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DEVELOPMENT AND VALIDATION OF SIMULTANEOUS ESTIMATION OF FAMOTIDINE AND DOMPERIDONE IN BULK AND PHARMACEUTICAL DOSAGE FORM BY RP-HPLC

SANTHIPRIYA Y*[1], SIVA PRASAD M[2], PRACHET P[3], ANEESHA A[4] AND RAMA RAO N[5]

1: M.Pharmacy, Department of Pharmaceutical analysis, Chalapathi institute of pharmaceutical sciences, Chalapathi nagar, Lam, Guntur, Andhra Pradesh, India-522034

2: Assistant Professor, Department of Pharmaceutical analysis, Chalapathi institute of Pharmaceutical sciences, Chalapathi Nagar, Lam, Guntur, Andhra Pradesh, India-522034

3: Assistant professor, Department of Pharmaceutical analysis, Chalapathi institute of Pharmaceutical sciences, Chalapathi Nagar, Lam, Guntur, Andhra Pradesh, India-522034

4: Assistant professor, Department of pharmaceutical analysis, Chalapathi institute of Pharmaceutical sciences, Chalapathi Nagar, Lam, Guntur, Andhra Pradesh, India-522034

5: Principal, Chalapathi institute of Pharmaceutical sciences, Chalapathi Nagar, Lam, Guntur, Andhra Pradesh, India- 522034

***Corresponding Author: Yadavalli Santhipriya: E Mail: santhipriya724@gmail.com**

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ABSTRACT

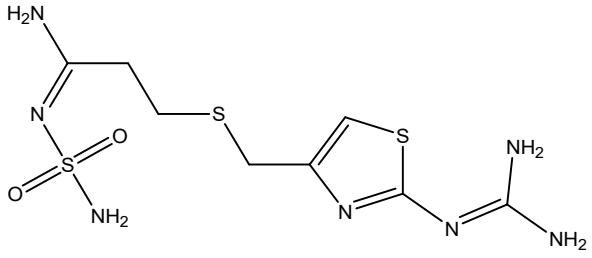
The main goal of this research is to estimate and validate the concentrations of Famotidine and Domperidone in bulk and marketed formulations. Famotidine belongs to the H2 blocker family. It is used to protect you and treat heartburn. Domperidone is a dopamine receptor antagonist used to treat dyspepsia, nausea, and anti-emetic symptoms. The stationary phase used was Shimadzu column, while the mobile phase was methanol: 0.1% Trifluroacetic acid in water: acetonitrile in the ratio 30:40:30 v/v, with a flow rate of 0.8 ml/min. The injection volume was 10µl, and the detection wavelength was 280 nm. According to ICH Q2 (R1) recommendations, system suitability, specificity, linearity, accuracy, precision, limit of detection, limit of quantification, and robustness were all tested. The linearity of famotidine and domperidone was determined to be 4-20µg/mL and 2-10µg/mL, respectively, with correlation values of 0.9993 and 0.9993. It is a simple, precise, accurate, cost-effective, and robust method and hence used for routine analysis.

Key words: Famotidine, domperidone, RP-HPLC, ICH

INTRODUCTION:

Famotidine $C_8H_{15}N_7O_2S_3$is a pharmaceutical substance that competitively blocks histamine H2 receptors thus, inhibits histamine H2 receptors competitively, reducing gastric secretion by lowering the acid content and decreasing the volume of secretion **[1, 2]**. It's used to treat ulcers in the stomach and duodenum, as well as other hyper secretion states, as well as to prevent recurrent ulcers and gastric acid aspiration during general anaesthesia. Famotidine comes in the form of tablets, capsules, and powder for oral suspensions or injectable solutions. Chemically known as 3-[[2-[(Aminoiminomethyl)amino]-4-thiazolyl]methyl]thio]-N-(aminosulfonyl)propanimidamide with Molecular weight 337.45 gm/mol. Famotidine comes in the form of tablets, capsules, and powder for oral suspensions or injectable solutions **[3, 4]**.

Domperidone is chemically: 6-chloro-3-[1-[3-(2-oxo-3H-benzimidazol-1-yl)propyl]piperidin-4-yl]-1H-benzimidazol-2-one. Domperidone blocks receptors in the chemoreceptor trigger zone at the floor of the fourth ventricle, acting as a peripherally selective antagonist of dopamine D2 and D3 receptors and providing relief from nausea. It aids in preventing you from feeling or being ill (nausea or vomiting).If you're receiving end-of-life care, it can also be used to alleviate stomach pain (palliative care).Domperidone is available in tablet form or as a liquid to ingest **[5]**.



famotidine

Figure 1: Structure of famotidine

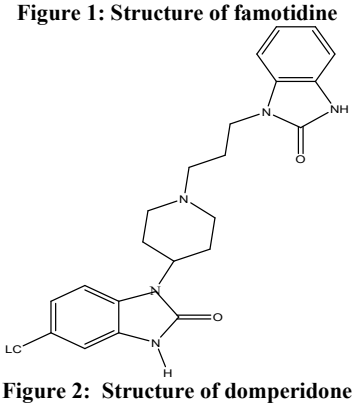


Figure 2: Structure of domperidone

METHODOLOGY:

Materials:

Famotidine and Domperidone Tablets were purchased from the local market.

Instrumentation:

The chromatographic separation was carried out on HPLC Shimadzu 2030C 3D plus with photo diode array detector, Shimadzu column, The mobile phase consisting of methanol: buffer (0.1 ml Trifluroacetic acid in 100 ml water): acetonitrile in the ratio 30:40:30 v/v into the column at a flow rate of 0.8 ml/min. The injection volume was set to be 10 µl with detection at 280 nm.

Preparation of famotidine and domperidone standard solutions:

Accurately weighed quantity of 10mg of Famotidine and 10 mg of Domperidone into different 10ml volumetric flask and made up to the volume with diluent (Tetrahydrofuran with water (1:1)) . From the above stock solution pipette out 1ml, transfer into a 10 ml volumetric flask and make up the volume with methanol (100µg/ml).

Sample preparation:

20 Tablets were weighed and their average weight were determined. They were crushed into fine powder, weigh the tablet powder equivalent to 10mg of drug and transferred into volumetric flask and dissolved in mixture of tetrahydrofuran with water (1:1).the solution is filter through 0.45µ membrane filter which gives the concentration of 1000µg/ml and this solution were used as a sample stock solution.

METHOD VALIDATION:

The developed method was evaluated for system suitability, specificity, linearity, accuracy, precision, and robustness using the ICH recommendations. The following parameters were evaluated as part of the validation study.

System suitability:

The chromatographic conditions were used to optimise the HPLC system. In the chromatographic system, 10µl of drug standard solutions were injected. To determine the suitability of the system for the proposed method, parameters such as retention time, number of theoretical plates, tailing factor, and % RSD were calculated and compared to the system's standard specification.

Specificity:

The chromatograms of the blank, standard, and sample were compared to determine the method's specificity.

Linearity:

The method's linearity was tested by generating calibration curves with various concentrations of standard solutions. The peak area and concentration of the standard solutions were used to plot the calibration curve. Using least square regression analysis, linearity was established for

famotidine from 4 to 20 µg/ml and domperidone from 2 to10 µg/ml.

Accuracy:

It is analysed by conducting three different concentrations of the working standards. With the percentage of 50%, 100%, 150% inject each concentration three times into HPLC and calculate the average percentage recovery. The mean percentage recovery of Famotidine and Domperidone is 100.51% and 99.44%.

Precision:

Six replicate injections of a known concentration of Famotidine (12µg/ml) and Domperidone (6 µg/ml) have been analysed by injecting them into a HPLC column. The peak area of all injections was taken and standard deviation, % relative standard deviation (RSD), was calculated.

Robustness:

Robustness should be considered during the development process and varies depending on the procedure under study. The ability of a method to remain unaffected by small changes in parameters such as mobile phase pH, temperature, % organic solvent strength, and buffer concentrations, among others, is known as robustness. To evaluate the method's robustness, experimental conditions were purposefully changed, and chromatographic characteristics were assessed. We change the ratio of mobile phase and mobile phase flow rate in this study.

RESULTS AND DISCUSSION:

System suitability:

The system suitability parameters of famotidine and domperidone were found to be within the acceptance standards, as shown in **Table 1**.

Acceptance criteria: The %RSD should be NMT 2.0%.

Specificity:

The approach is specific because the blank solution does not interact with the standard or sample, as shown in **Table 2**. **Figures 3, 4, 5** illustrate blank, standard, and sample chromatograms.

Linearity:

The method was linear with good correlation coefficient values and these are represented in **Table 3**.

Accuracy:

The method was accurate with good % recovery and these results are represented in **Table 4**.

Precision:

The method was precise with %RSD NMT 2 for method precision and intermediate precision these results are represented in **Table 5 and Table 6**.

Robustness:

With % RSD values NMT 2 for various robustness criteria such as flow rate change and mobile phase ratio, the approach was sufficiently robust**.**

Assay:

The % assay of Famotidine and Domperidone was represented in **Table 7**.

Table 1: System suitability parameters of famotidine and domperidone:

Parameters	Famotidine	domperidone	Acceptance criteria
Tailing factor	0.975	1.274	NMT 2.0
Number of theoretical plates	6284	8909	NLT 2000
%RSD	0.49	0.53	NMT 2.0
Retention time	3.047	4.699	NA

Table 2: Specificity of Famotidine and Domperidone

	Retention time	
Name	Famotidine	Domperidone
Blank	Not detected	Not detected
Standard	3.407	4.699
Sample	3.131	4.800

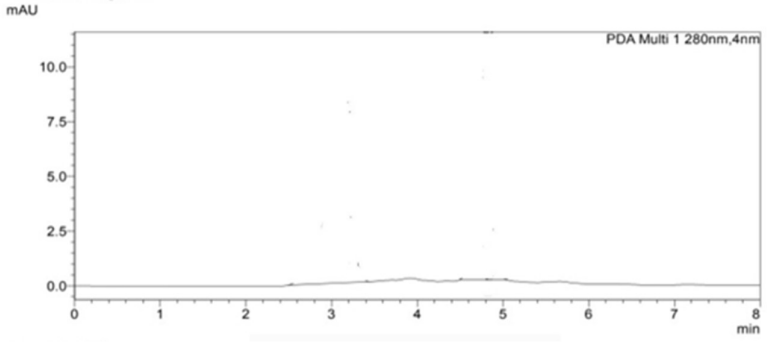


Figure 3: Blank chromatogram

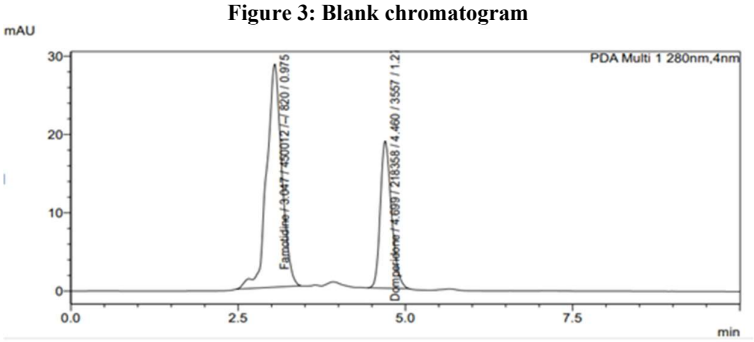


Figure 4: Standard chromatogram

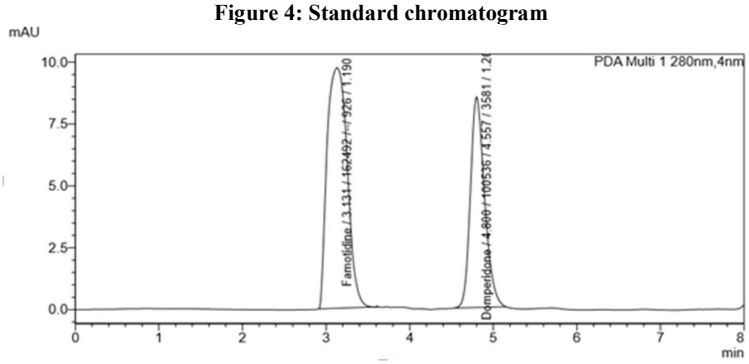


Figure 5; Sample chromatogram

Table 3: Linearity ranges for famotidine and domperidone

S.NO	Famotidine		Domperidone	
	Concentration(µg/ml)	Peak area	Concentration(µg/ml)	Peak area
1.	4	82261	2	42550
2.	8	177443	4	82491
3.	12	268365	6	122614
4.	16	364163	8	167595
5.	20	463122	10	202470
6.	Correlation coefficient	0.9993	Correlation coefficient	0.9993

Acceptance criteria: The correlation coefficient (R^2) should be NLT 0.999.

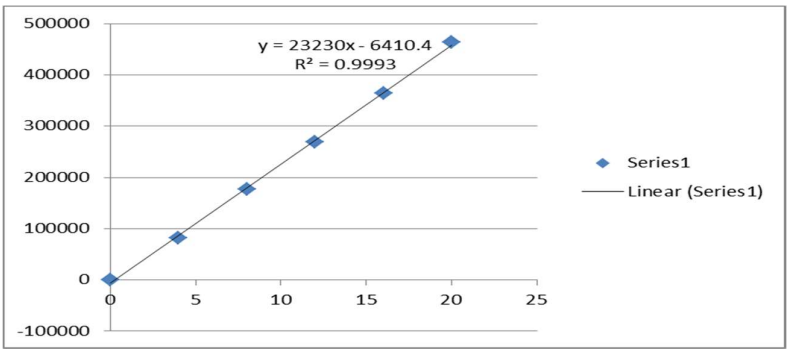


Figure 4: Calibration curve of famotidine

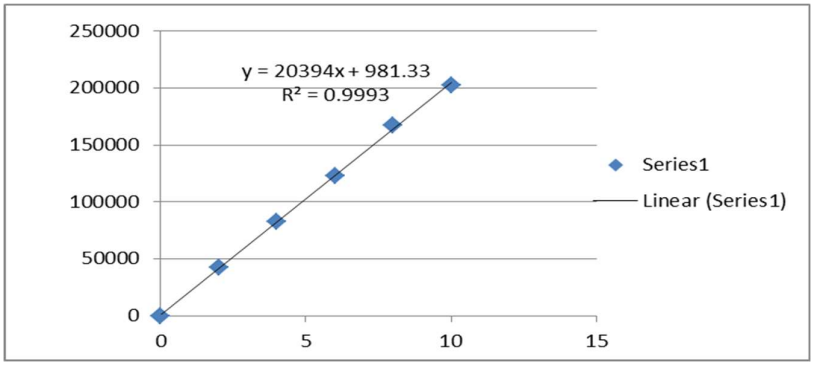


Figure 5: Calibration curve of domperidone

Table 4: Accuracy for Famotidine and Domperidone

% Level	% Recovery		Average % Recovery	
	Famotidine	Domperidone	Famotidine	Domperidone
50%	99.52	99.52	100.50%	99.44%
	101.63	99.11		
	100.62	99.79		
100%	100.52	99.24		
	100.86	99.65		
	100.39	99.17		
150%	100.51	99.70		
	100.26	99.54		
	100.27	99.34		

Acceptance criteria: The mean % recovery at each level should be not less than 98% and NMT 102%.

Table 5: System Precision for Famotidine and Domperidone

Injection number	Peak area	
	Famotidine	Domperidone
1.	240984	122652
2.	239671	121865
3.	241689	123899
4.	241954	123216
5.	242016	123312
6.	242769	123049
Average	241514	122999
SD	1070.402058	687.593315
%RSD	0.44	0.56

Acceptance criteria: The %RSD for the peak area should be NMT 2.0.

Table 6: Method precision for Famotidine and Domperidone

Injection number	Peak area	
	Famotidine	Domperidone
1.	240458	122662
2.	238671	120965
3.	241899	123789
4.	241844	124206
5.	242106	123122
6.	242869	123089
Average	241308	122972
SD	1509.064	1126.994484
%RSD	0.63	0.92

Acceptance criteria: The %RSD for the peak area should be NMT 2.0.

Table 7: % Assay

Name	% Assay
Famotidine	100.01%
Domperidone	99.44%

CONCLUSION:

Here, we have described a new method which is simple, precise, accurate, economic and robust for the simultaneous estimation of Famotidine and Domperidone in bulk and marketed formulation by using RP-HPLC. The influence of the stationary phase shimadzu column was more in order to achieve the better separation of the drugs using the mobile phase of methanol:0.1 ml Trifluroacetic acid in 100 ml water: acetonitrile in the ratio 30:40:30 v/v was pumped into the column at a flow rate of 0.8 ml/min for the faster elution. The injection volume was 10 µl with photo diode array detector for the detection of drugs at 280 nm. Further, validation of the developed method was done adapting the ICH guidelines and the results like correlation coefficient for Famotidine 0.9993 and Domperidone 0.9993 and parameters like theoretical plates, resolution, tailing factor were within the limits with %RSD of NMT 2.0. Finally, the developed method can be effectively applied in the routine analysis in the laboratories, industries and institutes.

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