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Development and Validation of Spectrophotometric Methods for Simultaneous Estimation of Ibuprofen and Famotidine in Combined Pharmaceutical Formulation

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ABSTRACT

Two simple, rapid, precise and accurate spectrophotometric methods have been developed for simultaneous analysis of Ibuprofen (IBU) and Famotidine (FAMO) in their combined dosage form. Method A, absorbance correction method involves measurement of amplitudes at 220 nm (for IBU) and 288 nm (for FAMO) in zero derivative spectra. Method B, ratio derivative spectrophotometry, involves division of spectra of IBU by one selected standard spectrum of FAMO and then measuring amplitudes at 234.2 nm in ratio derivative spectra for estimation of IBU. Similarly, spectra of FAMO are divided by one selected standard spectrum of IBU and then amplitudes at 277.8 nm in ratio derivative spectra are measured for estimation of FAMO. Developed methods were validated according to ICH guidelines. The calibration graph follows Beer's law in the range of 2 to 60 µg/ml for IBU and 3.8 to 4.6 µg/ml for FAMO with R^2 value greater than 0.999. Accuracy of all methods was determined by recovery studies and showed % recovery between 98 to 102%. Intraday and Interday precision was checked for both the methods and mean %RSD was found to be less than 2 for these methods. The methods were successfully applied for estimation of IBU and FAMO in marketed formulation.

Keywords: Ibuprofen, Famotidine, Absorbance correction method, first order ratio derivative method

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INTRODUCTION:

Ibuprofen (IBU) α-methyl-4-(2-methylpropyl)benzene acetic acid, 2-(p-Isobutyl phenyl)propanoic acid, 4-Isobutylhydratropic acid is a nonsteroidal anti-inflammatory drug (NSAID) used for relief of symptoms of arthritis, constipation, fever, as an analgesic (pain reliever), especially where there is an inflammatory component and dysmenorrhoea. Ibuprofen is known to have an antiplatelet effect, though it is relatively mild and somewhat short-lived when compared with aspirin or other better-known antiplatelet drugs. In general, ibuprofen also acts as a vasodilator, having been shown to dilate coronary arteries and some other blood vessels. Famotidine (FAMO) is a histamine H_2 receptor antagonist that inhibits stomach acid production, and it is commonly used in the treatment of peptic ulcer disease (PUD) and gastro oesophageal reflux disease (GERD/GORD). Unlike cimetidine, the first H_2 antagonist, famotidine has no effect on the cytochrome P450 enzyme system, and does not appear to interact with other drugs. A large Number of methods have been reported in literature based on UV and HPLC including LC – MS. But a few randomly selected references are mentioned. for the individual analysis of IBU based on UV[11, 12], HPLC[4, 5] etc. and for FAMO by area under curve in UV method[3], first order derivative spectroscopy[3], HPLC[6, 7, 10]., However to our knowledge, no article related to simultaneous estimation of IBU and FAMO by UV and RP-HPLC methods has ever been mentioned in literature.

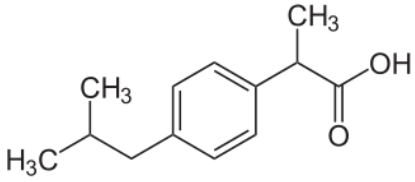

Figure 1: structure of Ibuprofen

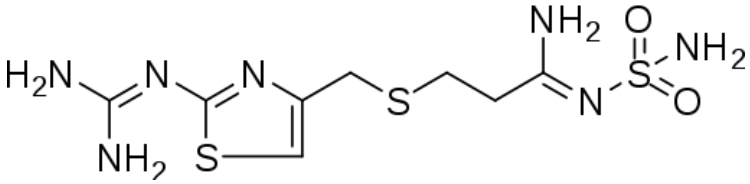

Figure 2: structure of Famotidine

MATERIALS AND METHODS

Instrumentation: Shimadzu UV-1700 double beam spectrophotometer connected to a computer loaded with Shimadzu UVProbe 2.10 software was used for all the spectrophotometric measurements. The absorbance spectra of the reference and test solutions were measured in 1 cm quartz cells over the range of 200-400 nm.The samples were weighed on A×120, Shimadzu electronic analytical balance.

Reagents and Chemicals

AR grade methanol (SPECTROCHEM Pvt ltd, Mumbai, India). Standard sample IBU and FAMO were provided by TORRENT PHARMA. LTD (Ahmadabad) and SULESHWARI PHARMA (Ankleshwer) as gift samples. Methanol - AR grade was used as solvent.

Preparation of Standard solutions

Accurately weighed IBU and FAMO (in quantities of 10 mg and 10 mg respectively) were transferred to two separate 10 ml volumetric flasks, dissolved with the use of methanol and volume was made up to the mark with methanol. From this, standard stocks solution of IBU (1000 µg/ml) 5 ml aliquot was transferred to to 50 ml volumetric flask and making up the volume with methanol and that will become 100 µg/ml. five standard IBU solutions in the range of 24 to 48 µg/ml were prepared by subsequent dilution of this solution. For FAMO, an aliquot of 1 ml from the standard stock solution (1000 µg/ml) was diluted to 10 ml with methanol; five standard FAMO solutions in the range of 3.8 to 4.6 µg/ml were prepared by subsequent dilution of this solution.

Preparation of Sample solutions

The combined dosage formulation of IBU and FAMO is not available in India, though it is available in US. A laboratory sample was prepared using the excipients mentioned in the literature [1] and by following the standard procedure [13], formula for the laboratory sample used for analysis was,

Table 1: Formula for the laboratory sample

Sr no.	Chemical	Quantity (mg)
1	Famotidine	26.5
2	Ibuprofen	800
3	Anhydrous lactose	160
4	Povidone	10
5	Aerosil	2
6	Magnesium stearate	2
Total		**1000.5**

Synthetic mixture was weighed and dissolved in methanol to make up the volume to 100 ml. the solution was further diluted with methanol to obtain the final sample solutions in the concentration range of 24 to 36 µg/ml for IBU and 3.8 to 4.2 µg/ml for FAMO for recovery study.

Method A: Ratio Derivative Spectrophotometry

In this method, the zero order absorption spectra of IBU and FAMO were divided by one standard spectrum of FAMO and IBU respectively. For selecting the standard solution as divisor, appropriate concentrations of IBU and FAMO were tested and based on better signal to noise ratio values, 4.2 µg/ml of FAMO and 24 µg/ml of IBU were selected as divisor concentration. The spectra of IBU ranging from 24 to 48 µg/ml were recorded in the region of 200 to 400 nm and were divided by standard spectrum of 4.2 µg/ml FAMO to obtain ratio spectra. These ratio

spectra were derivatised with Δλ = 16 nm and scaling factor 100. Ratio derivative spectra are shown in figure 3 and 4. Analytical wavelength of 234.2 nm was selected because of higher correlation co efficient for estimation of IBU. Calibration graph at this wavelength is plotted and shown in figure 5 and 6. Similarly, the spectra of FAMO ranging from 3.8 to 4.6 µg/ml were recorded and divided by standard spectrum of 24 µg/ml IBU. These ratio spectra were derivatised with Δλ = 16 nm and scaling factor 100. For estimation of FAMO, analytical wavelength of 277.8 nm was selected. Ratio derivative spectra (Figure 3 and 4) and calibration graph (Figure 5 and 6) are shown in Result and Discussion.

Method B: Absorbance Correction Method [2]

Absorbance spectra of IBU (24 to 48 µg/ml) and FAMO (3.8 to 4.6 µg/ml) in the range of 200 to 400 nm were taken. Overlain zero order spectra of both drugs are shown in Figure 7. This method involves measurement of absorbance at 220 nm and 288 nm. At 288 nm, IBU shows no absorbance and FAMO can be estimated directly without any interference of IBU. IBU shows maximum absorbance at 220nm where FAMO is having considerable interference. So, absorbance of FAMO at 220 nm is corrected from total absorbance and then it is related to concentration of IBU. Calibration graphs are prepared at 320 nm and 288 nm for IBU and FAMO respectively.

- $C_Y = \frac{A_{288\ nm}}{A\ (1\%,\ 1cm)_{288\ nm\ of\ FAMO}}$
- $Ay_{220\ nm} = Cy * A\ (1\%,\ 1cm)_{220\ nm\ of\ FAMO}$
- $CAx_{220\ nm} = A_{220\ nm} - Ay_{220\ nm}$
- $C_x = \frac{CAx_{220\ nm}}{A\ (1\%,\ 1cm)_{220\ nm\ of\ IBU}}$

Where,

- Cx = Conc. Of IBU in gm/100ml
- Cy = Conc. Of FAMO in gm/100ml
- $A_{220\ nm}$ = Absorbance of mixture at 220 nm
- $A_{288\ nm}$ = Absorbance of mixture at 288 nm
- $CAx_{220\ nm}$ = Corrected absorbance of IBU at 220 nm
- $Ay_{220\ nm}$ = Absorbance of FAMO at 220 nm

Assay of Commercial Formulation by Method A and B

Synthetic tablet powder was weighed and an amount equivalent to 10 mg IBU and FAMO was weighed and dissolved in 10 ml of Methanol. Solutions were filtered using Whatmann filter paper grade 1. Appropriate dilutions were prepared in methanol taking suitable aliquots of the

clear filtrates and subjected to analysis using the two methods described above. The result of analysis is reported in Table 2 in Result and Discussion.

RESULTS AND DISCUSSION

The spectra and calibration curve for method A - Ratio Derivative Spectrophotometry are shown below.

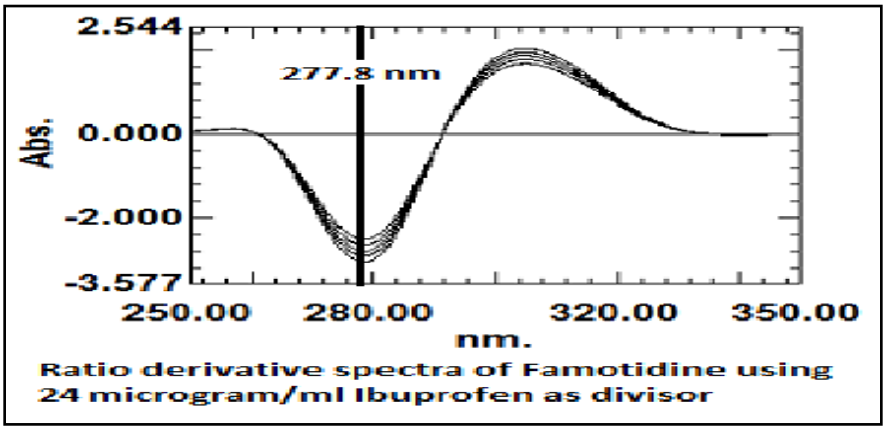

Figure 3: Ratio derivative spectra of FAMO

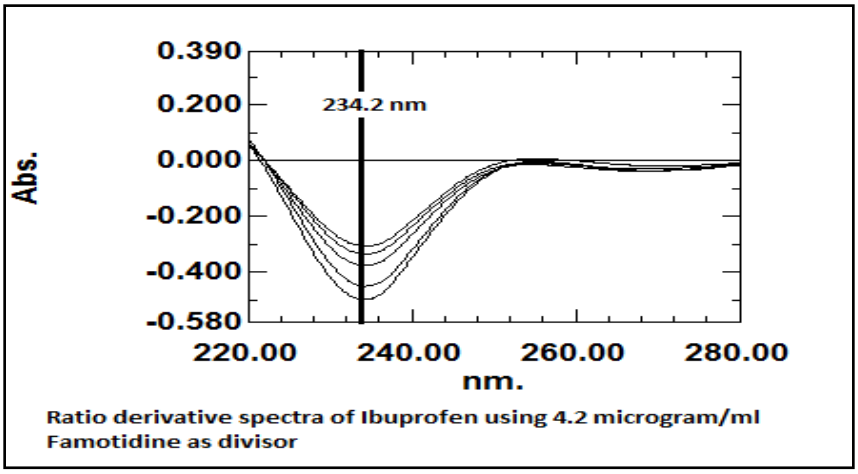

Figure 4: Ratio derivative spectra of IBU

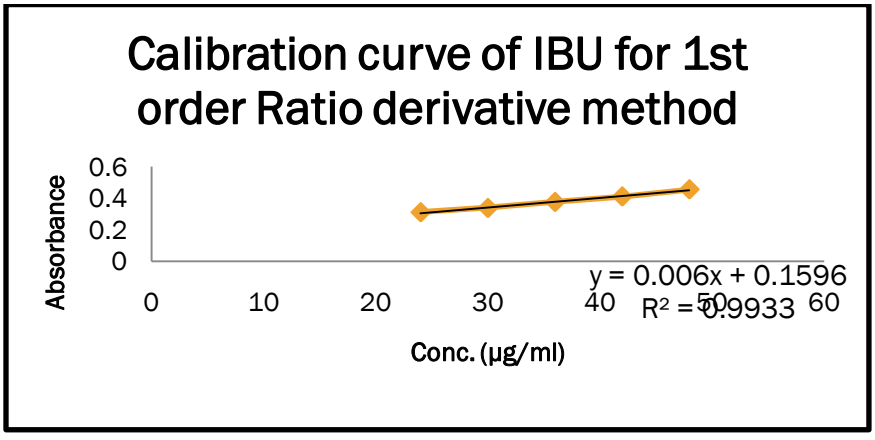

Figure 5: Calibration graph of IBU by ratio derivative spectrophotometry

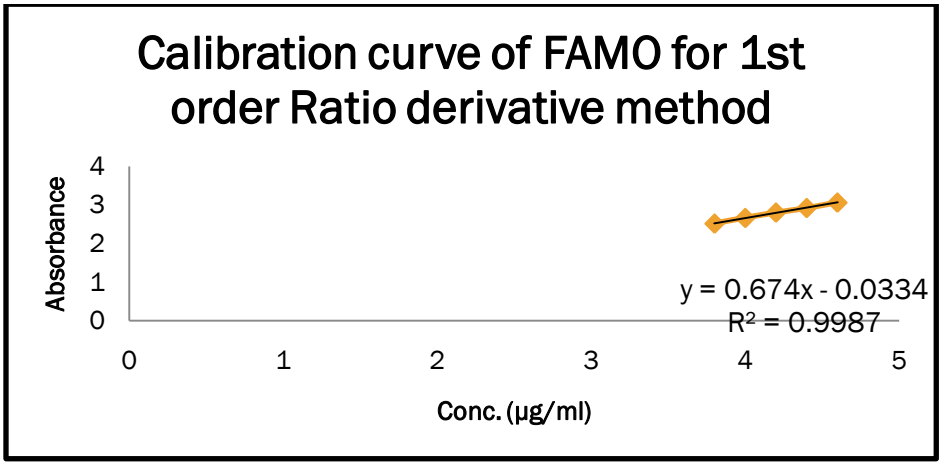

Figure 6: Calibration graph of FAMO by ratio derivative spectrophotometry

The spectra and calibration curve for method B - Absorbance Correction Method are shown below.

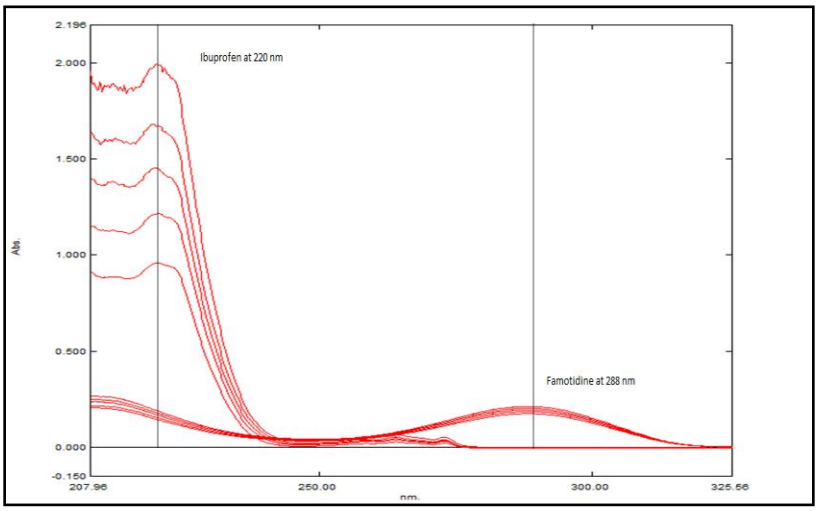

Figure 7: Zero order overlain spectra of IBU at 220 nm and FAMO at 288 nm

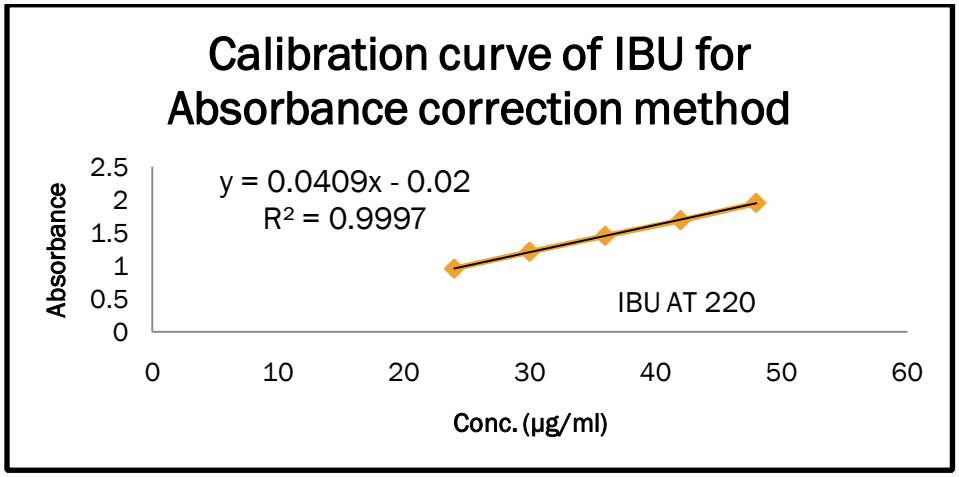

Figure 8: Calibration graph of IBU by absorbance correction method

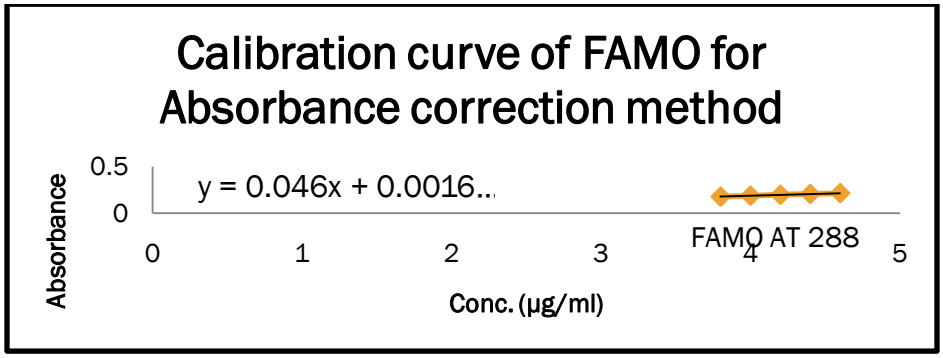

Figure 9: Calibration graph of FAMO by absorbance correction method

Table 2: Results of Simultaneous Estimation of laboratory scale synthetic mixture For Method A and B.

Labelled claim :- IBU : FAMO (800 mg : 26 mg)		
Method	IBU*	FAMO*
A	99.50 ± 0.82 %	99.85 ± 0.83 %
B	99.31 ± 1.65 %	99.10 ± 0.74 %

* Mean value of five determinations

Developed spectrophotometric methods for the simultaneous analysis of IBU and FAMO were validated according to ICH guidelines and data complying with the standards were obtained. The results of validation parameters for the two methods are reported in Table 3.

Table 3: Summary of Validation Parameters by Developed Methods [14]

Parameters		**Method A**		**Method B**	
		IBU	**FAMO**	**IBU**	**FAMO**
Analytical wavelength (nm)		234.2	277.8	220	288
Beer's range (µg/ml)		24 to 48	3.8 to 4.6	24 to 48	3.8 to 4.6
Regression coefficient		0.9933	0.9987	0.9997	0.9995
Intraday precision (%RSD)		0.88642	0.36020	0.154	0.958
Interday precision (%RSD)		0.71906	0.10103	0.147	0.536
LOD (µg/ml)		1.80	0.049	0.192	0.131
LOQ (µg/ml)		4.64	0.151	0.257	0.399
% Recovery	80% standard addition*	101.66% ± 0.75	99.73% ± 1.23	99.50% ± 0.87	100.43% ± 0.98
	100% standard addition*	100.64% ± 0.98	101.29% ± 0.96	99.10% ± 0.74	100.09% ± 1.02
	120% standard addition*	102.75% ± 0.56	101.58% ± 0.87	99.31% ± 0.99	99.85% ± 0.83

* Mean value of three determinations

CONCLULSION

Spectrophotometric methods were developed for simultaneous estimation of IBU and FAMO in their combined formulation without prior separation. Spectra of IBU were completely overlapped

by FAMO and derivatisation was used as a powerful tool for simultaneous determination. Methods were found to be precise and accurate as can be reflected from validation data. Developed methods were successfully applied for estimation of IBU and FAMO in marketed formulation.

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