Anew spectrophotometric method for determination of Famotidine drug

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Abstract

Anew and simple sensitive reproducible spectrophotometric method was used for determination of famotidine drug(FA) in bulk sample and pharmaceutical formulation . The determination depend on formed the prussian blue by reacting the drug with iron(III) chloride to form iron(II) which reacts with potassium hexacyanoferrate(III). The product measurable spectrophotometrically at 744 nm. Regression analysis of Beers plot good correlation in the concentration range (1.00-6.00) µg.ml^{-1}

No interference was observed from the usually existing additive in the pharmaceutical formulation and the applicability of the method was examined by analyzing tablets containing (FA).

The correlation coefficient of 0.9982, a relative standard deviation (RSD%)of (2.07%) and the detection limit was (3.50×10^{-5}) µg.ml^{-1}and the sandell sensitivity was (1.70×10^{-4} µg.cm). Recoveries were (98.25-100.5)% .

التقدير الطيفي لعقار الفاموتودين

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الكلمات المفتاحية: فوماتودين ,الطرق التطبيقية

الخلاصة :طريقة طيفية جديدة بسيطة وحساسة لتقدير مركب الفاموتودين, التقدير يعتمد على تكوين الصبغة البروسية الزرقاء بتفاعل الدواء مع الحديد الثلاثي ليكون الحديد الثنائي الذي يتفاعل بدوره مع سداسي سيانيد الحديديك البوتاسيومي ’ الناتج يقاس طيفيا عند 744 nm, التحاليل الخطية لقانون بيير لمبيرت اظهر مدى الخطية (1.00-6.00)µg.ml^{-1} ومعامل الارتباط 0.9982 وكان الانحراف القياسي النسبي (2.071%) وحد الكشف (3.50×10^{-5}) µg.ml^{-1} وكانت حساسية ساندل (1.7×10^{-4} µg.cm). كان معدل الاستيعادية بين (98.25-100.5)%.

Introduction

Famotidine is a white or yellowish-white crystalline powder has a chemical formula of $C_8H_{15}N_7O_2S_3$ 3-[[[2-[(Diamino methylene) amino]thiazol-4-yl] methyl] sulphanyl]- N-sulphamoylpropanimidamide[1]. The famotidine is histamine H_2-receptor antagonists are reversible competitive blockers of histamine at H_2-receptors. H_2-receptors are found in the stomach, hence their stimulation causes gastric acid secretion. They compete with histamine for H_2-receptors and block gastric acid secretion and some effects of histamine[2].

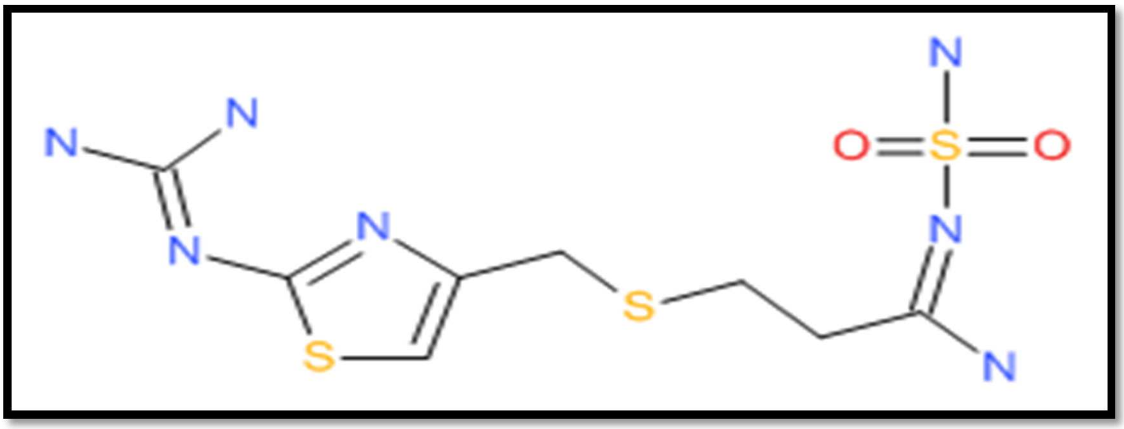

Figure (1):-The structure of famotidine

There are various analytical methods for determination of famotidine such as HPLC[3-8], potentiometry[9] electrochemical[10-12], UV spectrophotometry[13-20]. The objective of this study to find a new reproducible method for determination of famotidine in bulk sample and pharmaceutical formulation.

Experimental

- **Apparatus:**
  1. A shimadzu Uv-vis 1800 spectrometer Japan) equipped with a quarts cell of 1.0 cm width was used for the determination and all absorbance measurements.
  2. Lab-tech water bath manufacture of lab instruments.
  3. Denver sensitive balance instrument ISO 9001 .

- **Reagents and Solution:**

All Analytical reagents grade chemicals and distilled water were used throughout.

-Pure drug were provided by SDI.

-The stock standard solutions of FA (100 µg mL^{-1}) were prepared by dissolving precisely weighed 10 mg of pure drug in 100 mL 0.1M hydrochloric acid. The working concentrations were prepared by approximate dilution of standard drug solution(15) .

-Dosage forms containing the studied drug being purchased from local mark sources provided by SDI

-Iron chloride(III) $3.00x10^{-2}$ M solution: was prepared by dissolving 0.486gm of $FeCl_3$ in 1ml concentrated HCl and made up to 100 ml of distilled water.

-Potassium hexacyanoferrate(III)1.00x 10^{-3} M solutions: was prepared by dissolving 0.032gm of $K_3Fe(CN)_6$ in 100 ml of distilled water.

Preliminary investigation

General procedure:

Aliquots containing 1.0–6.0 µg mL^{-1} of standard FA (100 µg mL^{-1}) were transferred quantitatively to 25 mL calibrated standard flasks. To that, 1 mL of (0.03M) $Fecl_3$ solution was added and shake well followed by addition of 1.5mL (0.00lM) of $K_3Fe(CN)_6$ and the volume was brought to 25 mL with distilled water and allow the reaction to stand for 15min. The absorbance were measured at 744 nm against the reagent blank prepared in the same way but containing no famotidine. The color of product is stable for at least 60min.

Procedure for pharmaceutical preparations:

Twenty tablets of FA were powdered, and portion of powder equivalent to 100 mg of famotidine (average weight four tablets) was weighted, and dissolved in 100 mL of 0.1M hydrochloric acid to obtained 1000µg mL^{-1} of famotidine solution. The solution was filtrated and 10ml of filtrate was transferred into100ml volumetric flask and diluted with distilled water to the marks to obtain 100µg

mL^{-1}. The solution was suitable to analyze by taking a convenient volumes in the range of calibration curve under a general procedure.

Results and discussion

The Uv-visible Spectrum

The famotidine drug reacts with iron(III) to produce iron(II) which in presence of potassium hexacyanoferrat(III) to forms blue complex measurable at 744 nm. The absorbance of the blue is directly related to the concentration of the famotidine and can be used for its spectrophotomotic determination. The development of the color is dependent on the reaction conditions. Therefore it is very important to optimize the reaction conditions.

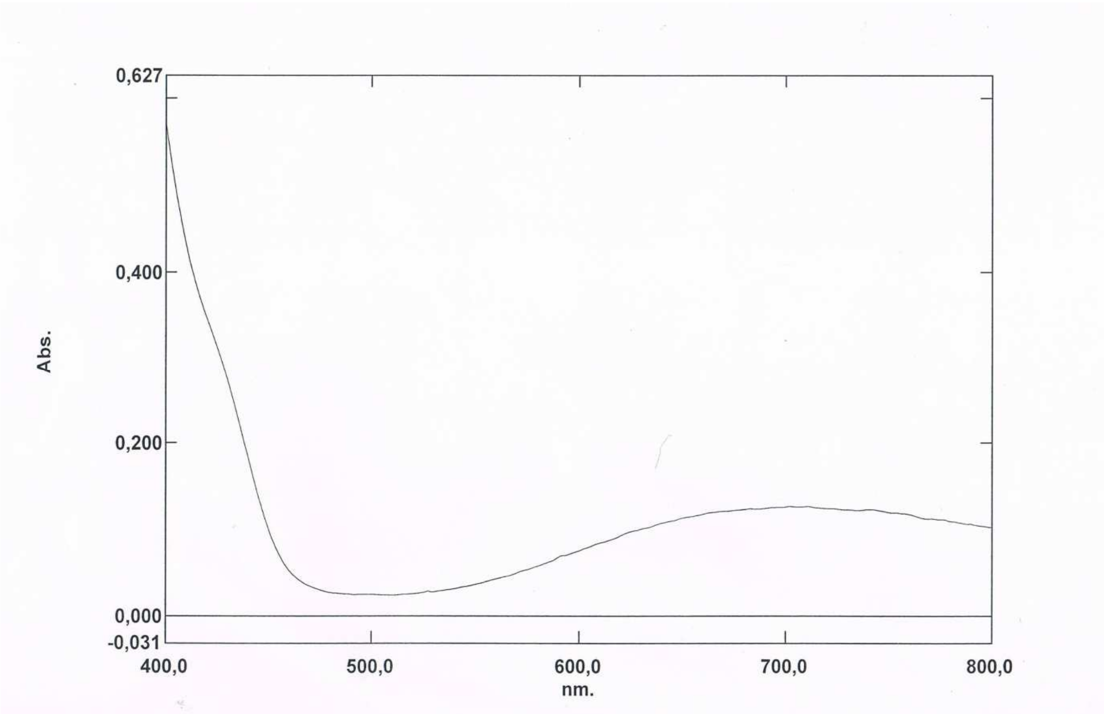

Fig.2- UV-Vis spectropotometric of blue species formed by reaction famotidine (5ppm) with sodium ferric chloride (0.03M) and 0.00lM of $K_3Fe(CN)_6$ against reagent blank.

Study the best condition of complex famotidine:

The effect of Iron(III)Chloride.

The effect of Iron(III)Chloride concentration on the production of Prussian blue color product was investigated in the range of ($0.6x10^{-3}$-$3.60x10^{-3}$ M). The concentration ($1.20x10^{-3}$ M) gave the highest absorbance as shown in Fig.3.Therefore, $1.20x10^{-3}$ M was considered to be the preferred concentration of Iron(III)Chloride ($1.20x10^{-3}$M) as shown in figure.3

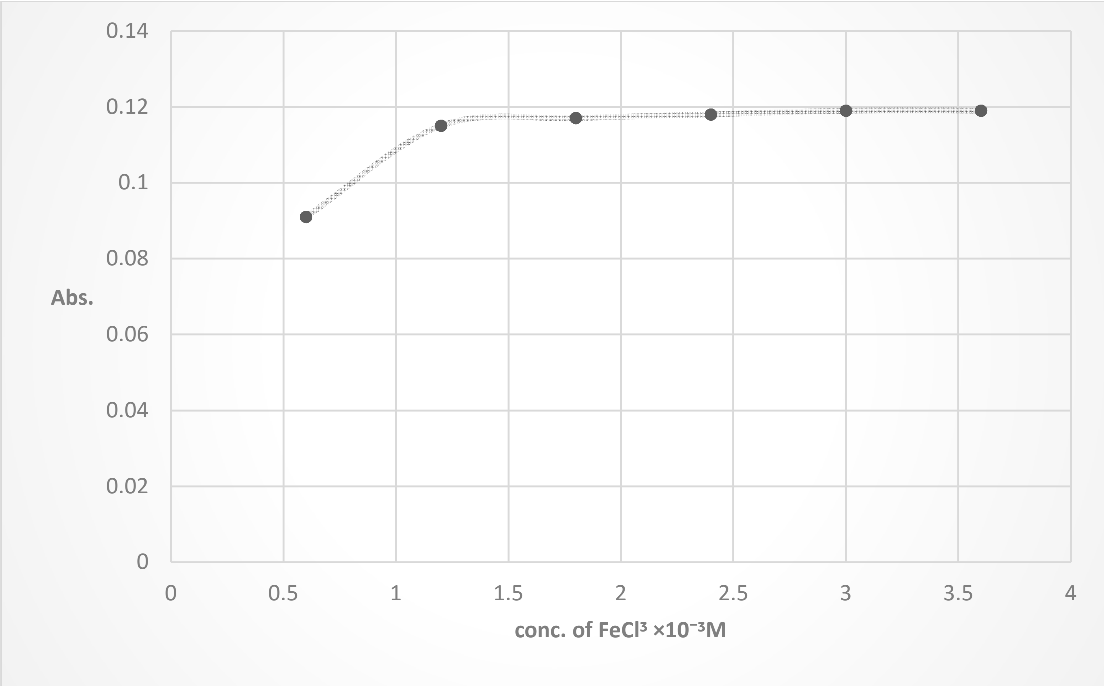

Fig. 3: Effect of variation of reagent concentration(Iron(III)chloride) on the intensity of the colored product.

Effect of potassium hexacyanoferrate(III):

The effect of potassium-hexacyanoferrate(III) concentration was similary studied in the range of (0.2×10^{-4}- 1.2×10^{-4} M) in a final volume 25 ml. The concentration 0.6×10^{-4} M, gave the highest absorbance as shown in Fig.4 .Therefore, $0.6\ x10^{-4}$ M was considered to be the preferred concentration of potassium-hexacyanoferrate(III) ($0.6\ x10^{-4}$M) as shown in figure.4

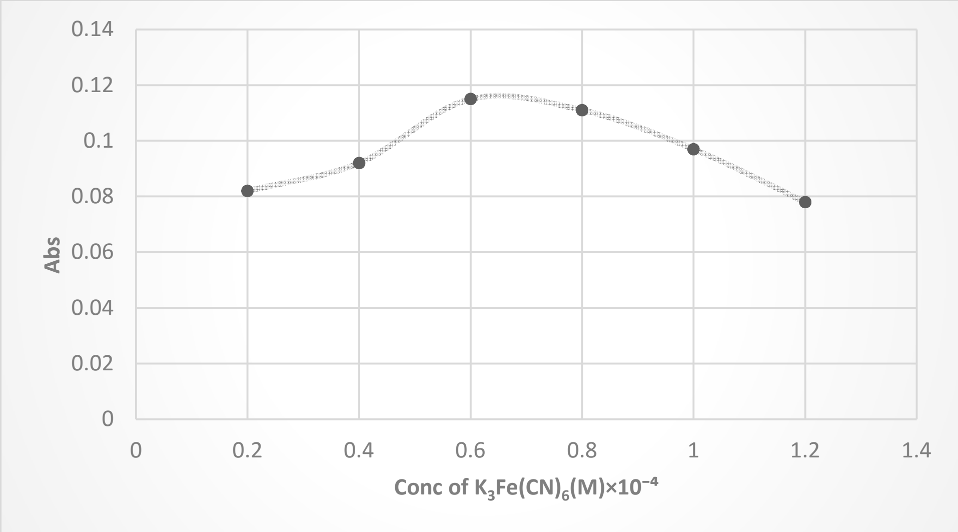

Fig. 4: Effect of variation of reagent concentration($K_3Fe(CN)_6$) on the intensity of the colored product

Effect of Temperature:

The effect of temperature on the color intensity of the blue dye was studied. In practice, the absorbance of the sample was low at 10^{o}C whereas at 50^{o}C a high value for the blank was obtained. Therefore, it is recommended that the color reaction be carried out at room temperature(25^{o}C).

Table(1) Effect of temperature:

Temperature (°C)	Absorbance
10 °C	0.095
25 °C	0.115
50 °C	0.125

Effect of order of addition:

The influence of chemical addition on intensity of the absorbance. Prussian blue color product was studied. Table 2, shows there is no effect for order of addition on the absorbance. Therefore the order of addition could be followed drug, $FeCl_3$,$K_3Fe(CN)_6$.

Effect of order of addition:

The measurements obtained indicated that the order of addition of the chemicals involved in the formation of colored product have no effect on the sensitivity and intensity of the product formed. Thus, the recommended addition shown in calibration curve construction was used through out this work.

Table(2) Effect of order of addition

Order of addition	absorbance
Drug:$Fecl_3$+$K_3Fe(CN)_6$	0.115
Drug: $K_3Fe(CN)_6$ + $FeCl_3$	0.095
$K_3Fe(CN)_6$+ $FeCl_3$+drug	0.111
$K_3Fe(CN)_6$+drug+ $FeCl_3$	0.0102
$FeCl_3$+drug+ $K_3Fe(CN)_6$	0.109
$FeCl_3$+ $K_3Fe(CN)_6$+drug	0.107

Effect of reaction time:

The color intensity reached a maximum after mixing the famotidine with $Fecl_3$ and $K_3Fe(CN)_6$ for 15 min Therefore .15 min development was selected as optimum time in the general procedure. The color obtained was stable for at least 60 min as shown in Fig 5.

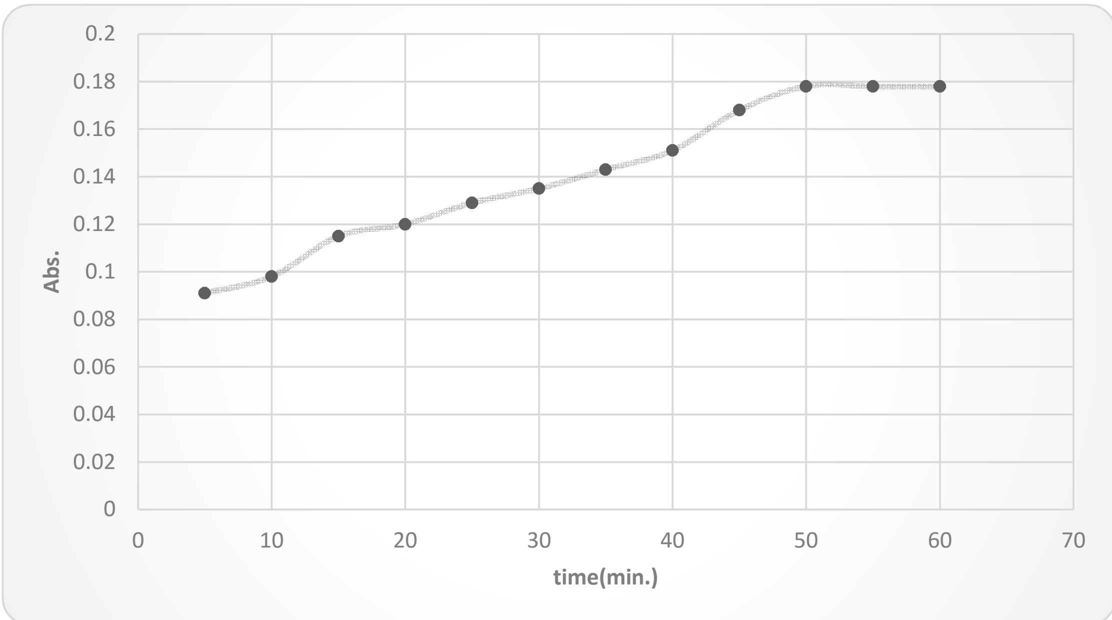

Figure (5):- Effect of reaction time (min.)

Calibration Graph:

Under the described experimental conditions, standard calibration curve for the studied famotidine were constructed by plotting the absorbance versus concentration. Conformity to Beer's Law was evident over the concentration range of ((1.00-6.00)µg.mL^{-1}) Fig 6, with the mean correlation coefficient of 0.9982.The conditional molar absorptivity of the Prussian blue color product was found to be (5.00×10^{4} L $mole^{-1}$ .cm^{-1}) and the sandell sensitivity was (1.70×10^{-4} µg.cm^{-2})

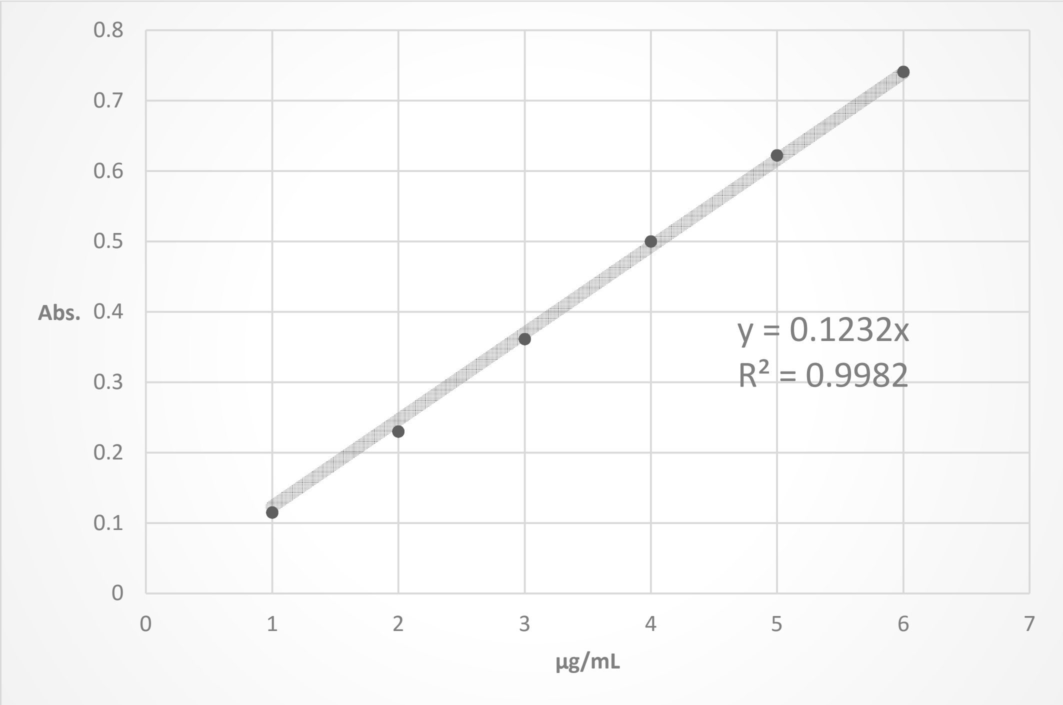

Figure (6):- Calibration curve for the determination of famotidine.

Accuracy and Precision:

Famotidine was determined at two different concentrations with 4 replicated. The results obtained are shown in table (3) .A satisfactorily precisian accuracy could be obtained using the proposed method.

Table(3):-Accuracy and Precision of the method

Con.(μg.mL^{-1})	Mean	S.D	R.S.D	Error%
2.00	0.231	0.00479	2.071	4.00
6.00	0.739	0.00330	0.446	-1.83

Pharmacetical Application:-
The pharmaceutical formulation of famotidine was determined according to the study method, the result obtained in table (4).

Table(4):- Application of the method for determination of famotidine in pharmaceutical tablets

Con. Of FAM(μg.m L^{-1})		S.D	R.S.D	Error%	Recovery
Taken	Found				
2.00	2.01	0.0041	1.77	4.00	100.5%
4.00	3.93	0.0026	0.52	-1.75	98.25%

Conclusion:

The new method provides a simple and sensitive means of determining the studied famotidine in pharmaceutical preparations. It has also the advantages of acceptable accuracy and precision. This method is also easier, cheaper and performance than other method and do not require expensive reagents. These advantages coupled with acceptable precision make the method suitable routine quality control. The famotidine reacts with iron(III) chloride and the resulting iron (II) reacts with potassium hexacyanoferrate(III) and a blue product is resulted.

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