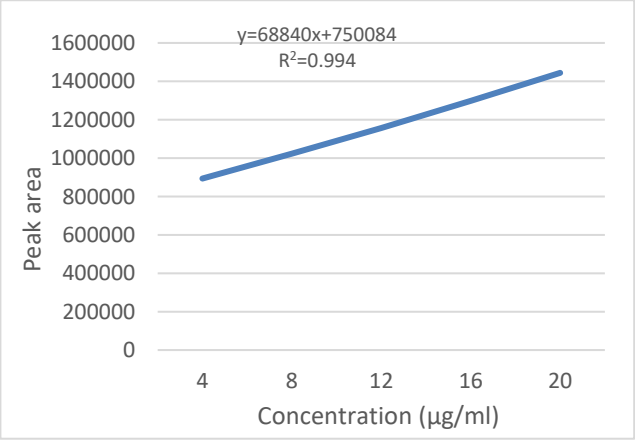


Figure 4: Calibration curve of Famotidine

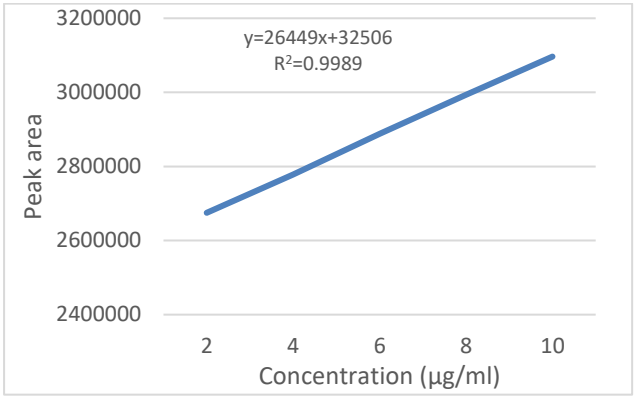


Figure 5: Calibration curve of Omeprazole

Recovery

Recovery was performed by spiking the sample with 80%, 100%, and 120% standard solutions, these are analyzed by the selected method and recovery % and relative standard deviation (RSD) were calculated.

Precision

The precision of the method was determined by 6 repeated assays of the sample and the RSD (%) was calculated. Intermediate precision was determined by inter and intra-day methods and expressed in terms of standard deviation (SD) and % RSD.

Limit of detection and limit of quantification

LOD and LOQ values are determined from the calibration curve plotted in concentration ranges of 4-20 µg/ml of FAM and 2-10 µg/ml of OME.

Table 1: Regression analysis data

	Famotidine	Omeprazole
Concentration range (µg/ml)	4-20	2-10
Correlation Coefficient (r^2)	0.994	0.998
LOD (µg/ml)	0.3022	0.231
LOQ (µg/ml)	0.916	0.7

Robustness

Robustness was studied by deliberate variations in the chromatographic parameters. The parameters evaluated were mobile phase composition (± 2 ml), flow rate altered by ± 1 ml, and detection wavelength altered by ± 2 nm.

Table 2: Calibration data of Famotidine and Omeprazole

Famotidine		Omeprazole	
Concentration (µg/ml)	Peak area (mV)	Concentration (µg/ml)	Peak area (mV)
4	89344	2	2674892
8	1023120	4	2778541
12	1156231	6	2888130
16	1298832	8	2993216
20	1443986	10	3096542

Table 3: Precision -Repeatability data for FAM (12 µg/ml) and OME (6 µg/ml)

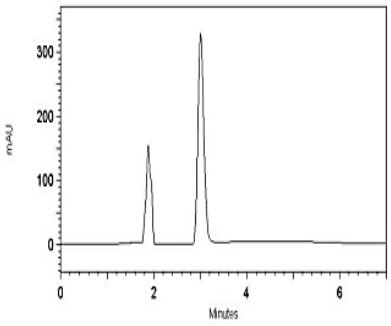
SL no	Famotidine (12 µg/ml)	Omeprazole (6 µg/ml)
1	1156234	2888131
2	1156245	2888142
3	1156249	2888156
4	1156230	2888124
5	1156258	2888149
6	1156263	2888159
% RSD	0.0010	0.0043

Table 4: Intermediate precision (reproducibility) data for FAM (12 µg/ml) and OME (6 µg/ml)

SL. No	Intraday (n=3)		Intraday (n=3)	
	Famotidine	Omeprazole	Famotidine	Omeprazole
1	1156258	2888131	1156229	2888137
2	1156231	2888124	1156267	2888174
3	1156263	2888163	1156246	2888159
%RSD	0.0012	0.0005	0.0013	0.0005

Table 5: Accuracy data (n=3)

Drug	Level of Recovery	% Recovery	% RSD
FAM	80%	96.29	0.918
	100%	97.5	
	120%	98.48	
OME	80%	98.61	0.300
	100%	97.91	
	120%	98.10	



Spectrum Max Plot

Pk #	Retention Time	Area	Area %	Height	Height %
FAM	1.877	1156224	12.537	154850	22.544
OME	3.008	2888130	31.316	328281	47.793
TOTAL		4044354	43.853	483131	70.337

Figure 3: Chromatogram of a combination of FAM (12µg/ml) and OME (6 µg/ml) in optimized chromatographic condition

Table 6: System suitability (n=6)

Parameters	FAM± SD	OME± SD
Retention time	1.883±0.034	3.010±0.053
Tailing factor	1.375±0.432	0.636±1.034
Theoretical plates	2542.6±0.122	649.63±0.060

RESULTS AND DISCUSSIONS

To optimize the RP-HPLC parameters, several mobile phase compositions were tried. A satisfactory separation and good peak symmetry for FAM and OME were obtained with a mobile phase Methanol: Water (60:40 v/v) at a flow rate of 1.4 ml/min to get better reproducibility and repeatability. The retention time was found to be 1.877 and 3.008 for FAM and OME respectively.

CONCLUSION

The developed RP-HPLC method allows accurate, precise, and reliable estimation of OME and FAM in combined dosage forms. The method was validated for linearity, accuracy, method precision, intra-day and inter-day precision, the limit of detection, and the limit of quantification. The RSD of all validation parameters was satisfactory. The developed method can be used for routine simultaneous estimation of FAM and OME in combined dosage forms.

REFERENCES

1. Yang R, Schulman SG, Zavala PJ. Acid–base chemistry of omeprazole in aqueous solutions. Analytica chimica acta. 2003 Mar 28;481(1):155-64.
2. Aybay C, Imir T, Okur H. The effect of omeprazole on human natural killer cell activity. General Pharmacology: The Vascular System. 1995 Oct 1;26(6):1413-8.
3. Nataraj KS, Duza MB, Pragallapati K, Kumar DK. Development and validation of RP-HPLC method for the estimation of omeprazole in bulk and capsule dosage forms. International current pharmaceutical journal. 2012 Oct 3;1(11):366-9.
4. Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. World journal of gastrointestinal pharmacology and therapeutics. 2014 Aug 8;5(3):105.
5. Hung PD, Schubert ML, Mihas AA. Zollinger-Ellison syndrome. Current treatment options in gastroenterology. 2003 Apr;6(2):163-70.
6. Kayesh R, Sultan MZ, Rahman A, Uddin MG, Aktar F, Rashid MA. Development and validation of a RP-HPLC method for the quantification of omeprazole in pharmaceutical dosage form. Journal of Scientific Research. 2013 Apr 22;5(2):335-42.
7. Campoli-Richards DM, Clissold SP. Famotidine. Drugs. 1986 Sep;32(3):197-221.
8. Naveed S, Zafar F. UV spectrophotometric assay of Famotidine formulations. American Journal of Pharmacy and Pharmacology. 2014;1(3):28-31.

9. Ku MS. Use of the biopharmaceutical classification system in early drug development. The AAPS journal. 2008 Mar;10(1):208-12.

10. Attimarad M, Shahzad Chohan M, Ahmed Balgoname A. Simultaneous determination of moxifloxacin and flavoxate by RP-HPLC and ecofriendly derivative spectrophotometry methods in formulations. International journal of environmental research and public health. 2019 Apr;16(7):1196.

11. Zhang WQ, Hu CQ. Theory of selectivity of RP-LC C18 column and its application. Yao xue xue bao= Acta Pharmaceutica Sinica. 2010 May 1;45(5):555-9.

12. Borman P, Elder D. Q2 (R1) validation of analytical procedures. ICH Quality guidelines. 2017 Sep 29;5:127-66.

13. Kumari K, Yadav S. Linear regression analysis study. Journal of the practice of Cardiovascular Sciences. 2018 Jan 1;4(1):33.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.