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DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF IBUPROFEN AND FAMOTIDINE

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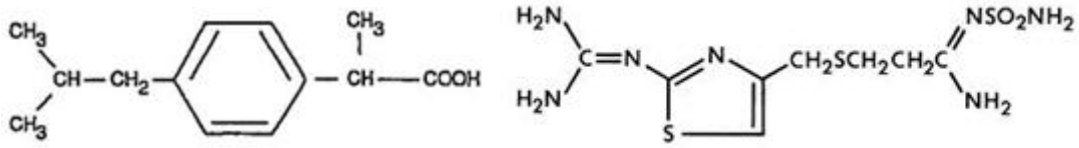
ABSTRACT

The present work describes a simple reverse phase HPLC method for the determination of Ibuprofen and Famotidine in synthetic mixture. The determination was carried out on a Phenomenex C_{18} column (250 mm x 4.6 mm i.d., 5 µm particle size) column using a mobile phase consisting of Acetonitrile : Buffer(KH2PO4) (75 : 25 , v/v) having pH 3.0 using 0.2% Triethylamine at a flow rate and run time of 1.0 ml/min and 7 min respectively. The eluent was monitored at 222 nm. The method was reproducible, with good resolution between Ibuprofen and Famotidine. The detector response was found to be linear in the concentration range of 120-600 µg/ml and 4-20 µg/ml for Ibuprofen and Famotidine. The methods were validated as per ICH guidelines (Q2R1).

INTRODUCTION

Ibuprofen is a NSAID (Non Steroidal Anti-inflammatory drug) indicated for the relief of signs and symptoms of the rheumatoid arthritis and osteoarthritis, but the side effect of gastric ulceration was the big problem, Famotidine is a H_2 Receptor Antagonist. Ibuprofen individually gives relief from Rheumatoid and Osteoarthritis but side effect of Gastric ulceration was the big problem, but in combination with the Famotidine the side effect of gastric ulceration was also removed along with the above diseases. The present work involves the development of RP-HPLC method for the above combination. A survey of literature revealed no chromatographic method has been reported till now for the above combination. Hence an attempt was made to develop RP-HPLC method with greater precision, accuracy and sensitivity.



a. **b.**

Figure 1: Chemical structure of Ibuprofen (a) and Famotidine (b)

MATERIALS AND METHODS

Pure Ibuprofen (IBU) was obtained as a gift sample from GLPL, Vadodara, Gujarat (India) and pure Famotidine (FAM) was obtained as a gift sample from Alembic Ltd., Vadodara, Gujarat (India). All HPLC grade solvents and distilled water were used throughout the study. A Shimadzu HPLC (LC Solution) system was used coupled with SPD 20A UV detector. Separations were carried out on a Phenomenex C_{18} column (250 mm x 4.6 mm i.d., 5 µm particle size) as the stationary phase. The mobile phase consisting of Acetonitrile: Buffer (KH2PO4) (75: 25, v/v) having pH 3.0 using 0.2% Triethylamine was pumped at a flow rate 1 ml per min, the detection was monitored at 222 nm and the run time was 7 min.

PREPARATION OF STANDARD STOCK SOLUTION

- Accurately weighed 120.0 mg of Ibuprofen and 4 mg of Famotidine were transferred into 100 ml volumetric flask, dissolved and diluted up to mark with mobile phase to give a stock solution having strength of 1200 µg/ml Ibuprofen and 40 µg/ml of Famotidine.
- Prepared solution was sonicated for 5 minutes.

PREPARATION OF WORKING STANDARD SOLUTION

- 10 ml of standard stock solution was transferred into 100 ml volumetric flack and diluted up to mark with mobile phase to get 120 µg/ml of Ibuprofen and 40 µg/ml of Famotidine.
- Prepared solution was sonicated for 5 minutes.

RESULTS AND DISCUSSION

Several systematic trials were performed to optimize the Chromatographic conditions for developing a sensitive, precise and accurate RP-HPLC method for the analysis of Ibuprofen and Famotidine in synthetic mixture. The present method contains mobile phase Acetonitrile: Buffer(KH2PO4) (75: 25, v/v) having pH 3.0 using 0.2% Triethylamine, which was found to be the most suitable as the chromatographic peaks obtained with this system were better defined and resolved and all almost free from tailing. Under the above conditions the retention time obtained for Famotidine and Ibuprofen was 2.107, 5.951min respectively. A model Chromatogram was shown in Fig.2 and overlaid chromatogram of Ibuprofen and Famotidine was shown in Fig. 3.

LINERITY AND RANGE

The linearity and range for RP-HPLC method was determined at six concentration levels for Ibuprofen and Famotidine. The linearity and range was found as 120-600 µg/ml and 4-20 µg/ml at 222.0nm. The calibration curve was constructed by plotting peak area against concentration of drugs. The representative linear regression equation found were $y = 38024x + 84251$ (R^2=0.998) and $y = 36890x + 30649$ (R^2=0.999) for Ibuprofen and Famotidine respectively as shown in Fig. 4 & 5.

ACCURACY

The accuracy of the methods was determined by the method of standard addition at three different levels. The recovery studies were carried out for tablets by spiking standard of each drugs equivalent to 80%, 100%, and 120% to the original amounts present in each drug formulations. The recovery data are given for Ibuprofen and Famotidine in Table 1 & 2 respectively.

PRECISION

The precision of the method for the determination of Ibuprofen and Famotidine was studied using the parameters i.e. system precision, intraday precision and intermediate precision. System precision was determined by six replicate injections of standard solution injected in to the HPLC

system. The relative standard deviation was less than 2%. Intraday precision and Interday precision was determined by the 3 replicates of 3 concentration injected to the HPLC system. The relative standard deviation was less than 2%. Robustness of the method was determined by flow rate change (±0.2ml/min) and wavelength change (±2nm). The data on precision were reported in Table 3.

LIMIT OF DETECTION AND QUANTIFICATION

The limit of detection (LOD) and limit of Quantification (LOQ) was estimated from the standard calibration curve. The residual standard deviation of regression line or standard deviation of y intercepts of regression lines used to calculate LOD and LOQ. Here, LOD=3.3* D/S and LOQ=10*D/S. Where, D is the standard deviation of y intercept of regression line and S is the slope of calibration curves. The data on LOD and LOQ were reported in Table 3.

Table 1: % Recovery Data for Ibuprofen

Level of recovery	Amt of Std IBU added (µg/ml)	Total amt of IBU (µg/ml)	Amt of IBU found (µg/ml)	Amount of IBU recovered (µg/ml)	% Recovery	Mean % recovery ± SD
80%	96	216.02	215.91	95.89	99.88	99.96 ± 0.09
	96	216.02	215.97	95.95	99.94	
	96	216.02	216.09	96.07	100.07	
100%	120	240.02	240.06	120.04	100.03	99.96 ± 0.06
	120	240.02	239.91	119.89	99.90	
	120	240.02	239.97	119.95	99.95	
120%	144	264.02	264.01	143.99	99.99	99.98 ± 0.05
	144	264.02	263.91	143.89	99.92	
	144	264.02	264.06	144.04	100.03	

Table 2: % Recovery Data for Famotidine

Level of recovery	Amt of Std FAM added (µg/ml)	Total amt of FAM (µg/ml)	Amt of FAM found (µg/ml)	Amount of FAM recovered (µg/ml)	% Recovery	Mean % recovery ± SD
80%	3.2	7.25	7.21	3.16	98.75	99.06 ±0.32
	3.2	7.25	7.23	3.18	99.38	
	3.2	7.25	7.22	3.17	99.06	
100%	4.0	8.05	8.01	3.96	99.00	99.00

	4.0	8.05	7.99	3.94	98.50	±0.05
	4.0	8.05	8.03	3.98	99.50	
120%	4.8	8.85	8.81	4.76	99.16	99.23 ±0.32
	4.8	8.85	8.80	4.75	98.96	
	4.8	8.85	8.83	4.78	99.58	

Table 3: Validation Parameters for RP-HPLC method

Parameters		**RP-HPLC method**	
		Ibuprofen	**Famotidine**
Slope		38024	36890
Intercept		84251	30649
Correlation coefficient		0.999	0.999
Linearity range (µg/ml)		120-600	4-20
LOD (µg/ml)		0.32	0.02
LOQ (µg/ml)		0.97	0.06
Precision (%RSD)	Intraday	1.20	1.28
	Interday	1.37	1.04

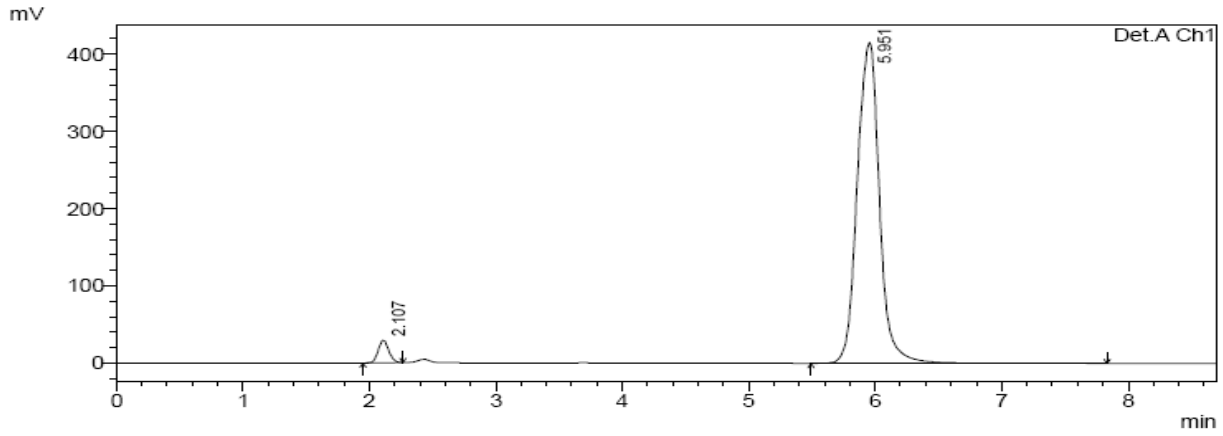


Figure.2: Standard chromatogram of Ibuprofen and Famotidine

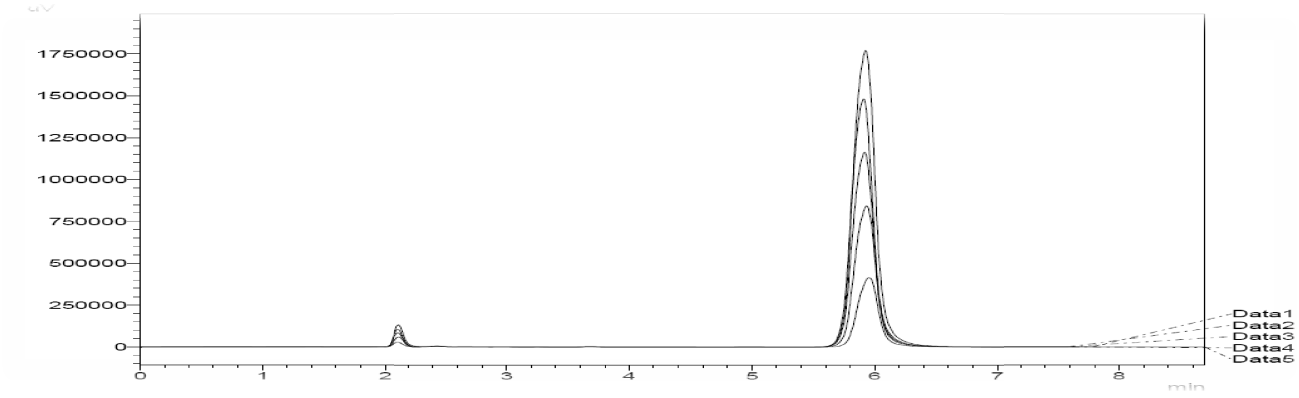
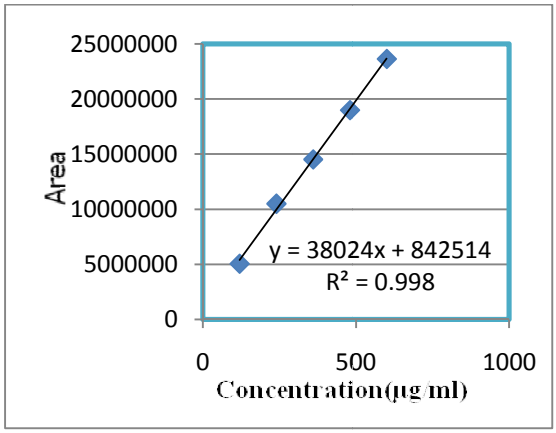


Figure.3: Overlaid chromatograms of Ibuprofen and Famotidine



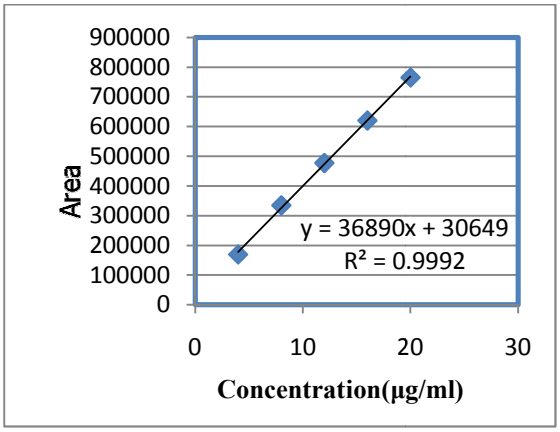


Figure 4: Calibration curve of Ibuprofen

Figure 5: Calibration curve of Famotidine

CONCLUSION

RP-HPLC method was developed for the determination of Ibuprofen and Famotidine in synthetic mixture. The low value of relative standard deviation for repeated measurement indicates that the method is precise. The value of SD in recovery study is less than two, which indicates that the methods can be used for estimation of the Ibuprofen and Famotidine without any interference. Hence proposed method is simple, accurate, precise, rapid and useful for routine analysis.

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