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Development of UV Spectrophotometric Method for the Simultaneous Estimation of Ibuprofen and Famotidine in Tablet Dosage Form by Absorbance Correction Method and Absorbance Ratio Method

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ABSTRACT

Two new UV-spectrophotometric methods have been developed and validated for simultaneous estimation of ibuprofen and famotidine in a tablet dosage form (DUEXIS). The first method, the absorbance correction method was based on the measurement of the absorbance at two wavelengths, namely, 287nm at which ibuprofen has no absorbance while at wavelength 264 nm both drugs have considerable absorbance. The second method was the absorbance ratio method, which involves formation of Q-absorbance equation at 274.5 nm (isoabsorptive point) and also at 264 nm (λmax of ibuprofen). The methods were found to be linear between the range of 50-800 g/ml for ibuprofen and 3-27 g/ml for famotidine for both methods. The mean percentage recovery was found in the range of 101.1%-101.84% and 101.84-102.84% for the Absorbance correction method and 99.93-101.14 and 101.62-102.57 for the absorbance ratio method, for ibuprofen and famotidine, respectively, at three different levels of standard additions. The precision (intra-day, inter-day) of methods were found within limits (RSD <2%). It could be concluded from the results obtained in the present investigation that the two methods for the simultaneous estimation of ibuprofen and famotidine in tablet dosage form are simple, rapid, accurate, precise and economical and can be used, successfully in the quality control of pharmaceutical formulations and other routine laboratory analysis.

KEY WORDS: Ibuprofen, Famotidine, DUEXIS, Absorbance Correction Method, Absorbance Ratio Method, Validation Parameters.

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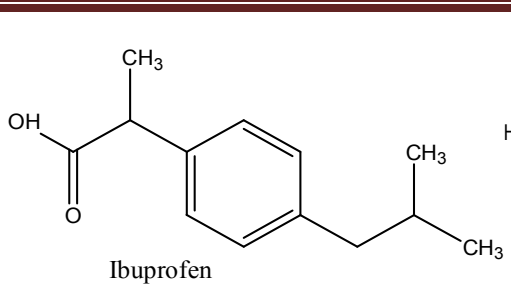
INTRODUCTION

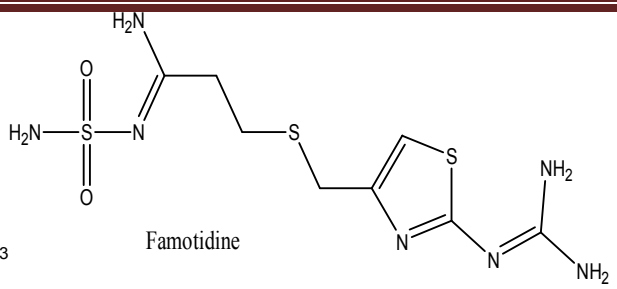
Ibuprofen, 2-[4-(2-methyl propyl) phenyl] propanoic acid, is an NSAID. Its anti-inflammatory properties may be weaker than those of some other NSAIDs. It is used in the management of mild to moderate pain and inflammation in conditions such as dysmenorrhoea, headache including migraine, postoperative pain, dental pain, musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis including juvenile idiopathic arthritis, peri-articular disorders such as bursitis and tenosynovitis, and soft-tissue disorders such as sprains and strains; it is also used to reduce fever[1]. Ibuprofen contains a chiral carbon atom on the propionic acid side-chain; therefore it exists as two enantiomers. It is usually marketed as a 50:50 mixture of the *S*- and *R* enantiomers, even if it is known that the pharmacological activity is due almost exclusively to the *S*- enantiomer[2].

Famotidine N2- (aminosulfonyl)-3-[[[2[(diaminomethylene) amino] thiazol-4 yl] methyl] thio] propanamidine is a potent histamine H2-receptor antagonist widely used in the treatment of gastric and duodenal ulcers[3]. Famotidine belongs to a class of drugs known as histamine H2 receptor antagonist used in the treatment of gastric and duodenal ulcers. It inhibits gastric acid secretion by blocking the H2 receptors located on parietal cells[4].

Famotidine and Ibuprofen both are official in IP[5], USP[6], BP[7], JP[8] and EP[9] which includes HPLC method, Potentiometric titration for estimation of famotidine and ibuprofen respectively. Famotidine and Ibuprofen are available in a combined tablet dosage known as DUEXIS (Horizon Pharma). It was approved by US-FDA. The combination of these two drugs is not official in any pharmacopoeia. Although a number of analytical procedures have been described in the l;iterature for the estimation of both drugs in either single dosage form, or in combination with other drugs[10-14], yet the estimation of ibuprofen and famotidine in tablet dosage form by the two uv-spectrophotometric methods that have been adopted in the present work have not been reported in the literature. It is noteworthy to mention that, ibuprofen and famotidine in tablets have been estimated via only, one reported method, the first order derivative method[15]. It was this endeavour that prompted us to carry out the present research investigation. One of the objectives of the present work is, also, to develop and validate new analytical methods, namely, the Absorbance Correction Method and the Absorbance Ratio Method, for simultaneous determination ibuprofen and famotidine in tablet dosage forms.



Ibuprofen



Famotidine

EXPERIMENTAL SECTION (MATERIALS AND METHODS)

Instruments:

Shimadzu UV-1800, UV-Visible double beam Spectrophotometer with matching pair of 1 cm quartz cuvettes (Shimadzu Corporation, Kyoto, Japan). The spectral bandwidth is 0.5 nm.

Reagents and Chemicals

Pure drug samples of Ibuprofen and Famotidine were obtained as gift sample from EL-ALAMIA Pharmaceuticals Ltd., Yemen. Combined dose tablet formulation (DUEXIS) was procured from market. NaOH (0.1%) was used as solvent.

Preparation of stock solution

Accurately weighed ibuprofen (800 mg) and famotidine (30 mg) were transferred to a 100 ml volumetric flask and dissolved and diluted up to the mark with NaOH (0.1%) to produce 8000 g/ml for ibuprofen and 300 g/ml for famotidine stock solution.

DETERMINATION OF MAXIMUM WAVELENGTH AND ISOABSORPTIVE POINT

The stock solutions of Ibuprofen and famotidine were diluted further with NaOH (0.1%) to get working standard solution of 200 g/ml of ibuprofen and 6 g/ml of famotidine. These standard solutions were used for the spectrophotometric determination runs. The diluted solutions were scanned in the spectrum mode over the range of 200-400 nm against NaOH (0.1%) as blank runs. The overlain spectra of the two drugs were conducted and being recorded. Ibuprofen showed an absorbance peak at 264 nm whereas famotidine shows an absorbance peak at 287 nm. The overlain spectra also showed isoabsorptive points at 265.50 nm. Due to difference in absorbance maxima and having no interference

with each other, both drugs can be simultaneously estimated by Absorption Correction Method (Method-I) and absorbance ratio method (Method-II).

The Calibration curves were prepared for ibuprofen and famotidine in the concentration range of 50-800 g/ml and 3-27 g/ml at selected wavelengths by diluting aliquot portions of stock solution of each drug. The plots of Beer's law limit are shown in Fig. 1 and Fig. 2.

Method I: Application of Absorption Correction Method

The overlain spectrum of ibuprofen and famotidine in NaOH (0.1%), (Fig. 1) showed that ibuprofen has zero absorbance at 287nm, whereas famotidine has shown a substantial absorbance. Therefore, famotidine was estimated at 287nm with no interference from ibuprofen. To estimate the concentration of ibuprofen, the absorbance of famotidine was, firstly, being measured at 264nm using standard solution of famotidine (6.65 g/ml). Then the concentration of ibuprofen was deducted from the total absorbance of sample mixture at 264nm. The calculated absorbance for ibuprofen is known as ibuprofen Corrected Absorbance. (The concentration of ibuprofen was determined from calibration curve at 264 nm using corrected absorbance).

METHOD II (ABSORBANCE RATIO METHOD)

Two wavelengths were selected, from the overlain spectrum of ibuprofen\ and famotidine: one λ max at 274.5 nm which is the isoabsorptive point for both drugs and the other λ max at 264 nm which is λ max of ibuprofen. The absorbances of the sample solutions were performed in a similar manner as described in the previous experiment. Wavelengths of absorptions were measured and the absorbance ratio values for both drugs at selected wavelengths were also calculated. The method employs Q-values and the concentration levels of drugs in sample solution were determined by using the following formulae:

$$Cx = \frac{Q\,m - Qy}{Qx - Qy} * \frac{A}{ax} \qquad (1)$$

$$Cy = \frac{Qm - Qx}{Qy - QX} * \frac{A}{ay} \qquad (2)$$

Where,

Cx and Cy are concentrations of ibuprofen and famotidine respectively,

Qx = the ratio of absorptivity of ibuprofen at 264 and 274.5 nm.

Qy = the ratio of absorptivity of famotidine at 264 and 274.5nm.

Qm = the ratio of absorbance of mixture at 264 and 274.5nm

A = the absorbance of mixture at isoabsorptive point.

ax = the absorptivity value of ibuprofen at isoabsorbtivepoint

ay =the absorptivity value of famotidine at isoabsorptivepoint.

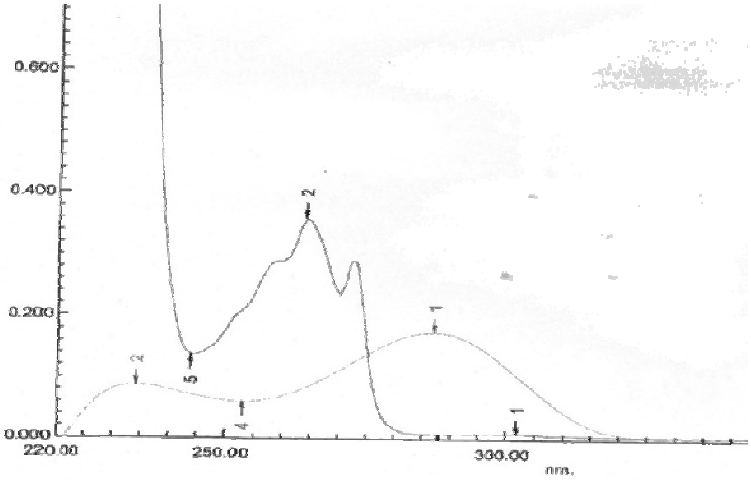


Figure 1: Overlay spectra of ibuprofen and famotidine

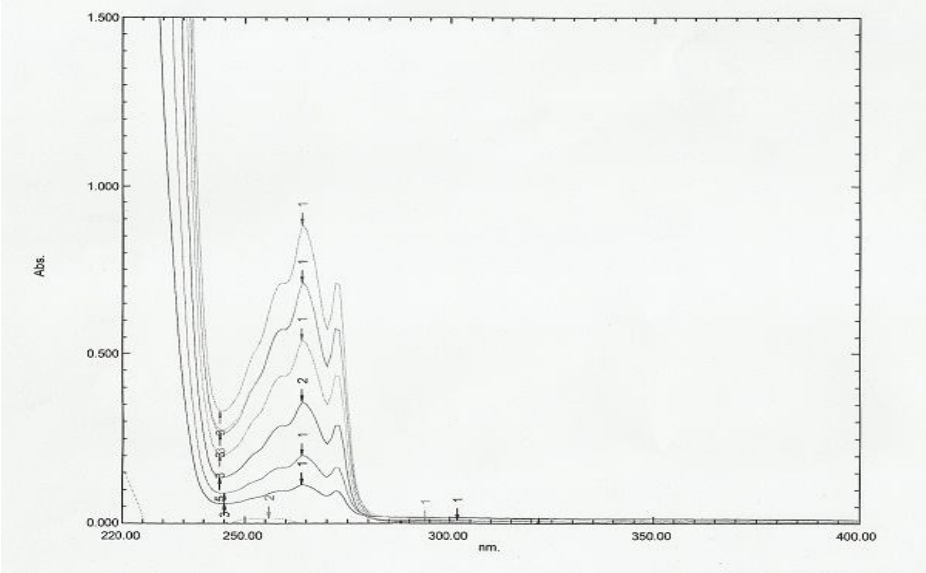


Figure 2: Overlay Spectra of Ibuprofen.

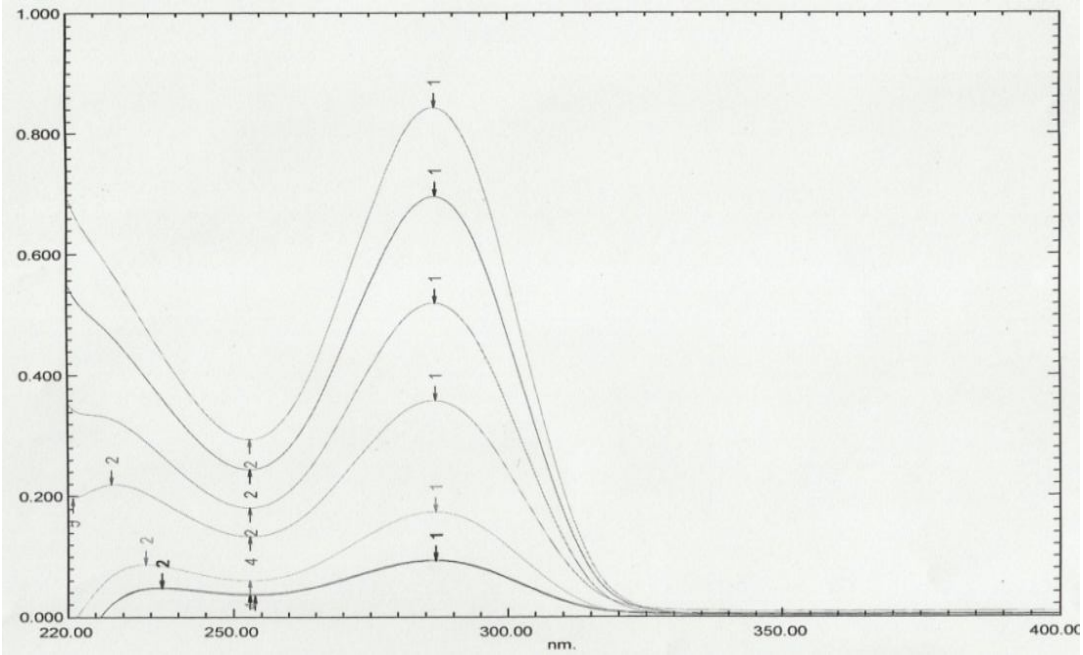


Figure 3: Overlay Spectra of Famotidine

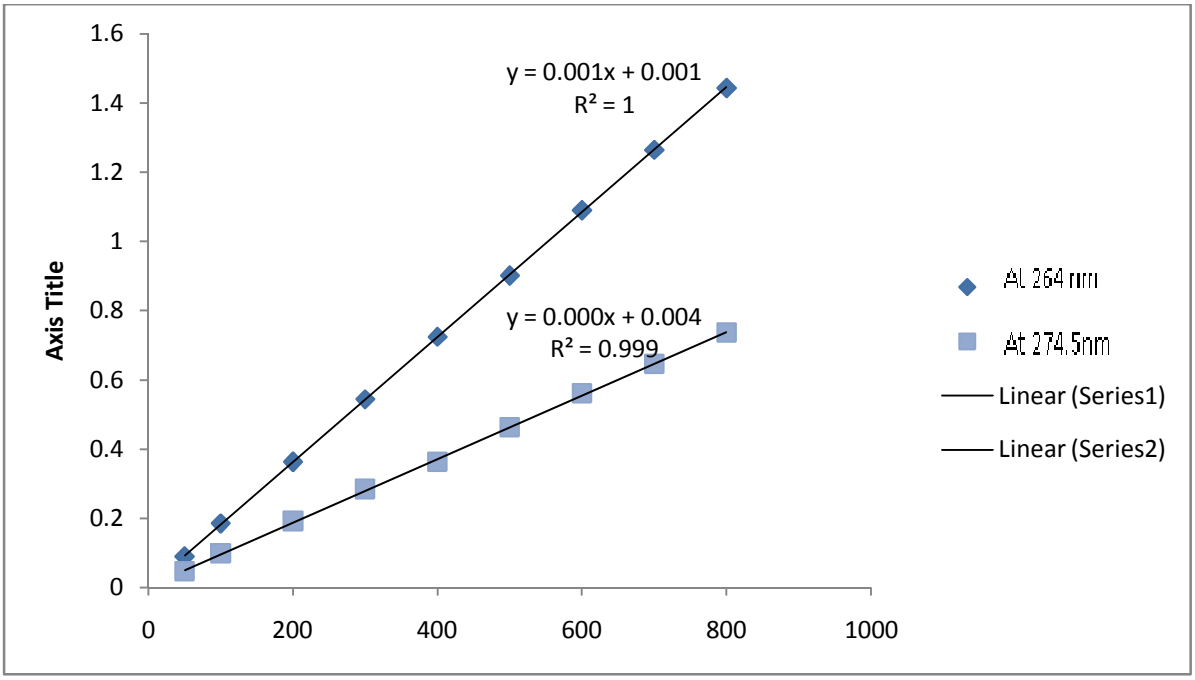


Figure 4: Calibration Curve of Ibuprofen.

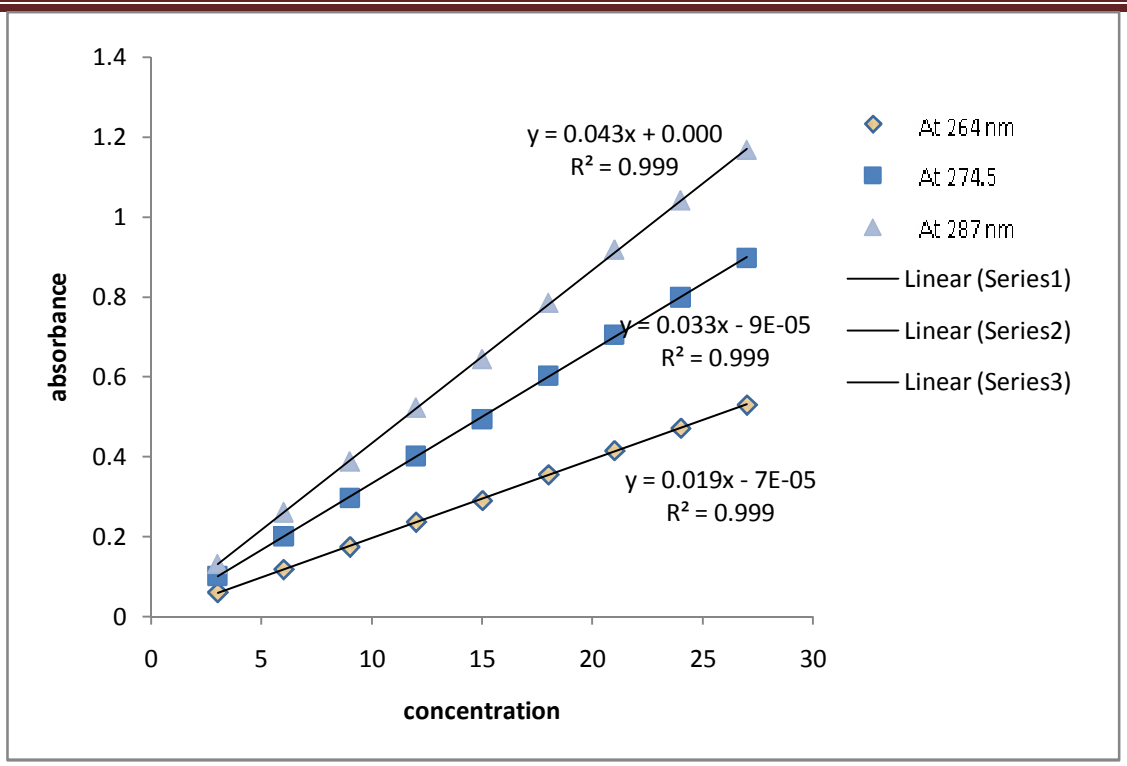


Figure 4: Calibration Curve of Famotidine.

ANALYSIS OF MARKETED FORMULATION (DUEXIS)

Twenty tablets were taken and their average weight of a single tablet was then determined. The tablets were crushed to fine powder. An amount equal to 400 mg of ibuprofen was taken in 100-ml volumetric flask. The amount of famotidine present in this tablet powder was 13.3mg; both drugs are in the ratio of 30:1 and shaken for about 10 min with 50 mL of NaOH (0.1%), diluted up to the mark with NaOH 0.1%. The contents of the flask were filtered using a Whatman No.41 filter paper. AnAliquot portion of the filtrate was further diluted to achieve a concentration of 200 g/mL of Ibuprofen and 6.65 g/mL respectively (On labeled claim basis). The absorbance of sample solution was measured at selected wavelengths. The content of ibuprofen and famotidine in sample solution of tablet was calculated by using absorption correction method and absorbance ratio method (equations 1 and 2). The analysis procedure was repeated six times.

VALIDATION:

The method was validated according to ICH Q2B guidelines validation of analytical procedures for the determination of the following validation parameters [16].

ACCURACY

To check the accuracy of the developed methods and to study the interference of the excipients in the formulation, analytical recovery experiments were carried out using the standard addition method at 80, 100, 120% levels. The percentage recovery was calculated from the total and the amount of drug yields. The results revealed no interference of excipients (Table 3).

PRECISION

The precision of the methods could be evaluated by the determination of the following parameters such as repeatability, intermediate precision. Accordingly, six dilutions in three replicates were analyzed in the same day, in two different days and by two analysts for day to day and analyst to analyst variation. The low value of standard deviation showed that the methods were precise (Table 4).

SENSITIVITY

The limit of detection (LOD) was calculated using the following equation LOD=3.3σ/s where σ is standard deviation of y intercept of the calibration curve (n=6) and s is the slope of regression equation (Table 1).

Table 1: Optical Characteristics of ibuprofen and famotidine:

Parameter	Absorption correction method		Absorbance Ratio Method	
	ibuprofen	famotidine	famotidine	ibuprofen
λ_{max}(nm)	264	287	274.5	274.5
Linearity range (μg/ml)	50-800	3-27	3-27	50-800
Molar absorptivity (liter,mole-1 cm-1)	371.31	14644.46	112364.2	185.652
Sandell's sensitivity (g/cm2 -0.001absorption units)	0.555556	0.02304147	0.003003	1.111111
Slope	0.0018	0.0434	0.0333	0.009
Intercept	0.0011	0.0008	0	0.0041
Regression coefficient (r^2)	1	0.9998	0.998	0.996
LOD	1.69025	0.06086	0.051207	3.994816
LOQ	5.121969	0.184425	0.155171	12.1055

Table 2: Results of Analysis of Tablet Formulations:

Drugs	Labelled Claim	Absorption correction method	Absorbance Ratio Method
		% ± SD (n=6)	% ± SD (n=6)
Ibuprofen	800	101.66±0.37	101.24±0.66
Famotidine	26.6	100.20±0.45	99.96±0.27

Table 3: Results of Recovery Studies:

Level of % recovery	**Absorption correction method***		**Absorbance Ratio Method***	
	famotidine	ibuprofen	famotidine	ibuprofen
80%	102.06±1.54	101.66±1.07	102.57±1.121	101.00±0.79
100%	101.84±0.647	101.10±3.31	101.62±0.75	99.94±1.81
120%	102.84±0.463	101.85±1.38	101.87±0.95	101.14±1.32

*Average of nine determinations

Table 4: Results of Precision:

Parameter		Method I		Method II	
		Ibuprofen	famotidine	ibuprofen	Famotidine
Precision (Mean ± % R.S.D.)	Repeatability	102.09 ±0.86	99.60±1.47	101.80±0.97	101.08±0.92
	Day to Day	101.03±1.41	99.54±1.21	100.66±1.48	100.77±0.94
	Analyst to Analyst	100.21±0.91	99.10275±1.87	101.5065± 1.13	100.66± 1.24

*Average of six determinations

RESULTS AND DISCUSSION

The proposed two methods are based on spectrophotometric simultaneous estimation of ibuprofen and famotidine in UV region using NaOH (0.1%) as solvent. The absorbance spectral analysis shows the maximum absorbance at 264 nm for ibuprofen and 287nm for famotidine. Method I is based on absorbance correction method which involves correction of absorbance at λ_{max} 264.0 nm for estimation of ibuprofen and the estimation of famotidine was done at λ_{max} 287 nm directly with no interference of ibuprofen.. Method II is based on absorbance ratio method. It involves formation of Q-absorbance equation at 274.5 nm (isobestic point) and λ_{max} 264 nm. The latter is the maximum wavelength of absorption of ibuprofen)

Beer's law is obeyed in the concentration range of 50-800 g/mL and 3-27 g/mL for both drugs. The correlation coefficients were found to be in between 0.998 -0.999 which shows the good linear relationship for both components. The results of optical characteristics such as Beer's law limits, correlation coefficient, slope, intercept and absorptivity coefficient values were summarized in Table 1 for method I and method II.

The tablet assay results obtained by the two proposed methods were very close to the labeled claim with a low value of standard deviation, suggesting that the two developed methods have high precision (Table 2). In order to check the accuracy of the developed methods, known quantities of standard drugs of ibuprofen and famotidine in three different concentration levels were added to its preanalyzed tablet sample and analyzed by the developed methods. The results of recovery determinations are given in Table 3. The mean percentage recoveries have indicated the non interference of the excipients in the tablet formulations. Precision test was determined between different time intervals, days and analysts. The results in (Table 4) have shown no statistical difference between different analysts, time and days, suggesting that the developed methods were rugged

CONCLUSION

The proposed two analytical UV spectrophotometric methods: the Absorbance Correction and the Absorbance Ratio Methods were developed and validated thoroughly for quantitative determination of ibuprofen and famotidine in tablets.

The developed methods were found to be simple, rapid, accurate, precise and economical and give an acceptable recovery of the analytes, which can be directly and easily applied to the analysis of ibuprofen and famotidine and other pharmaceutical tablet formulations.

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