Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 1, 2013

Research Article

UV-VIS SPECTROPHOTOMETRIC STUDY FOR DETERMINATION OF CEFIXIME IN PURE FORM AND IN PHARMACEUTICALS THROUGH COMPLEXATION WITH Cu(II) USING ACETATE–NaOH BUFFER IN WATER:METHANOL

ABDUL AZIZ RAMADAN*, HASNA MANDIL, MARWA DAHHAN**

Dept. of Chemistry, Faculty of Sciences, Aleppo University, Syria. *Email: dramadan@scs-net.org

Received: 10 Oct 2012, Revised and Accepted: 16 Nov 2012

ABSTRACT

UV-Vis spectroscopic method for the analysis of cefixime (CEFI)in pure form and pharmaceutical formations through complexation with Cu(II) using acetate-NaOH buffer in mixture water: methanol has been developed. Optimal temperature and time for coupling were established at 25±5°C with time ranging from 0 to10 min. The formation complex, CEFI: Cu(II) gives maximum absorbance of the yellow color occurred at λ= 410 nm and the molar absorptivity is 5.12 x 10^3 $L.mol^{-1}.cm^{-1}$. The reaction between CEFI and Cu(II) occurred at a stoichiometric ratio of 1:1. All reaction conditions have been optimized to obtain the complex. Under optimum conditions Beer's law was obeyed at concentrations ranging from 0.2267 to 22.671µg.$mL^{-1}$with correlation coefficients≥0.9995 in all cases with RSD generally less than 4.0%. The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.030µg.mL^{-1} and 0.091µg.mL^{-1}, respectively. The proposed method was simple, economic, accurate and successfully applied to the determination of CEFI in pharmaceuticals with average recovery of 98.00 to 103.00%, the results obtained agree well with the contents stated on the labels.

Keywords: Cefixime (CEFI), complex (CEFI:Cu^{2+}), Methanol:Water, Pharmaceuticals, Spectrophotomety.

INTRODUCTION

Cefixime (CEFI) (6*R*,7R)-7- [2-(2-amino-4-thiazolyl)glyoxylamido] -8-oxo-3-vinyl-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid, 7-(*Z*)- [*o*-(carboxymethyl)-oxime] trihydrate is third-generation cephalosporin antibiotic [1], see Figure 1.

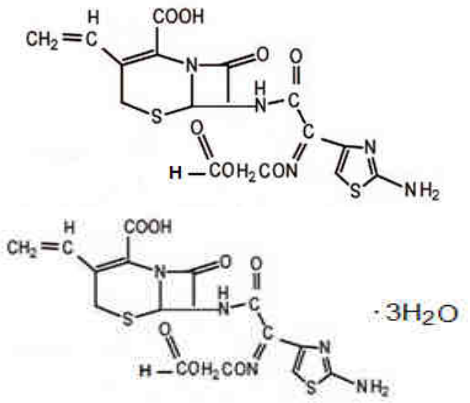

Fig. 1: Scheme of cefixime and cefixime three hydrate.

Cefixime Cefiximetrihydrate

A simple and sensitive spectrophotometric method has been developed for the determination of five cephalosporins namely cefpodoxime, ceftizoxime, ceftazidime, ceftriaxone, and cefixime. This method is based on the formation of yellow to yellowish brown complex between palladium (II) chloride and the investigated cephalosporins in the presence of sodium lauryl sulphate (SLS) as surfactant. The reaction conditions were studied and optimized. For each drug, the composition of this complex as well asits stability constant was also investigated. The proposed method was used for the determination of the above-mentioned drugs in their commercial preparations. The results were compared statistically with either official or published methods and showed no significant difference between the two methods [2].

A new, simple, sensitive and accurate spectrophotometric method has been developed for the assay of metoprolol tartrate (MPT), which is based on the complexation of drug with copper(II) [Cu(II)] at pH 6.0, using Britton-Robinson buffer solution, to produce a blue adduct. The latter has a maximum absorbance at 675 nm and obeys Beer's law within the concentration range 8.5-70 µg.mL^{-1}. Regression analysis of the calibration data showed a good correlation coefficient (r = 0.998) with a limit of detection of 5.56 µg/mL. The proposed procedure has been successfully applied to the determination of this drug in its tablets. In addition, the spectral data and stability constant for the binuclear copper(II) complex of MPT ($Cu_2MPT_2Cl_2$) have been reported [3].

Cephalexin, cefixime, ceftriaxone and cefotaxime were determined spectrophotometrically in the pure form and in pharmaceutical formulations by using ferrihydroxamate method. Using cefotaxime sodium as model drug with ester functional group, it was shown that proposed method gives equally accurate and precise results even in the presence of ester functional group [4].

Interaction of norfloxacin and ofloxacin with copper(II) and copper(II)/phenanthroline has been studied in aqueous solution and the stability constants of the binary complexes Cu(II)/fluoroquinolone and of the ternary complexes Cu(II)/phenanthroline/fluoroquinolone have been determined by potentiometry and UV–vis spectrophotometry [5].

Cefixime reacts with transition metal(II) ions to give $[M(cefixi)(H_2O)_2]$ complexes (M = Mn, Co, Ni and Cd) and $[Fe(cefixi)Cl(H_2O)]$, which were characterized by physicochemical and spectroscopic methods, and an octahedral geometry is suggested for their structure. The complexes have been screened for antibacterial activity against several bacteria, and the results are compared with the activity of cefixime [6].

A sensitive, accurate and rapid flow injection analysis (FIA) method for the determination of cefotaxime, cefuroxime, ceftriaxone, cefaclor, cefixime, ceftizoxime, and cephalexin is proposed. Aliquots of each cephalosporin were hydrolyzed for 15 min with 0.1 M NaOH at 80°C and then oxidized with Fe^{3+} in sulfuric acid medium to produce Fe^{2+}. The produced Fe^{2+} is then complexed by *o*-phenanthroline (*o*-phen) in citrate buffer at pH 4.2 to form the red complex, $Fe(o\text{-phen})_3^{2+}$, which exhibits an absorption maximum at 510 nm. The method was successfully applied to the analysis of pharmaceutical preparations. The results have been compared with those obtained using the official methods. Excellent agreement between the results of the proposed method and the official methods was obtained [7].

Two spectrophotometric methods have been developed for the determination of cefixime in pure and in its pharmaceutical formulations. In UV method cefixime showed absorption maximum at 290 nm in aqueous medium, where as in visible

spectrophotometric method it reacts with Folin-Ciocalteu (FC) reagent under alkaline conditions forming a blue coloured chromogen having absorption maximum at 720 nm. These methods obey Beer's law in the concentration range of 1 to 15 µg.mL^{-1} and 5 to 25 µg.mL^{-1} respectively. The methods are statistically evaluated for accuracy and precision [8].

Three simple and sensitive spectrophotometric, difference spectroscopic, and liquid chromatographic (LC) methods are described for the determination of cefixime. The first method is based on the oxidative coupling reaction of cefixime with 3-methyl-2-benzothiazolinon hydrazone HCl in presence of ferric chloride. The absorbance of reaction product was measured at the maximum absorbance wavelength (λ_{max}), 630 nm. The difference spectroscopic method is based on the measurement of absorbance of cefixime at the absorbance maximum, 268 nm, and minimum, 237 nm. The conditions were optimized, and Beer's law was obeyed for cefixime at 1 to 16 µg.mL^{-1} and 10 to 50 µg.mL^{-1}, respectively. The third method, high-performance LC, was developed for the determination of cefixime using 50 mM potassium dihydrogen phosphate (pH 3.0) methanol (78 + 22, v/v) as the mobile phase and measuring the response at λ_{max} 286 nm. The analysis was performed on a Lichrospher RPC18 column. The calibration curve was obtained for cefixime at 5 to 250 µg.mL^{-1}, and the mean recovery was 99.71-0.01%. The results obtained in the analysis of dosage forms agreed well with the contents stated on the labels [9].

A simple, accurate and precise colorimetric method for the analysis of pharmaceutical formulation containing both ofloxacin and cefixime was developed. The method has been successfully applied for the analysis of drugs in pharmaceutical formulation. Results of analysis were validated statistically and by recovery studies [10].

A simple, precise and accurate kinetic spectrophotometric method for determination of cefradine anhydrous, cefaclor monohydrate, cefadroxil monohydrate, cefalexin anhydrous and cefixime in bulk and in pharmaceutical formulations has been developed. The method has been successfully applied to the determination of the studied drugs in commercial pharmaceutical formulations [11].

A simple, accurate and precise spectrophotometric method has been proposed for the determination of eleven cephalosporins, namely; cefaclor monohydrate, cefadroxil monohydrate, cefalexin anhydrous, cefradine anhydrous, cefotaxime sodium, cefoperazone sodium, ceftriaxone sodium, ceftazidime pent hydrate, cefazolin sodium, cefixime and cefpodoxime proxetil in bulk drug and in pharmaceutical formulations. The method depends on hydrolysis of the studied drugs using 0.5M NaOH at 100°C and subsequent reaction of the formed sulfide ions with NBD-Cl (4-chloro-7-nitrobenzo-2-oxa-1, 3-diazole) to form a yellow- colored chromogen measured at 390 nm. Under the optimum conditions, linear relationships with good correlation coefficients (0.9990- 0.9999) were found in the range of 5-160 µg mL^{-1}for all studied drugs. The limits of assay detection and quantitiation ranged from 0.289 to 5.867 and from 0.878 to 17.778 µg.mL^{-1}; respectively. The method was successfully applied for analysis of the studied drugs in their pharmaceutical formulations and the recovery percentages ranged from 96.6 to103.5% [12].

A simple specrtophotometric method for the determination of cefoxamide with variamine blue is presented. The determination is based on the hydrolysis of β-lactum ring of cefixime with sodium hydroxide which subsequently reacts with iodate to liberate iodine in acidic medium. The liberated iodine oxidizes variamine blue to violet colored species of maximum absorption at 572 nm. The absorption is measured within the pH range of 4.0-4.2. Beer's law is obeyed in the range of 0.5-5.9µg.mL^{-1} for cefixime. The analytical parameter was optimized and the method is successfully applied for the determination of Cefixime [13].

An accurate and precise colorimetric method is presented for the determination of ofloxacin and cefixime in same pharmaceutical formulation. Ofloxacin forms an orange colored product in the presence of ferric chloride solution in acidic medium and the absorbance of orange colored species formed was measured at 435 nm against reagent blank and Beer's law was obeyed in the concentration range of 15-75 µg.mL^{-1}. While cefixime forms a greenish colored product with Fehling solution and the absorbance of greenish colored species formed was measured at 490 nm against reagent blank and Beer's law was obeyed in the concentration range of 5-40 µg.mL^{-1}. The amount of cefixime and ofloxacin present in the sample was computed from calibration curve **[14].**

A simple, sensitive, rapid, accurate, precise and economic dual wavelength spectrophotometric method was developed for the simultaneous determination of cefiximetrihydrate (CEFI) and ofloxacin (OFLO) in combined tablet dosage form. The method was based on determination of ofloxacin at 350 nm using its absorptivity value and cefixime at 264 nm after deduction of absorbance due to ofloxacin. The two drugs follow Beer-Lambert's law over the concentration range of 2-14 µg.mL^{-1}. The method was successfully applied to pharmaceutical dosage form because no interference from the tablet excipients was found [15].

A new simple, accurate and cost-effective spectrophotometric method has been developed for the analysis of some cephalosporins (ceftriaxone, ceftazidime, cefixime, cefotaxime and cefuroxime) in bulk samples and pharmaceutical dosage forms. The reaction involves a two-step process of diazotization of the cephalosporins with acidified $NaNO_2$ at 0–5°C and coupling with acidified p-dimethylaminobenzaldehyde (DMAB). Beer's law was obeyed at concentrations ranging from 5 to 60 µg.mL^{-1} with correlation coefficients >0.9980 in all cases. Overall recoveries were of the order of 95–103% with errors generally less than 6%. The method was successfully applied to the determination of the cephalosporins in dosage forms [16].

An accurate, precise and ecofriendly spectrophotometric method is presented for the determination of Cefixime based on the formation of a yellow colour product with ninhydrin in the presence of bicarbonate with an absorption maximum at 438 nm. The reaction proceeds quantitatively at 97 ± 1°C in 15 min. The calibration curve is linear over the range of 45-65 µg.mL^{-1} with a regression coefficient (r) of 0.9987 (n = 5). The calculated molar absorptivity and Sandell sensitivity values are 4.1536 x 10^3 L.mol^{-1}.cm^{-1} and 0.0072 µg/cm^2, respectively. The limits of detection (LOD) and quantification (LOQ) calculated as per ICH guidelines are 1.13 and 3.40 µg.mL^{-1}, respectively [17].

Spectroscopic analytical study for the determination of cefixime in pure and its Syrian pharmaceutical formations through complexation with Cu(II) in acetate buffer at pH = 7.8 has been developed. The method is based on the formation pink colour complex between cefixime and Cu(II). The maximum absorbance of the coloured complex occurred at l = 546 nm and the molar absorptivity is 3.28 × 10^3 L mol^{-1}cm^{-1}. The reaction conditions have been optimized to obtain the complex. Under optimum conditions the absorbance of complex was found to increase linearly with increase in concentrations of cefixime, which corroborated with the correlation coefficient values (1:1). The linear range of the calibration curve was 0.453-9.069 mg mL^{-1} with correlation coefficients = 0.9975 in all cases. Overall recoveries were of the order of 98.00-101.50 %. The limit of detection and limit of quantification was found to be 0.075 mg mL^{-1} and 0.22 mg mL^{-1}, respectively. The proposed method was simple, economic, accurate and successfully applied to the determination of cefixime in Syrian pharmaceuticals, the results obtained agree well with the contents stated on the labels [18].

A simple, accurate, sensitive and validated RP-HPLC method for simultaneous determination of Cefixime and Ofloxacin in combined tablet dosage form has been developed. Separation was carried out on Jasco HPLC system equipped with HiQ-SiL C $_8$Neosphere column (150 × 4.6 mm i.d.) and UV/VIS detector using Methanol: 0.025 mM potassium dihydrogen phosphate buffer in ratio of (70:30, v/v) as mobile phase and detection was carried out at 290 nm. Ambient temperature conditions were maintained. Results were linear in the range of 1-10 mg mL^{-1}for both the drugs. The method has been successfully applied for the analysis of drugs in pharmaceutical formulation. Results of analysis were validated statistically and by recovery studies [19].

The spectrophotometric (UV and Vis) [1-18,20,21],chromatographic (HPLC, GC and TLC) [9,19,22,23] and electrochemical (polarography, voltammetry and other) [24-29] methods most prevalentto identify different drugs in pure and pharmaceutical dosage forms.

In the present work, spectroscopic analytical study for the analysis of cefixime in pure and its pharmaceutical formations through complexation with Cu(II) using acetate-NaOH buffer in methanol: water (8:92, v/v) has been applied.

MATERIALS AND METHODS

Instruments and apparatus

Spectrophotometric measurements was made in a Biotech E.M.UV-Visible spectrophotometer with 1.00 cm quartz cells. The pH measurement was performed with EUTECH COPERSCAN-500. A ultrasonic processor model POWERSONIC 405 was used to sonicate the sample solutions. The solution was kept in a thermostat at 30°C. The diluter pipette model DIP-1 (Shimadzu), having 100 µL sample syringe and five continuously adjustable pipettes covering a volume range from 20 to 5000 µL (model PIPTMAN P, GILSON), were used for preparation of the experimental solutions.

Reagents

Cefixime tree hydrate(99.0%) was of pure from Parabolic Drugs-INDIA, the purity 88.6% as cefixime, which was determined by HPLC method [9].Copper perchloratehexahydrate was of pure from Fluka (Switzerland). Sodium acetate, NaOH and all other reagents were of analytical grade, and alcohols were of extra pure from Merck (Germany). Buffer solution 0.0016 M NaCH3COO + 0.04 M NaOH was prepared in water: methanol (8:92, v/v). A stock solution of cefixime (a) $2.5x10^{-3}$mol.L^{-1}(1.1336 mg.mL^{-1}) and (b) $2.5x10^{-4}$ mol.L^{-1}(113.36 µg.mL^{-1}) were prepared in buffer solution. A stock solution of Cu(II)(c) $2.5x10^{-2}$mol.L^{-1} and (d) $2.5x10^{-5}$ mol.L^{-1} were prepared in buffer solution.

Sample preparation

A commercial formulations (tablet and capsule) were used for the analysis of cefixime by using spectrophotometric analysis. The following commercial formulations were subjected to the analytical procedures:

(1) ***Bioxime***(tablet), Shifa pharmaceutical industries –Aleppo–SYRIA, Each tablet contains: 400 mg cefixime.

(2) ***Cefix***(capsule)**,** Alpha, Aleppo pharmaceutical industries - Aleppo–SYRIA, Each capsule contains:400 mg cefixime**.**

(3) ***Cifime***(capsule)**,**Delta for medicaments -Aleppo–SYRIA, Each capsule contains:400 mg cefixime.

(4) ***Cefixime-ElSaad*** (tablet), ElSaad pharma-Aleppo–SYRIA, Each tablet contains: 400 mg cefixime.

(5) ***Supraxime***(tablet), Asia pharmaceutical industries-Aleppo – SYRIA, Each tablet contains: 400 mg cefixime.

(6) ***Cifime*** (tablet), Delta for medicaments – Aleppo – SYRIA, Each tablet contains: 200 mg cefixime.

(7) ***Supraxime***(tablet), Asia pharmaceutical industries-Aleppo – SYRIA, Each tablet contains: 200 mg cefixime.

(8) ***Cefixime-ElSaad*** (tablet), ElSaadpharma-Aleppo–SYRIA, Each tablet contains: 200 mg cefixime.

Crushed three tablets (or the contents of three capsules) of each studied pharmaceutical formulations, mix well and weigh equivalent tenth the weight of one tablet (or content one capsule), solve it in 40 ml buffer solution by using ultrasonic, filtered over a 50 mL flask and diluting to 50 mL with buffer solution (Stock solution of pharmaceutical formulations). The stock solutions content: 40, 40, 40, 40, 40, 20, 20 and 20mg/50mL of cefixime for pharmaceuticals: *Bioxime*(tablet,400mg), *Cefix*(capsule, 400mg), *Cifime*(capsule, 400mg), *Supraxime*(tablet, 400mg), *Cefixime-ElSaad*(tablet, 400mg), *Cifime*(tablet, 200 mg), *Supraxime*(tablet, 200mg) and *Cefixime-ElSaad* (tablet, 200mg), respectively. Working solutions of pharmaceuticals were prepared daily by diluting 0.050 mL from stock solution of pharmaceutical formulations in 20 mL buffer solution and 2.00 mL from stock solution (c) of Cu(II) anddiluting to 25 mL with buffer solution [working solution of *Bioxime*(400mg), *Cefix*(400mg), *Cifime*(400mg), *Supraxime*(400 mg), *Cefixime-ElSaad* (400 mg), *Supraxime*(200 mg), *Cifime*(200 mg) and *Cefixime-ElSaad* (200 mg) content:1.60, 1.60, 1.60, 1.60, 1.60, 0.80, 0.80 and 0.80µg.mL^{-1}cefixime, respectively]. Working standard addition solutions of pharmaceuticals were prepared as the follows: same mentioned volumes of stock solutions of pharmaceuticals in 20 mL buffer solution and 2.00 mL stock solution (c) of Cu(II) with 0.100, 0.200, 0.400, 0.800and 1.000mL from stock solution (b) of cefixime and diluting to 25 mL with buffer solution.

Procedure

A 25 mL volume of a solution containing an appropriate concentration of cefixime and Cu(II) in buffer solution(or working solutions of pharmaceuticals or working standard addition solutions of pharmaceuticals) at temperature 25 ± 5°C within 0-10 minat λ= 410 nm be ready for measurement.

RESULTS AND DISCUSSION

The different experimental parameters affecting the produced color of cefixime: Cu(II) complex were extensively studied in order to determine the optimal conditions for the determination of cefixime.

Spectrophotometric results

UV-Vis spectra by using acetate-NaOH buffer as blank were studied. The Cu(II) solutions and cefixime solutions do not absorb in range 400-600 nm, while cefixime solutions have one maximum absorbance at λ= 283 nm, the molar absorptivity are2.08×10^4 L.mol^{-1} cm^{-1}. When the cefixime: Cu(II) complex solutions in acetate-NaOH buffer have absorption at 410 nm, the molar absorptivity are $5.12x10^3$ L.mol^{-1} cm^{-1} (Figure 2).

The effect of ratio of water in methanol

First, the influence of ratio of water in methanol on the absorption was studied. The maximum absorption using acetate-NaOH buffer occurs at approximately 8:92 of water: methanol, Figure 3.

The effect of acetate-NaOH buffer in water

Methanol (8:92, v/v) the better buffer was continue sodium acetate (0.0016 M) and NaOH (0.04 M) in water: methanol (8:92, v/v).

The effect of temperature

The effect of temperature on the produced adduct was studied. It was found that heating at 25±5°C was better than another temperature.

The effect of time

The effect of time on formation of complex was studied. It was found that better time was 0-10 min.

The effect of concentration of Cu(II)

The effect of concentration of Cu(II) on formation of complex was studied. It was found that better concentration was 2-5 times of concentration cefixime.

Composition of cefixime: Cu(II)complex

The stoichiometric ratio between CEFI and Cu(II) of investigated macrolides in water: methanol using acetate-NaOH buffer and formation of cefixime: Cu(II) complex were employed to determine by mole-ratio and Job's method of continuous variation as follows:

Molar ratio method

The stoichiometry of cefixime: Cu(II) complex by molar ratio method according to following equation: A_{max}= f([Cu(II)] / [cefixime]), confirms that the ratio of complex cefixime: Cu(II) is equal to 1:1. Where the concentration of cefixime is constant (5×10^{-5} M) and the concentrations of Cu(II) is change from 0 to$10x\ 10^{-5}$ M (Fig. 4 and

5).Figure 4 showed that, UV-Vis spectra have one isosbestic point at 314 nm, and Figure 5 indicated a molar ratio of 1:1 drug to Cu(II). In figure 6 offered the stoichiometry of cefixime: Cu(II) complex by molar ratio method according to following equation: A_{max}= f([CEFI] / [Cu(II)]),where the concentration of Cu(II) is constant (5×10^{-5} M) and the concentrations of CEFI is change from (0 to$10x10^{-5}$ M). In this case too confirms that the ratio of complex cefixime:Cu(II) is equal to 1:1.

Job's method

Job's method of continuous variation of cefixime: Cu(II) complex systems according to following equation: A_{max}= f{ [Cu(II)] /([CEFI] + [Cu(II)])} were studied. Figure 7 shoed that, the ratio of complex cefixime: Cu(II) is equal to 1:1.

Calibration curve

The calibration curves for cefiximein pure form through complexation with Cu(II){CEFI: Cu(II) complex} showed excellent linearity over concentration ranges of 0.2267-22.671 µg.mL^{-1}, see Figure8. The spectra characteristics of the cefixime: Cu(II) solutions as ε, λ_{max}, Beer's law, the equation (y=0.0113x+0.0002; y=absorbance, x=concentration of cefiximein µg.mL^{-1}, 0.0002 = intercept and 0.0113 = slope) and the correlation coefficient (R^2=0.9995) are summarized in Table-1.

Analytical results

Spectrophotometric determination of cefixime through complexation with Cu(II) using acetate-NaOH buffer in optimal conditions using calibration curve was applied. The results, which summarized in Table 2 showed that, the determined concentration of cefixime was rectilinear over the range of 0.2267to 22.671µg.mL^{-1} with relative standard deviation (RSD) was not than 4.0%. The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.030µg.mL^{-1} and 0.091µg.mL^{-1}, respectively. The proposed method was validated statistically and through recovery studies. The method was successfully applied for the determination of cefixime in pure and dosage form with percent recoveries from 98% to 104%. The results obtained from the proposed method have been compared with the official HPLC method[9] and good agreement was found between them.

Table 1: The optimum parameters established for spectrophotometric determination of cefixime in pure form through complexation with Cu(II) using acetate-NaOH buffer in water:methanol (8:92, v/v).

Parameters	Operating modes
Time of maximum color intensity	0-10 min
λ_{max} of complex	410 nm
Molar absorptivity of complex at λmax, (ε)	5.12 x 10^3 L.mol^{-1}.cm^{-1}
$\lambda_{isosbestic}$	314 nm
λ_{max} of CEFI	283 nm
Molar absorptivity of CEFI at λ_{max}, (ε)	2.08 x 10^4 L.mol^{-1}.cm^{-1}
Spectra range	280 – 600 nm
Buffer solution	0.0016 M $NaCH_3COO$+0.04 M NaOH
Solvent	Water: methanol (8:92, v/v)
Temperature of solution	25 ± 5°C
Concentration of Cu(II)	More than 2-5 times of C_{CEFI}
Beer's Law Limit,µg.mL^{-1}	0.2267 – 22.671
LOD(3.3SD), µg.mL^{-1}	0.030
LOQ (10SD), µg.mL^{-1}	0.091
Regression equation:	
Slope	0.0113
Intercept	0.0002
Correlation coefficient (R^2)	0.9995
RSD%	4.0

Table 2: UV-Vis spectrophotometric determination of cefixime in pure form through complexation with Cu(II) using acetate-NaOH buffer in water: methanol (8:92, v/v).

x_i, µg.mL^{-1} (taken)	$*\overline{X}$, µg.mL^{-1} (found)	SD, µg.mL^{-1}	$\frac{SD}{\sqrt{n}}$, µg.mL^{-1}	$\bar{x} \pm \frac{t.SD}{\sqrt{n}}$, µg.mL^{-1}	RSD %
0.2267	0.227	0.0091	0.0041	0.227±0.011	4.0
0.4534	0.454	0.018	0.0080	0.454± 0.022	4.0
0.9069	0.908	0.035	0.0156	0.908± 0.043	3.9
1.3604	1.36	0.052	0.0233	1.36± 0.065	3.8
1.8138	1.81	0.065	0.0290	1.81± 0.081	3.6
2.7207	2.70	0.092	0.0411	2.70± 0.11	3.4
3.6276	3.63	0.12	0.0537	3.63± 0.15	3.2
4.5345	4.54	0.14	0.0626	4.54± 0.17	3.0
5.6681	5.67	0.16	0.0716	5.67± 0.20	2.9
6.8018	6.82	0.19	0.0850	6.82± 0.24	2.8
7.9354	7.91	0.21	0.0939	7.91± 0.26	2.7
9.0690	9.08	0.24	0.1073	9.08± 0.30	2.7
13.603	13.61	0.38	0.1699	13.61± 0.47	2.8
18.137	18.08	0.52	0.2325	18.08± 0.65	2.9
22.671	22.54	0.72	0.3220	22.54± 0.89	3.2

* n=5, t= 2.776

Table 3: Regression equations and correlation coefficients for spectrophotometric determination of cefixime in pharmaceuticals through complexation with Cu(II) using acetate-NaOH buffer in water:methanol (8:92, v/v)(m'= intercept/slope, µg.mL^{-1})

Pharmaceutical preparations	Operating modes		
	Regression equations*	Correlation coefficients	Amount of cefixime (m), mg/tab. or caps.
Bioxime-400 mg/tab.	y=0.0112x+0.01796	R^2=0.9986	$m_{CEFI/tbl.}$=250m'=401
Cefix- 400 mg/caps.	y=0.0114x+0.01838	R^2=0.9984	$m_{CEFI/caps.}$=250 m'=403
Cifime- 400 mg/caps.	y=0.0113x+0.01817	R^2=0.9986	$m_{CEFI/caps.}$=250m'=402
Supraxime-400 mg/tab.	y=0.0113x+0.01813	R^2=0.9984	$m_{CEFI/caps.}$=250m'=401
Cefixime-ElSaad- 400 mg/tab.	y=0.0114x+0.01838	R^2=0.9984	$m_{CEFI/tbl.}$=250m'=403
Cifime- 200 mg /tab.	y=0.0115x+0.009016	R^2=0.9980	$m_{CEFI/tbl.}$=250m'=196
Supraxime-200 mg /tab.	y=0.0113x+0.009311	R^2=0.9982	$m_{CEFI/caps.}$=250m'=206
Cefixime-ElSaad- 200 mg/tab.	y=0.0114x+0.009334	R^2=0.9981	$m_{CEFI/tbl.}$=250m'=205

*y= A, x= concentration of cefixime (µg.mL^{-1})=m'.

APPLICATIONS

Many applications for the determination of cefixime in some pharmaceutical preparations with a spectrophotometric method through complexation with Cu(II) using acetate-NaOH buffer in water: methanol (8:92, v/v) in optimal conditions were proposed. Regression equations and correlation coefficients were included in Table 3. Standard addition curves for determination of cefixime in different pharmaceutical preparations were used.The amount (m) of cefixime in one tablet (or one capsule by mg/tab., or mg/caps.) calculated from the following relationship: m = h. m', where: m' is the amount of cefixime in tablet, or capsule, calculated from the standard additions curve according to the following regression equation: y=a.x+b; when y=0;m'=x= b/a= intercept/slope (µg.mL^{-1}), h conversion factor is equal to 250 for all pharmaceuticals {***Bioxime***(tablet,400mg), ***Cefix***(capsule, 400mg)**,** ***Cifime*** (capsule, 400mg), ***Supraxime***(tablet, 400mg), ***Cefixime-ElSaad*** (tablet, 400mg), ***Cifime***(tablet, 200 mg), ***Supraxime***(tablet, 200mg) and ***Cefixime-ElSaad*** (tablet, 200mg)}. The results of quantitative analysis for cefixime in some pharmaceutical preparations were calculated using the standard additions method were summarized in Table 4. The proposed method was simple, economic, accurate and successfully applied to the determination of CEFI in pharmaceuticals with average recovery of 98.00 to 103.00%, the results obtained agree well with the contents stated on the labels. The results obtained by this method were validated by HPLC[9].

Table 4: Spectrophotometric determination of cefixime in pharmaceuticals through complexation with Cu(II) using acetate-NaOH buffer in water: methanol (8:92, v/v)

Commercial name	Contents	$\bar{x}$, mg/tab.or caps.	RSD%	Recovery %
Bioxime, Ctd.tab. Shifapharmaceutical industries Aleppo – SYRIA	400 mg/tab.	401	3.8	100.25
Cefix, Ctd.caps. Alpha, Aleppo pharmaceutical industries Aleppo – SYRIA	400 mg/caps.	403	3.9	100.75
Cifime, Ctd.caps. Delta for medicaments Aleppo–SYRIA	400 mg/caps.	402	3.8	100.50
Supraxime Asia pharmaceutical industries Aleppo–SYRIA	400 mg/tab.	401	3.8	100.25
Cefixime-ElSaad Al-Saad pharmaceutical industries Aleppo–SYRIA	400 mg/tab.	403	3.9	100.75
Cifime, Ctd.tab. Delta for medicaments Aleppo–SYRIA	200 mg/tab.	196	4.1	98.00
Supraxime Asia pharmaceutical industries Aleppo–SYRIA	200 mg/tab.	206	4.0	103.00
Cefixime-ElSaad Al-Saad pharmaceutical industries Aleppo–SYRIA	200 mg/tab.	205	4.0	102.50

*n=5

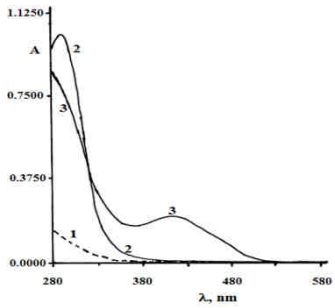

Fig. 2: UV-Vis spectra of: 1- 5x10^{-5} M Cu(II); 2- 5x10^{-5} M cefixime; 3- 5x10^{-5} M complex CEFI:Cu(II), 5x10^{-5} M cefixime with 5x10^{-5} M Cu(II) {using acetate-NaOH buffer in water:methanol (8:92,v/v); ℓ =1cm}.

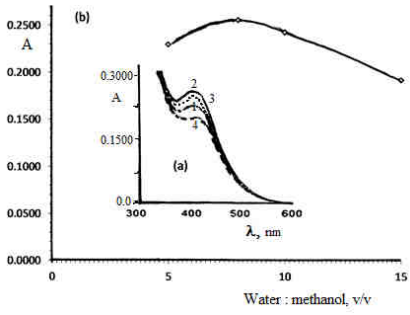

Fig. 3: The effect of ratio water in methanol on UV-Vis spectra of cefixime:Cu(II) complex using acetate-NaOH buffer in water:methanol (8:92,v/v) : 1- 5%, 2- 8%, 3- 10%, 4- 15% v/v; $C_{Cu(II)}$=C_{CEFI}= 5x10^{-5}M (ℓ =1 cm).

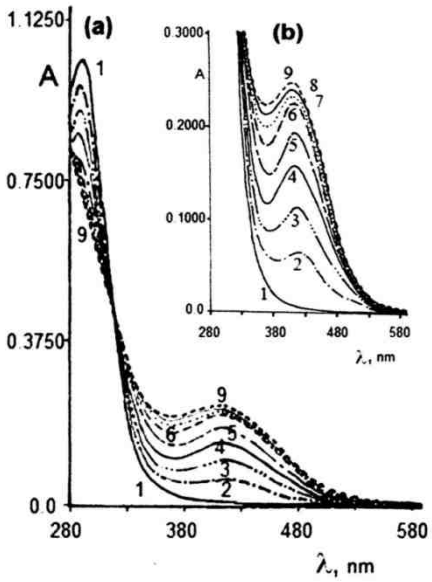

Fig. 4: UV-Vis spectra of 5.00x10^{-5} M cefixime with Cu(II) ; 0 to 9 concentration of Cu(II) were as the follow as: 1- 0; 2- 1.00x10^{-5}; 3- 2.00x10^{-5}; 4- 3.00x10^{-5}; 5- 4.00x10^{-5}; 6- 5.00x10^{-5}; 7- 6.667x10^{-5}; 8- 8.333x10^{-5}; 9- 1.000x10^{-4}M {using acetate-NaOH buffer in water:methanol(8:92,v/v); ℓ =1cm}.

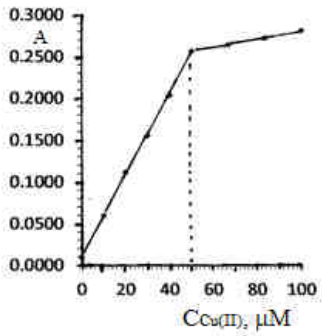

Fig. 5: Molar ratio method to calculate coupling ratio for cefixime:Cu(II) complex using acetate-NaOH buffer in water:methanol (8:92,v/v) as blank, C_{CEFI}=5x10^{-5}M, (ℓ =1 cm, λ_{max} = 410 nm).

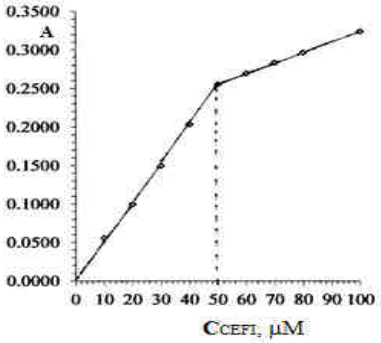

Fig. 6. Molar ratio method to calculate coupling ratio for cefixime:Cu(II) complex using acetate-NaOH buffer in water:methanol (8:92,v/v) as blank, $C_{Cu(II)}$=5x10^{-5}M, (ℓ =1 cm, λ_{max} = 410 nm).

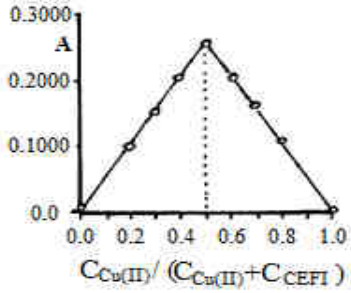

Fig. 7: Job's method of continuous variation of cefixime:Cu(II) complex using acetate-NaOH buffer in water:methanol (8:92,v/v) as blank, C_{CEFI}+$C_{Cu(II)}$=10x10^{-5}M, (ℓ=1cm, λ_{max} = 410 nm).

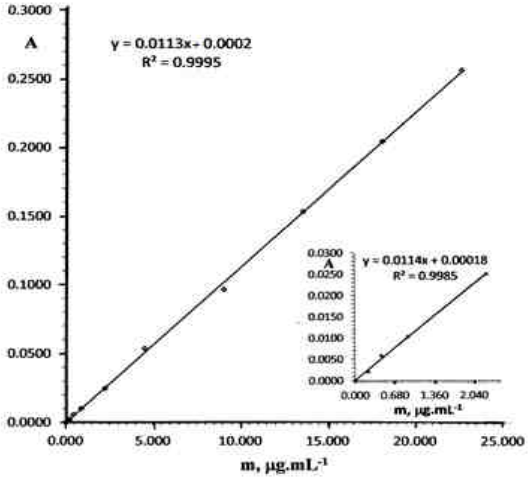

Fig. 8: Calibration curve for determination cefixime through complexation with Cu(II) using acetate-NaOH buffer in water:methanol (8:92,v/v) in optimal conditions (ℓ = 1 cm).

CONCLUSION

Spectrophotometric determination of cefixime in pure and its pharmaceutical formations through complexation with Cu(II) using acetate-NaOH buffer in water: methanol (8:92, v/v) has been developed. The maximum absorbance of the coloured complex occurred at λ= 410 nm and the molar absorptivity is 5.12 x 10^3 $L.mol^{-1}$ cm^{-1}. Reaction conditions have been optimized to obtain the complex. The linear range of the calibration curve was 0.2267-22.671µg.$mL^{-1}$with correlation coefficients ≥0.9995 in all cases. Overall recoveries were of the order of 98.0–103.0%.The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.030µg.mL^{-1} and 0.091µg.mL^{-1}, respectively. The proposed method was simple, economic, accurate and successfully applied to the determination of cefixime in pharmaceutical formulations and the results obtained agree well with the contents stated on the labels. The results obtained by this method were validated by HPLC[9].

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