Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 3, 2013

Research Article

DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHODS FOR THE ESTIMATION OF IBUPROFEN AND FAMOTIDINE

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Received: 27 Mar 2013, Revised and Accepted: 16 May 2013

ABSTRACT

Objective: Two simple, accurate, precise, reproducible and an economical spectrophotometric methods were developed for the simultaneous estimation of ibuprofen and famotidine in pharmaceutical bulk and synthetic mixture.

Methods: The first method was developed on the basis of Q-absorbance ratio method (method I) for analysis of both the drugs. Wavelengths selected for analysis in Q-absorbance ratio method were 263 nm (λ_{max} of ibuprofen) and 273.80 nm (iso-absorptive wavelength) in 0.1N NaOH. The second method was based on derivative spectrophotometric method (method II) involving the determination of both the drugs at their respective zero crossing point. The determinations were made at 252.8 nm (zero crossing point of famotidine) and 304 nm (zero crossing point of ibuprofen) in 0.1N NaOH.

Results: Both the method obeys Beer-Lambert's law in the concentration range of 150 - 750 µg/ml for ibuprofen and 5 - 25 µg/ml for famotidine. The assay result of synthetic mixture was found to be 99.13 ± 0.14 for IBU and 100.73 ± 0.57 for FAM by method I and 104.17 ± 1.96 for IBU and 100.88 ± 2.13 for FAM by method II. Proposed methods were validated according to ICH Q2 (R1) analytical method validation guidelines.

Conclusion: The proposed methods are suitable for the routine quality control analysis of ibuprofen and famotidine in pharmaceutical formulation.

Keywords: Ibuprofen, famotidine, Q-absorbance ratio method, First order derivative method.

INTRODUCTION

Ibuprofen (IBU) and famotidine (FAM) were co-formulated in oral tablet dosage form indicated for the relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastro-intestinal ulcer [1-2]. IBU and FAM are chemically incompatible. So, the tablet in tablet dosage form of IBU and FAM was formulated by Horizon Pharma USA which improves the stability of IBU and FAM under forced degradation condition [1].

Chemically, IBU (Fig. 1) known as (*RS*)-2-(4-(2-methylpropyl) phenyl) propionic acid is phenyl propionic acid derivative/ cyclooxygenase inhibitor from the class of nonsteroidal anti-inflammatory drug used in the treatment of fever, arthritis as an analgesic [2].

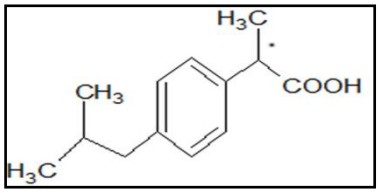

Fig. 1: Structure of IBU

Indian Pharmacopoeia [3], British Pharmacopoeia [4] and European Pharmacopoeia [5] described titrimetric method for the estimation of IBU in bulk form and titrimetric as well as liquid chromatographic method for the assay of tablet, cream, gel and oral suspension of IBU. United States Pharmacopoeia [6] described liquid chromatographic method for the estimation of IBU in bulk form and in tablet and oral suspension formulation. A number of methods have been described in the literature for the estimation of IBU as single formulation which includes spectrophotometric [7], spectrofluorimetric [8], HPLC [9, 10], HPTLC [11], and GLC [12, 13]. Also numerous methods have been reported for the estimation of IBU in multicomponent formulation which includes spectrophotometric [14-16], HPLC [17-19], UPLC [20], HPTLC [21, 22] and GC-MS [23].

Chemically, FAM (Fig. 2) known as 3-([2-(diamino- methylene amino) thiazol-4-yl] methylthio)-N′-sulfamoylpropanimidamide is a histamine H2 receptor antagonist used in the treatment of peptic ulcer and gastro esophageal reflux disease [2].

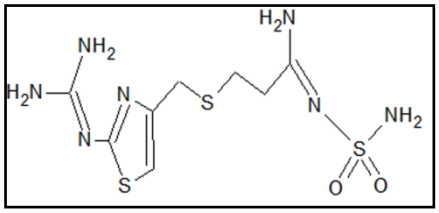

Fig. 2: Structure of FAM

Indian Pharmacopoeia [3], British Pharmacopoeia [4], European Pharmacopoeia [5] and United States Pharmacopoeia [6] described titrimetric method for the estimation of FAM in bulk form and liquid chromatographic method for the assay of tablet, injection and oral suspension of FAM. Few methods have been described in the literature for the estimation of FAM as single formulation which include spectrophotometric [24-27], spectrofluorimetric [28], HPLC [29-32], flow injection analysis [33], HPTLC methods [34, 35]. Also numerous methods have been developed for the estimation of FAM in multicomponent formulation which includes spectrophotometric [36], HPLC [37], flow injection analysis [38] and HPTLC methods [21, 39].

Research articles were published for the estimation of IBU and FAM in combination by using UV spectrophotometer. It includes first order derivative spectroscopy [40, 41], dual wavelength method [41], multicomponent mode of analysis [41], second order derivative spectroscopy [42] and simultaneous equation method [43]. In all the above method except simultaneous equation method methanol was used as solvent for the analysis of IBU and FAM in combination. But in the present work we use 0.1 N NaOH as solvent for the estimation of IBU and FAM in combination. Because NaOH is economical and non-volatile solvent.

Present work demonstrates the development, validation and application of two simple and economical spectrophotometric methods for the simultaneous analysis of IBU and FAM in combination.

MATERIALS AND METHODS

Reagents and chemicals

IBU and FAM were obtained as gift samples from Centurion Laboratories, Baroda, India. Analytical grade chemicals and distilled water was used during experimentation.

Instrument

A Shimadzu UV-1700 Pharma Spec UV-Visible spectrophotometer (UV probe 2.21 software) with a pair of 1.0 cm matched quartz cells were used for the measurement of absorbance.

Selection of solvent

About 0.1 N NaOH was selected as common solvent for studying spectral characteristics of IBU and FAM.

Preparation of standard solutions

Stock solution of IBU (3000 µg/ml) and FAM (100 µg/ml) was prepared in 0.1 N NaOH. Mixed working standard solution of 300 µg/ml of IBU and 10 µg/ml of FAM was prepared by dilution with water.

Method I: Q-absorbance ratio method

Volume of about 1.0 ml of IBU and FAM stock solution was separately transferred into 10 ml volumetric flask. The volume was adjusted to the mark with water to obtain concentration 300 µg/ml of IBU and 10 µg/ml of FAM. Absorbance of solution was measured at 263 nm (λmax of IBU) and 273.80 nm (Isoabsorptive wavelength) For IBU and FAM respectively. Concentration of both the drugs was determined using the formula mentioned below [44].

$$C1 = \frac{(Q0-Q2)}{(Q1-Q2)} \times \frac{A}{a} \qquad C2 = \frac{(Q0-Q1)}{(Q2-Q1)} \times \frac{A}{a}$$

Where,

C1- Concentration of IBU (µg/ml)

C2- Concentration of FAM (µg/ml)

A- Absorbance of sample at isoabsorptive point 273.80 nm

a- Absorptivity of IBU and FAM at isoabsorptivity wavelength 273.80 nm (0.001106 and 0.0339 for IBU and FAM respectively)

Q1- Ratio of absorbance of IBU at 263 nm to absorbance of IBU at 273.80 nm (1.6837)

Q2- Ratio of absorbance of FAM at 263 nm to absorbance of FAM at 273.80 nm (0.646)

Q0- Ratio of absorbance of sample solution at 263 nm to absorbance of sample solution at 273.80 nm

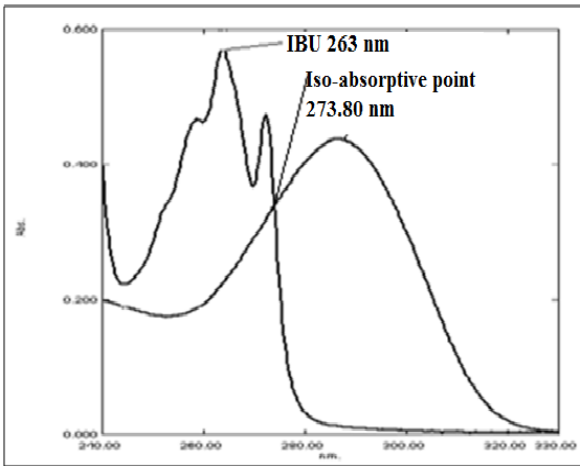

Fig. 3: Overlain UV spectra of IBU and FAM

Method II: First order derivative spectrophotometric method

Volume of about 1.0 ml of IBU and FAM stock solutions was separately transferred into 10 ml volumetric flasks. The volume was adjusted to the mark with water to obtain concentration 300 µg/ml of IBU and 10 µg/ml of FAM. Each spectrum was scanned in UV region 200 – 400 nm. The overlain UV spectra of IBU and FAM was shown in Fig. 3. The zero order spectra was transformed to first order derivative spectra with delta lambda 4 nm and scaling factor 1. From the overlain derivative spectra of IBU and FAM (Fig. 4), it was observed that IBU had zero crossing point at 304 nm whereas FAM had zero crossing point at 252.80 nm. The estimations were made at 252.80 nm for IBU (zero crossing point of FAM) and 304 nm for FAM (zero crossing point of IBU). Concentration and % drug content was determined by analyzing standard solutions simultaneously [45].

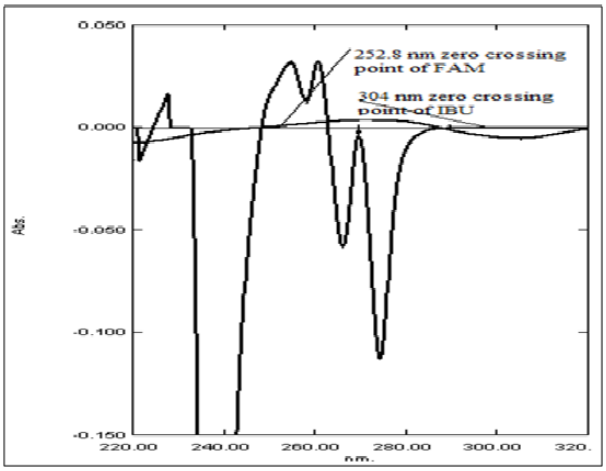

Fig. 4: Overlain of first order derivative spectra of IBU and FAM

Analysis of synthetic mixture

Excipients used in the tablet formulation were added to IBU + FAM mixture (30: 1 w/w) [1] (Table 1) and the mixture was sonicated for 20 minute after the addition of 0.1 N NaOH. The final volume was made with 0.1 N NaOH. The solution was filtered through Whatman filter paper. The working solution was prepared by dilution with water to obtain concentration of 300 µg/ml of IBU and 10 µg/ml of FAM. The working sample solution of synthetic mixture was analyzed by both UV spectrophotometric methods. The absorbance of sample solution was measured at 263 nm and 273.80 nm for Q-absorbance ratio method. For derivative spectrophotometric method, solutions were scanned in range 200 – 400 nm. Zero order spectra's were transformed to first derivative spectra, where amplitudes were measured at 252.80 nm and 304 nm against blank.

Table 1: Tablet formulation components

Material	%w/w	mg/tab
Famotidine	2.54	26.6
Lactose monohydrate	0.95	10.0
Microcrystalline cellulose	3.3	34.6
Croscarmellose sodium	0.38	4.0
Colloidal silicon dioxide	0.04	0.4
Magnesium stearate	0.11	1.2
Ibuprofen	89.75	800
Purified water	-	q. s.

Method validation

The method was validated according to ICH Q2 (R1) guidelines for validation of analytical procedures for parameters like linearity, accuracy, precision, LOD, LOQ and specificity for the analyte.

Linearity

Aliquot portions of 0.5 – 2.5 ml of IBU and FAM stock solutions were separately transferred into 10 ml volumetric flasks. The solution

was diluted with water to obtain concentrations 150 - 750 µg/ml of IBU and 5 - 25 µg/ml of FAM. For method I, absorbance of solution was measured at 263 nm for IBU and 273.80 nm for FAM. For method II, the amplitude from the first order derivative spectra was recorded at 252.80 nm for IBU and 304 nm for FAM. Calibration curve was constructed by plotting absorbance and peak amplitude versus concentration of solution.

Accuracy

The accuracy of the proposed method was determined by recovery study. The known amount of pure IBU and FAM was spiked to pre-analyzed synthetic mixture of IBU and FAM (300 µg/ml IBU + 10 µg/ml FAM). Analysis of IBU and FAM was carried out at three concentration levels such as 80%, 100% and 120% within the specified linearity and range.

The % recovery by proposed method was calculated using the formula as below.

$$\% \text{ recovery} = \frac{E}{T + P} \times 100$$

Where,

E: Total amount of drug estimated (µg/ml)

T: Amount of drug taken from pre-analyzed synthetic mixture (µg/ml)

P: Amount of pure drug added (µg/ml)

Precision

Precision was studied to find out intraday and inter-day variations in the test method of IBU and FAM. The repeatability study (intra-day precision) was performed by analyzing the samples of IBU and FAM repeatedly within the day. The inter-day precision study was performed by analyzing the samples of IBU and FAM repeatedly at different days. Six determinations of mixed working standard solution of IBU and FAM were performed. The results were expressed as SD, % RSD.

Limit of detection (LOD) and limit of quantitation (LOQ)

LOD and LOQ of IBU and FAM by developed analytical method was calculated using the formula mentioned below.

$$\text{LOD} = \frac{3.3 \times \sigma}{S}$$

$$\text{LOD} = \frac{10 \times \sigma}{S}$$

Where,

σ: Standard deviation of the response

S: Slope of calibration curve

Specificity study

Commonly used excipients like lactose, microcrystalline cellulose, magnesium stearate, croscarmellose sodium were added in the mixture of IBU and FAM (30: 1 w/w). Analysis of IBU and FAM was carried out in presence of mentioned excipients.

RESULT AND DISCUSSION

Two simple and an economical spectrophotometric methods were developed for the simultaneous estimation IBU and FAM in combination.

An overlain UV-absorption spectrum of IBU and FAM has shown severe overlap that made their direct determination in binary mixture very difficult. An overlain UV-absorption spectrum of IBU and FAM has shown iso-absorptive point at 273.80 nm (Fig. 3). So, we thought to develop Q-absorbance ratio method. Also, we have decided to develop derivative spectroscopic method which resolves the overlapped spectra (Fig. 4). In this method determination of both the drugs was carried out at zero crossing point of each other.

In concern with simultaneous equation method, analysis of both the drugs was carried out at λ_{max} of each other. But IBU has shown little and nonlinear absorbance at 286 nm (λ_{max} of FAM). So, simultaneous equation method was not developed for the analysis of IBU and FAM.

Selection of solvent

Different solvents were selected to dissolve the IBU and FAM. It includes methanol, 0.1M HCl, 0.1N NaOH and acetonitrile. IBU and FAM were insoluble in 0.1M HCl and acetonitrile, respectively. IBU and FAM were found to be freely soluble in methanol and 0.1 N NaOH.

UV spectra of IBU and FAM in methanol and 0.1 N NaOH

Separate working standard solution and mixed working standard solution of IBU and FAM in methanol was scanned in the range of 200-400 nm. IBU and FAM shown maximum absorbance at 263 nm and 286 nm respectively. UV spectrum of mixed working standard solution has shown two peak maxima at 263 nm (peak of IBU) and 266 nm (peak of FAM) instead of 286 nm (λmax of FAM) as shown in Fig. 5. This observed hypsochromic effect was might be due to quaternization of tertiary amine of FAM in methanol [45]. IBU and FAM in 0.1 N NaOH has shown maximum absorbance at 263 nm and 286.80 nm, respectively. Mixed working standard solution of IBU and FAM in 0.1 N NaOH did not shown any solvent effect on the wavelength of maximum absorbance in combination. Hence, 0.1 N NaOH was selected as a solvent for the simultaneous estimation of IBU and FAM. Effect of solvent on the absorption pattern of IBU and FAM in combination has shown in Fig. 5.

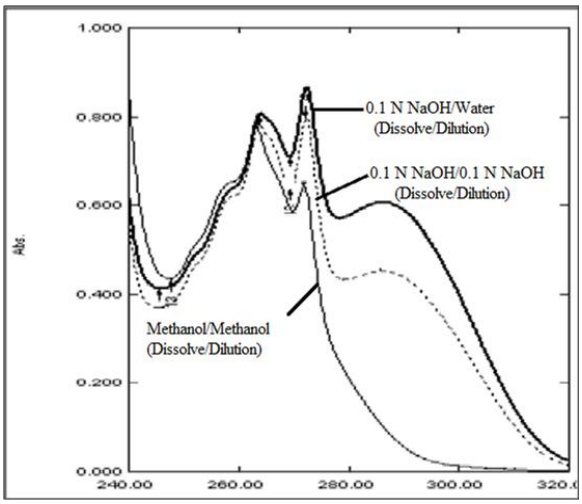

Fig. 5: Overlain spectra of IBU and FAM in different solvent system

Selection of diluent

The effect of diluent on absorbance of IBU and FAM was studied by using water and 0.1N NaOH as solvent. Mixed working standard solution of IBU and FAM diluted with water gave more absorbance than mixed working standard solution of IBU and FAM diluted with 0.1 N NaOH. So, 0.1 N NaOH was used as solvent to prepared stock solution of IBU and FAM whereas preferred diluent was water. Effect of diluent on the absorption of IBU and FAM has shown in Fig. 5.

The absorptivity value for IBU and FAM was found to be 0.001106 and 0.0339 respectively. Also, Q1 and Q2 value was found to be 1.6837 and 0.646 respectively.

Selection of derivative order

Normal spectrum of IBU and FAM was transformed to first, second and third order derivative spectrum. During linearity study it was observed that in second and third order derivative spectroscopic method IBU and FAM does not show linear response at zero crossing point of each other. In first derivative spectroscopic method IBU and

FAM has shown the linear response at 252.8 nm (zero-crossing point of FAM) and 304 nm (zero-crossing point of IBU) (Fig. 4). Therefore, first order of derivative spectrophotometric method at delta lambda (Δλ) of 4 nm and scaling factor 1 was used to resolve the spectral overlapping.

Analysis of synthetic mixture

The assay result of synthetic mixture was found to be 99.13 ± 0.14 for IBU and 100.73 ± 0.57 for FAM by method I and 104.17 ± 1.96 for IBU and 100.88 ± 2.13 for FAM by method II (Table 2).

Table 2: Application of proposed method for analysis of synthetic mixture

Drugs	Label Claim (mg)	Amount found (mg)		% Amount found		% RSD	
		Method I	Method II	Method I	Method II	Method I	Method II
IBU	300	303.11	315	99.13	104.17	0.14	1.96
FAM	10	9.93	10	100.73	100.88	0.57	2.13

Linearity study for IBU and FAM

The proposed spectroscopic method has shown linear relationship in the concentration range of 150 - 750 µg/ml for IBU and 5-25 µg/ml for FAM for both the methods (Table 3).

Accuracy

The mean % recovery was found to be 96.28 ± 1.44 for IBU and 98.97 ± 0.57for FAM by method I and 98.86 ± 1.27 for IBU and 97.32 ± 0.82 for FAM by method II (Table 4).

Precision

The results of inter-day precision were expressed as % RSD. It was found to be 1.02 and 1.05 for IBU and 1.96 and 2.13 for FAM by method I and method II, respectively. The results of intra-day precision were expressed as % RSD and it was found to be 0.70 and 1.21 for IBU and 2.02 and 2.13 for FAM by method I and method II, respectively. The % RSD value indicates the good precision of the method (Table 3).

Limit of detection (LOD) and limit of quantitation (LOQ)

Result of obtained LOD and LOQ value for simultaneous estimation of IBU and FAM by both the methods was given in Table 3.

Specificity study

From the results of specificity study, it was observed that tablet excipients did not interfere in the analysis of IBU and FAM in combination.

Table 3: Optical characteristics and validation of proposed method

Parameters	Method I		Method II	
	IBU	FAM	IBU	FAM
λmax (nm)	263	286.80	304	252.80
Iso-absorptive Point (nm)	--	273.80	--	--
Linearity Range (µg/ml)	150-750	5-25	150-750	5-25
Correlation coefficient	0.9999	0.9999	0.9995	0.9994
Slope	0.0019	0.0434	7E-05	0.0018
Limit of Detection (µg/ml)	9.7263	0.3346	1.3464	0.6954
Limit of Quantification(µg/ml)	29.4736	1.0138	4.0392	2.0862
Precision (% RSD)				
i. Intraday precision	0.70	1.21	2.02	2.13
ii. Interday precision	1.02	1.05	1.96	2.13

Table 4: Results of accuracy study

Drugs	Label claim (mg)	% Excess drug added	% Recovery	
			Method I	Method II
		80	96.28	99.07
IBU	300	100	95.85	97.50
		120	96.70	100
Mean			**96.28**	**98.86**
%RSD			**1.44**	**1.27**
		80	98.82	96.49
FAM	10	100	98.50	97.37
		120	99.59	98.09
Mean			**98.97**	**97.32**
%RSD			**0.57**	**0.82**

CONCLUSION

Two simple, accurate, precise, reproducible and an economical spectrophotometric methods were developed for the simultaneous estimation of ibuprofen and famotidine in pharmaceutical bulk and synthetic mixture. The proposed methods are suitable for the routine quality control analysis of ibuprofen and famotidine in pharmaceutical formulation.

ACKNOWLEDGMENT

We are thankful to Centurion Laboratories, Baroda (India) for providing gift sample of IBU and FAM for research purpose. We would also like to extend thanks to Dr. S. B. Bari Sir, Principal, H. R. Patel Institute of Pharmaceutical Education and Research, Shirpur for providing research facilities to carry out this project work.

REFERENCES

1. Xu J, Valley H, Tidmarsh, US Patent 8,067,033 B2, 2011; Stable compositions of famotidine and ibuprofen, Horizon Pharma, USA, pp. 1-11.
2. DUEXIS, Full Prescribing Information, 2011, Horizon Pharma, USA, pp. 1-20.
3. Indian Pharmacopoeia, I.P. Commission, Ghaziabad, 2010, p. 1331, 1479.

4. British Pharmacopoeia, Her Majesty's Stationary Office, London, 2009, p. 767, 791.
5. European Pharmacopoeia, Council of Europe (EDQM), France, 2119, 1865.
6. United States Pharmacopoeia, U.S.P.Convention, XXIV Rockville, 2009, p. 1865, 2607.
7. Afkhami A, Madrakian T, Khalafi L, Flow injection and batch spectrophotometric determination of Ibuprofen based on its competitive complexation reaction with phenolphthalein-B-cyclodextrin inclusion complex, Anal Lett 2007, 40(12): 2317-2328.
8. Damiani PC, Bearzotti M, Cabazon MA, Spectrofluorometric determination of ibuprofen in pharmaceutical formulations, J Pharm Biomed Anal 2001, 25(3-4): 679-683.
9. Glowka FK, Karazniewicz M, High performance capillary electrophoresis method for determination of ibuprofen enantiomers in human serum and urine, Anal Chim Acta 2005, 540(1): 95-102.
10. Cory WC, Harris C, Martinez S, Accelerated degradation of ibuprofen in tablets, Pharm Dev Technol 2010, 15(6): 636-643.
11. Save TK, Parmar DV, Devaranjan PV, High-performance thin-layer chromatographic determination of ibuprofen in plasma, J Chromatogr B 1997; 690(1-2): 315-319.
12. Hackett LP, Dusci LJ, Gas-liquid chromatographic determinaton of ibuprofen in human plasma, Clin Chim Acta 1978, 87(2): 301-303.
13. Vangiesse GJ, Kaiser DG, GLC determination of ibuprofen [dl-2-(p-isobutylphenyl)propionic acid] enantiomers in biological specimens, J Pharm Sci 1975, 64(5): 798-801.
14. Hassan WS, Determination of ibuprofen and paracetamol in binary mixture using chemometric-assisted spectrophotometric methods, Am J Appl Sci 2008, 5(8):1005-1012.
15. Nyola N, Govinda SJ, Kumavat M, Kalra N, Singh G, Simultaneous estimation of famotidine and ibuprofen in pure and pharmaceutical dosage form by UV-Vis spectroscopy, Int Res J Pharm 2012, 3(4): 277-280.
16. Palabiyik IM, Dinc E, Onur F, Simultaneous spectrophotometric determination of pseudoephedrine hydrochloride and ibuprofen in a pharmaceutical preparation using ratio spectra derivative spectrophotometry and multivariate calibration techniques, J Pharm Biomed Anal 2004, 34(3): 473-483.
17. Reddy PB, Reddy MS, RP-HPLC method for simultaneous estimation of paracetamol and ibuprofen in tablets, Asian J Res Chem 2009, 2(1): 70-72.
18. Ravisankar S, Vasudevan M, Gandhimathi M, Suresh B, Reversed-phase HPLC method for the estimation of acetaminophen, ibuprofen, chlorzoxazone in formulations, Talanta 1998, 46(6): 1577-1581.
19. Ge ZK., Luo YH, Zhao XY, Zang YJ, Zang H, Tian CC, Simultaneous determination of ibuprofen and diphenhydramine HCl in orally disintegrating tablets and its dissolution by reversed-phase high performance liquid chromatography (RP-HPLC), Afr J Pharm Pharmacol 2011, 5(18): 2100-2105.
20. Rao DD, Sait SS, Mukkanti K., Development and validation of an UPLC method for rapid determination of ibuprofen and diphenhydramine in presence of impurities in combined dosage form, J Chromatogr Sci 2011, 49(4): 281-286.
21. Dubey N, Jain DK, Jadhawani S, Stability indicating HPTLC method for simultaneous estimation of famotidine, paracetamol and ibuprofen in combined tablet dosage form, J Planar Chromatogr--Mod TLC 2012, 25(2): 162.
22. Soloman WDS, et al. Derivatized HPTLC method for simultaneous estimation of glucosamine and ibuprofen in tablets, Journal of Pharmacy Research and Health Care 2010, 2(2):156-162.
23. Dowling G, Gallo P, Fabbrocino S, Serpe L, Regan L, Determination of famotidine in human plasma and urine by high-performance liquid chromatography, Food Addit Conta 2008, 25(12): 1497-1508.
24. Darwish IA, Hussein SA, Mohmoud AM, Hassan AI, Sensitive indirect spectrophotometric method for determination of H2-receptor antagonists in pharmaceutical formulations, Int J Biomed Sci 2007, 3(2): 123-103.
25. Rahman N, Kashif M, Application of ninhydrin to spectrophtometric determination of famotidine in drug formulation, IL Farmaco 2003, 58(10): 1045-1050.
26. Ayad MM, Shalaby A, Abdellatef HE, Hosny MM, New colorimetric methods for the determination of trazodone HCl, famotidine and diltiazem HCl in their pharmaceutical dosage forms, Anal Boianal Chem 2003, 376(5): 710-714.
27. Okram ZD, Kanakapura B, Pavagada JR, Kanakapura BV, Simple and sensitive UV spectrophotometric methods for determination of famotidine in tablet formulations, Farmacia 2011, 59(5): 647-657.
28. Walash MI, El-Brashy A, El-Enany N, Wahba MEK, Spectrofluorimetric determination of famotidine in pharmaceutical preparations and biological fluids through ternary complex formation with some lanthanide ions: application to stability studies, Int J Biomed Sci 2009, 5(2): 158-168.
29. Zendelovska D, Stafilov T, High-performance liquid chromatographic determination of famotidine in human plasma using solid-phase column extraction, J Serb Chem Soc 2003, 68(11): 883-892.
30. Zarghi A, Shapaati A, Foroutan S M, Khoddam A, Development of a rapid HPLC method for determination of famotidine in human plasma using a monolithic column, J Pharm Biomed Anal 2005, 39(3-4): 677-680.
31. M Vamsi Krishna, G Madhavi, LA Rama Prasad, D Gowri Sankar, Impurity profiling of famotidine in bulk drugs and pharmaceutical formulations by RP-HPLC method using ion pairing agent, Der Pharm Lett 2010, 2(3): 1-11.
32. Helali N, Darghouth F, Monser L, RP-HPLC determination of famotidine and its potential impurities in pharmaceuticals, Chromatographia 2004, 60(7, 8): 455-460.
33. Tzanavaras PD, Verdoukas A, Balloma T, Optimization and validation of a dissolution test for famotidine tablets using flow injection analysis, J Pharm Biomed Anal 2006, 41(2): 437-441.
34. Singh S, Kumar S, Sharda N, Chakrabarti AK, New findings on degradation of famotidine under basic conditions: identification of a hitherto unknown degradation product and the condition for obtaining the propionamide intermediate in pure form, J Pharm Sci 2002, 91(1): 253-257.
35. Sathiyanarayanan L, Kulkarni PV, Nikam AR, Mahadik KR, Rapid densitometric method for simultaneous analysis of famotidine and domperidone in commercial formulations using HPTLC, Der Pharm Sin 2011, 3(1): 134-143.
36. Tajane DD, Gite SR, Shah AR, Kale AB, Gadhave RV, Choudhari VP, Spectrophotometric simultaneous determination of famotidine and domperidone in combined tablet dosage form by ratio derivative and area under curve method. Der Pharm Sin 2011, 2(3): 60-66.
37. Biffar SE, Mazzo DJ, Reversed-phase determination of famotidine, potential degradates, and preservatives in pharmaceutical formulations by high-performance liquid chromatography using silica as a stationary phase, J Chromatogr 1986, 363(2): 243-249.
38. Kamath BV, Shivram K, Shah AC, Determination of diclofenac sodium, famotidine and ketorolac tromethamine by flow injection analysis using dichloronitrophenol, J Pharm Biomed Anal 1994, 12(3): 343-346.
39. Pawar SM, Patil BS, Patil RY, Validated HPTLC method for simultaneous quantitation of famotidine and domperidone in bulk and formulation, Int J Adv Pharm Sci 2010, 1: 54-59.
40. Patel DP, Shah RR, Patel AP, Tank PK, Development and validation of first order derivative UV-spectroscopic method for estimation of ibuprofen and famotidine in synthetic mixture, Pharma Science Monitor 2012: 2506-2515.
41. Singhvi I, Prajapati A, Development and validation of analytical methods for simultaneous estimation of ibuprofen and famotidine in bulk and tablets using UV-visible spectroscopy, Inventi Rapid: Pharm Analysis & Quality Assurance 2012, 12: 19.
42. Shah DA, Suthar DJ, Nagda CD, Chhalotiya UK, Bhatta KP, Estimation of ibuprofen and famotidine in tablets by second order derivative spectrophotometric method, Arabian J Chem 2012, XXX, XXX-XXX: 1-4.

43. Kesur BR, Salunkhe VR, Magdum CS, Development and validation of UV spectrophotometric method for simultaneous estimation of ibuprofen and famotidine in bulk and formulated tablet dosage form, Int J Pharm Pharm Sci 2012, 4(4): 271-274.
44. Satheeshmanikandan TRS, Wali DC, Bariwal J, Kadam SS, Dhaneshwar SR, Simultaneous spectrophotometric estimation of ibuprofen and methocarbamol in tablet dosage form, Indian J Pharm Sci 2004, 66(6): 810-813.
45. Beckett AH, Stenlake JB, 1997. Practical pharmaceutical chemistry, 4thed. New Delhi: CBS publishers and distributors. p. 281.
46. Vijaya Laxmi, Spectrophotometric determination of amiloride in bulk and pharmaceutical formulations, Int J Pharm Pharm Sci 2013, 5(2): 298-302.
47. Lalitha G., Salomi P., Ravindra Reddy K., development of an analytical method and its validation for the analysis of atenolol in tablet dosage form by uv- spectrophotometry, Int J Pharm Pharm Sci 2013, 5(2): 197-199.
48. ICH Validation of analytical procedures: Text and methodology Q2 (R1), 2005.