Cloud point Extraction of antibiotic drug by Direct (UV- Vis) Spectrophotometer and Indirect(Flame Atomic Absorption) Technique

Saadiyah A. Dhahir and Noor J. Mohammed
sadiataher@yahoo.comnoor.jamal1987@yahoo.com
Department of chemistry, College of science for women, University of Baghdad

Abstruct

A new method for the determination of the Cefiximedrug in some Pharmaceuticals using ultra violet-visible (UV- Vis) and indirect Flame Atomic Absorption Spectrophotometry (FAAS) by Cloud point Extractionby usingTriton X-114 as surfactant, the method based to form chelating complex(CEF –Cu II) at 827nm ,variables parameters were studied such as the concentration of metal ion , effect of pH, Triton X-114 amount, equilibration temperature and incubation time.The best pH for the formation of chelatingcomplexwas(13). The best temperature on cloud-point extraction was 500C at 20 min. then complex extracted with ethanol .The mole-ratio method has been used to determine the structure of chelate (CEF- CuII) and found to be 1:1 L:M(Ligand : Metal). Beer's Law wasobeyed in the range 10-130 and 5-60µg/ml for UV-Vis and AAS respectively. Limit of Detection andLimit of QuantitationLOD values for these methodswere(1.6906,0.6081)µg/mland LOQ(5.6355, 2.02710)µg/ml respectively.the methodwas validated and successfully applied to drug formulations like Cefix capsules marketed in Iraq. The results of analysis have been validated statistically and by recovery studies and were found satisfactory

Keywords :Antibiotic drug, Cefixime ,Cloud Point Extraction, chelating complex

I. INTRODUCTION

Antibiotics are the chemotherapeutic agents that kill or inhibit the growth of microorganisms. These chemical agents are used to treat disease by destroying pathogenic microorganisms or inhibiting their growth at concentration low enough to avoid undesirable damage to the host. Antibiotics are drugs preparations which contain some chemical substances that are produced by microorganisms and by chemical synthesis. These substances at very low concentrations are known to totally destroy or partially inhibit microorganisms . Antibiotics have wide spread application in the treatment of bacterial disease (1) Cefixime is Chemically,(CEF) (6R, 7R)-7-[2-(2-amino-4- thiazolyl) glyoxylamido] - 8-oxo-3-vinyl-5-1- azabicyclo [4.2.0] oct-2- ene-2-carboxylicacid, 7-9z)-[o-carboxymethyl)-oxime] trihydrate.Molecular formula ofCefixime is C16H15N5O7S2, molecular weight (453.45 g/mol), It is third generation cephalosporin antibiotic. It is under the category of β-Lactam Antibiotics, Cell Wall inhibitor. It acts by inhibiting an enzyme Transpeptidase, involved in the building of Bacterial Cell Walls. It is used in Lower Respiratory Tract Infections, Acute Urinary Tract Infections, Biliary Tract Infections, Sinusitis, Acute Otitis Media, Peptic ulcer (2)It is used to treat or prevent infections that are proven or strongly suspected to be caused by bacteria. One of the major problems with this drug is its very poor solubility in biological fluids that results into poor bioavailability after oral administration. It shows erratic dissolution problem in gastric and intestinal fluid due to its poor water solubility. Rate of absorption and/or extent of bioavailability for such insoluble drugs are controlled by rate of dissolution in gastrointestinal fluids (3)The structures of drug are shown in (Fig.1)(4)

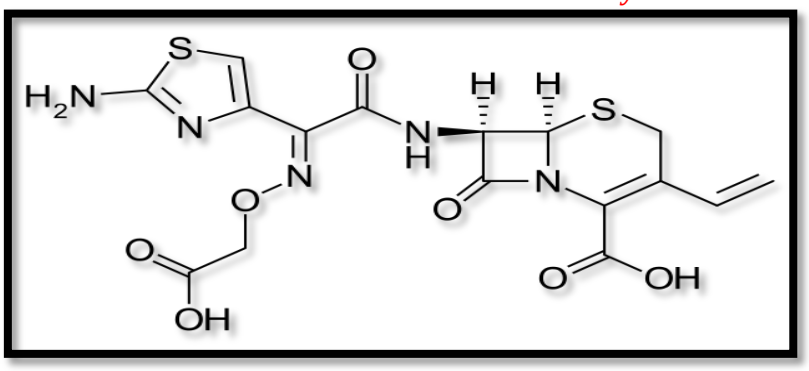

Figure (1) The structure ofCefixime(4)

The cloud point procedure (CPE) is based on the following phenomenon: an aqueous solution of some surfactant becomes turbid and separatesin to two isotropic phases if some condition such as temperature or pressure is changed or if an appropriate substance is added to the solution (5)which describes a liquid chromatographic method for its assay in bulk form. In order to assure the quantity of cefixime in dosage forms, several methods have been reported which include liquid chromatography-mass spectrometry(6),high performance liquid chromatography(7-10),high performance thin layer chromatography (11-12) derivative spectrophotometry (13) , voltammetry (14) , and capillary electrophoresis(15) .

II. MATERIALS AND METHODS

Apparatus

UV-Visible recording spectrophotometer (1986) Shimadzu Model (160A) (Japan) with a response time of 0.1s ,was used for spectrophotomatric determination A quartz cell of 5 ml internal volume and 1cm path length was used for absorbance measurements

Flame Atomic Absorption Spectrophotometer ,GBC (933 plus)

Hotplate Stirrer (Hotplate stirrer Model L-81 Labincobv)

Electric Balance (Sartorius, 4digitals, made in Germany)

Oven (Memmert , maximum temperature 250,made in western Germany.)

Water Bath (A thermostat water Bath, model Unitemp)

Centrifuge (Triup International corp ,TRIU 800 Centrifuge ,made in Korea).

PH-meter (model BP 3001).

Materials AND METHODS

A pure grade of Cefiximewas obtained from Drug Industries and Medical Appliance (SID) Samarra/ Iraq

All the chemical stock solution were prepared from analytical grade BDH

2.3.Preparation of Standard Solutions:

All glassware was used cleaned with distilled water and dried at 50˚C for 30 minute prior to use. Batch experiments were carried out in to ensure the reproducibility of results and the average value. All metal used were of the highest purity and most solutions were prepared in distill water.

A stock solution of 1000µg ml -1 or (2.205×10-3 M) for the drug Cefixime was prepared by dissolving 0.1g in minimum amount of water and diluted to mark with water in a 100 ml volumetric flask.

A solution of 1000 ppm of Cu+2 was prepared by dissolving 3.8gm of Cu(NO3)2.3H2O in small amount of water and complete the volume to 1000 ml by using volumetric flask.

A standard stock solution of sodium hydroxide NaOH (1M) was prepared by dissolving (4g) of the solid product in 100 ml of distill water Then 10 ml of the stock solution was diluted to100 ml with distilled water to Prepare 0.1M solution.

A 10% (v/v) of Triton X-114 was prepared by diluting 10 ml with water in a 100 ml volumetric flask

Interference Solutions of 1000 ppm

An amount of 1000 µg ml-1 stock solution of interferences is prepared by dissolving 0.1g of the different organic compound such as [Lactose, Starch, Arabic Gum, Glucose and Talc] and inorganic compound such as [0.2579g, 0.2500g] of Ca3(PO4)2 and CaCO3 respectively in distilled water and diluting them to the mark in 100 ml volumetric flask.

2.4 General procedure for CPE by UV-VIS Method

Aliquots 10 ml of a solution containing known amount of Cefixime drug was mixed with 1ml of 1000µg ml -1 Cu+2metal ion Then pH was adjusted by using 0.1M NaOHand 0.1 HCl then added 1ml of 10% (v/v) Triton x-114. The mixture was shaken for 1 min and left to stand in a thermo-stated bath at 50 oC, for 10 min. Separation of the phases was achieved by centrifugation at 3000 rpm for 10 min,Test tube taken in ice bath to increased viscosity micelles layer for 1min. then become easily separated was dissolved by1ml of ethanol, the measurements of absorbance of the complex were followed by UV-Vis spectrophotometer with used 1.0 cm quartz cell to get λ max for CFX - Cu (II) complex against blank which was prepared in the same way but without drug .

III. RESULTS AND DISCUSSION

3.1. Absorption Spectra

The absorption spectrum of the complex productCEF - Cu (II)formed was recorded against the corresponding blank between 200 to 900 nm before obtaining optimum conditions according to the recommended CPE procedure. Figure 2show an absorbance at λ max 827nm. The molar absorptivityvalue is 3 ×103 Lmol-1cm-1. The value of molar absorptivity enables to carry out the quantitative analysis of cefixime in Pharmaceuticalsdirectly .

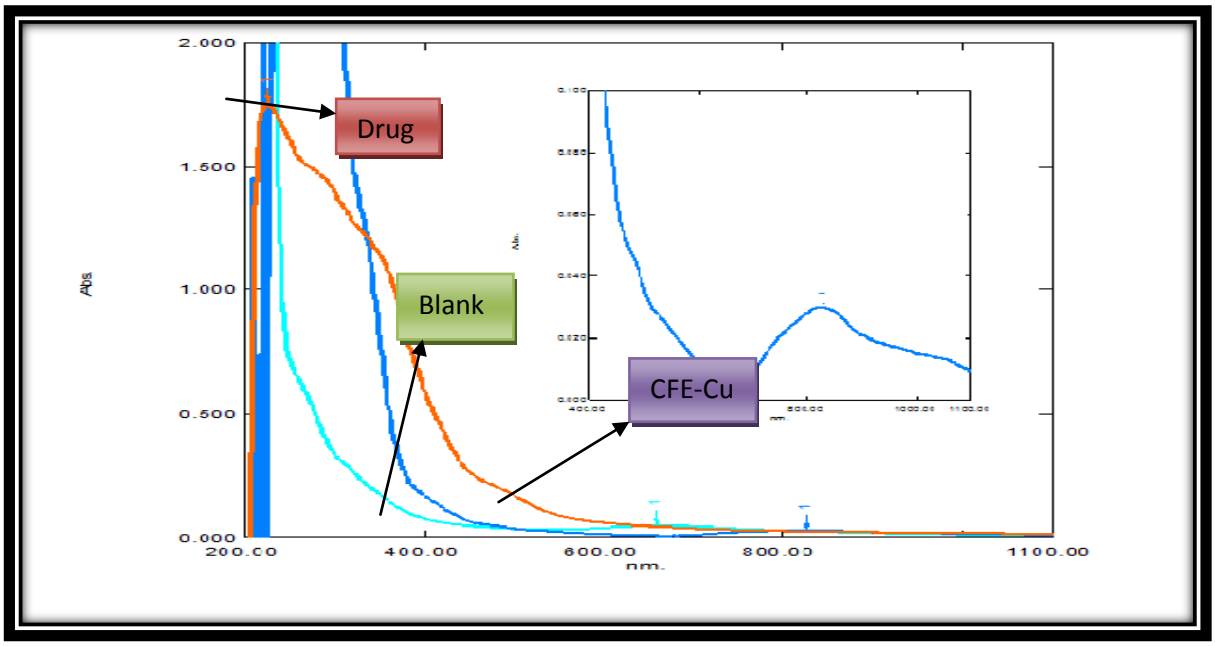

Figure 2. Absorption Spectra of (A) CEF Versus Distilled Water, and (B) metal Versus Distilled Water (C) Complex of the CEF - Cu(II) Against metal Blank

3. 2. Optimization of CPE Methodology

A group of experiments has been conducted to study the effect of several variables that affect the extraction efficiency of the CPE and maximize the sensitivity of the detection system for drug under study using a classical optimization. The variables such as the concentration of metal ion , best of pH ,best of buffer ,best of volume buffer, Triton X-114amount, equilibration temperature and incubation time.

3. 2.1. Effect of metal ions concentration

The effect of copper ion concentrations was studied by measuring the absorbance values according to the geranial procedure containing 1ml of 1000µg ml-1Cefixim, 1ml of 10% (v/v) Triton x-114 ofand varying volumes of the1000µg/mlCuII ranged from (0.2-2) ml.The optimum volume of the metal ions that gave maximum absorbance was 1.4ml as shown in Figure3.this volume was used throughout this study.

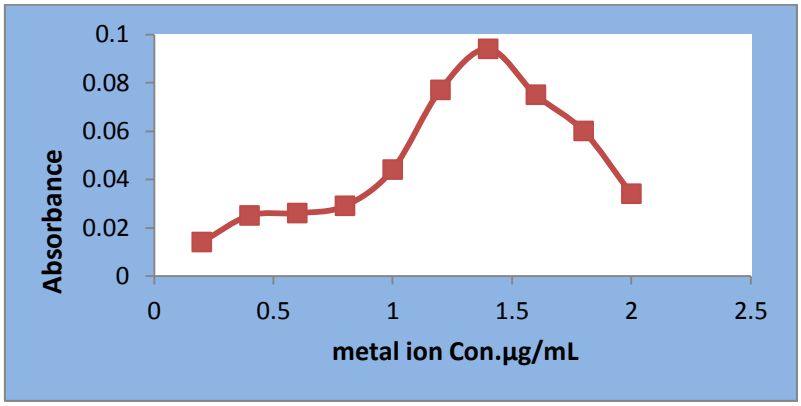

Figure 3 : Effect of Optimum concentration (Cu II) ion conc. on absorbance of CEF- (Cu II) complex

3.2.2. Effect of pH

The pH plays a unique role on metal-ligand formation and subsequent extraction, and is proved to be a main parameter for CPE(16). Set of similar experiments in the pH range of 1-14 were accomplishedaccording to the described procedure The maximum sensitivity andthe best separation for the complexes drug- Cu(II) was obtained at pH 13 .The results are shown in Figure4 and table1.

Table (1) Data of Absorbance to value of pH

value of pH	Absorbance at λmax 827 for (Cu II)
1	0.032
2	0.03
3	0.025
4	0.053
5	0.056
6	0.058
7	0.166
8	0.175
9	0.178
10	0.183
11	0.195

12	0.196
13	0.199
14	0.082

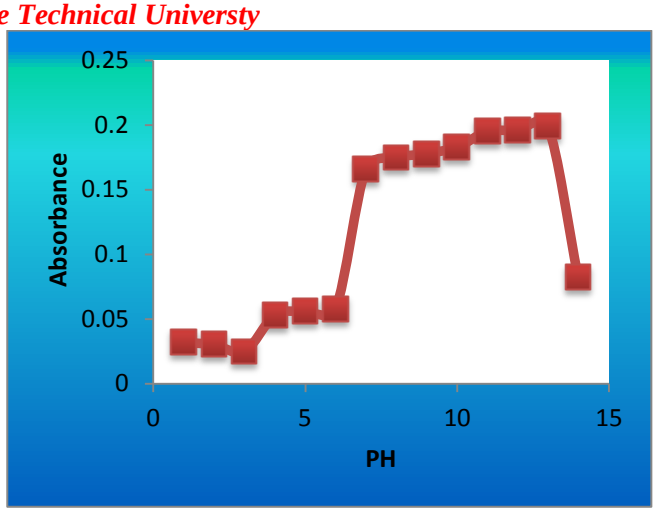

Figure 4: pH effect on the absorbance of (CEF- CuII)complex

It was shown that the sensitivity increase at pH 13. At higher pH, the drug is deprotonatedand it behaves like a hydrophilic molecule and easily gets solubilized in the micelles while at lower pH, the drug is protonated and its ionic characteristicsincrease and led to decrease in its solubilization in thehydrophobic micelles.

3.2.3. Effect of buffersolutions

The effect of buffer solutionpotassiumbuffer solutionswith basic function 13 was studied on the intensity of complex formation (Cu+ CEF)

The best intensity values ofpotassiumbuffer solutions as shown in table2.

Table 2: buffer pH 13

Preparation buffer pH	Absorbance
Potassium buffersolution كتب بخط عدل	0.469

3. 2.4.Effect of Volumes buffer solutions

Fig (5) shows the value of absorbance intensity for the CEF-Cu complex against the value of volumes of potassium buffer solution. It is evident that absorbance increase with increase the volume of buffer up 0.8ml, but suddenly decrease the absorbance because the decomposition happen when increase basicity.

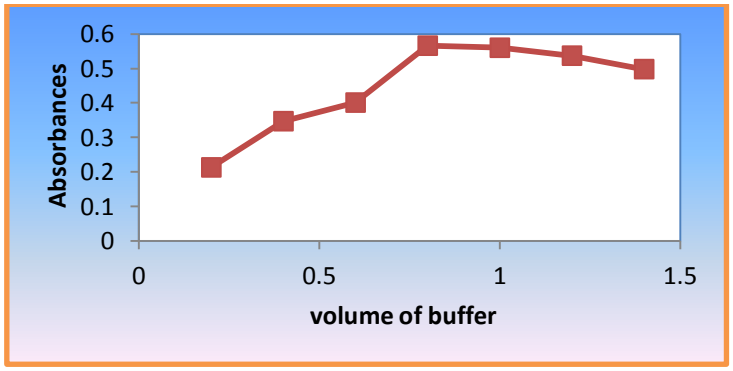

Figure 5: buffer of pH effect on the absorbance of CEF- CuIIcomplex

3.2.5. Effect Type of Surfactant with complex.

The type of surfactant plays very substantial role in cloud point extraction process where each surface owns spectral properties depend on practical basis of Micelles .Aliquots of 10ml of a solution contains [1ml cefixime ,

1.4 ml Cu , 0.8.ml buffer pH 13] in 10ml volumetric flask and use different surfactant [Tween 20, Tween80, CTAP, SDS, Triton X-100, Triton X-114] at 500C for 10 min incubation time then it centrifuged at 3000 rpm for 10min , separated the surfactant- rich phase and dissolved in 1ml ethanol then measured by UV-Vis at λmax= 827 nm for CEF-CuIIcomplexthe results shown inTable (3)

Table (3) Data of Absorbance of Type of Surfactant

N	Surfac	Absorbance λmax = 827 nm (II)
1	Tween	0.298
2	Tween	0.189
3	SDS	0.394
4	CTAP	0.151
5	Triton	0.368
6	Triton	0.569

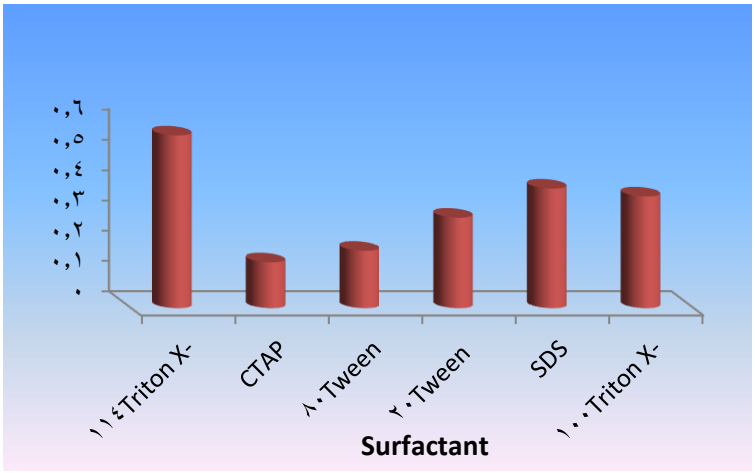

Figure (6): Effect of surfactant type onAbsorbance

It was observed that Triton X-114 which has maximum absorbance at 827 nm .It is clear from the results that the nonionic surfactant Triton X-114 is of high absorbance and the surface increases of the efficiency of thecloud point extraction.

3.2.6. Effect of Triton X-114 amount

Most studies confirm that the amount of an nonionic surfactant type Triton X-114 as an extracting medium plays an important role for maximizing the extraction efficiency by minimizing the phase volume ratio (Vs/Va) and therefore improving the pre-concentration factor of the CPE procedure, Therefore, the amount of Triton X-114 was investigated by varying the volume of 10% Triton X-114 between (0.2-2 mL) for CEF-CuII complex. The results are presented in Fig (7). It was noticed that the absorbance values of CEFdrug continued to increase dramatically and reached maximum at 1.6mL of 10% Triton X-114. These values were selected as optimal amount and used in the proposed methods for the detection of CEF.Plotting the absorbance values of the cloud point versus the volume of Triton X-114 is shown in Fig (7).

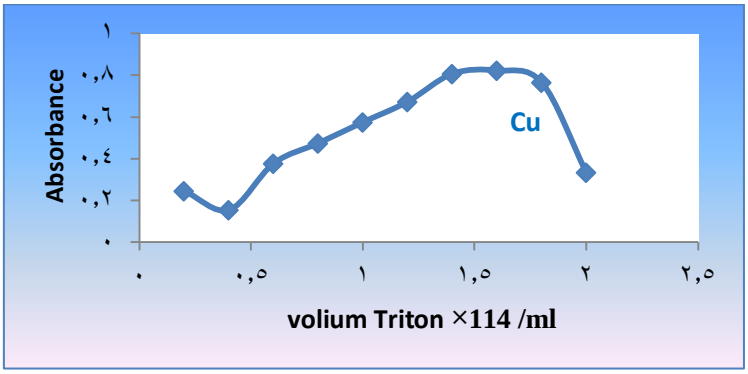

Figure 7: Effect of the Triton X-114 amount on absorbance of CEF- (Cu II) complex

3.2.7 Effect of the Equilibration Temperature and Time:

In order to optimize the method, it was necessary to examine the effect of the temperature on cloud-point extraction. Temperature that enhances higher range of (35 – 80)°C and (5 - 35)min, respectively, while keeping all other parameters constant. Excellent absorbance was found at temperature 500C as shown in figure 8 and table 4, therefor choose500C, higher than500C is probably due to the decomposition of the complex.

Table (4) Data of Absorbance in different Temperatures / 0C

Temperature /	Absorbance at 827 for Cu(II)
35	0.332
40	0.49
45	0.658
50	0.825
55	0.51
60	0.498
65	0.43
70	0.476
75	0.462
80	0.307

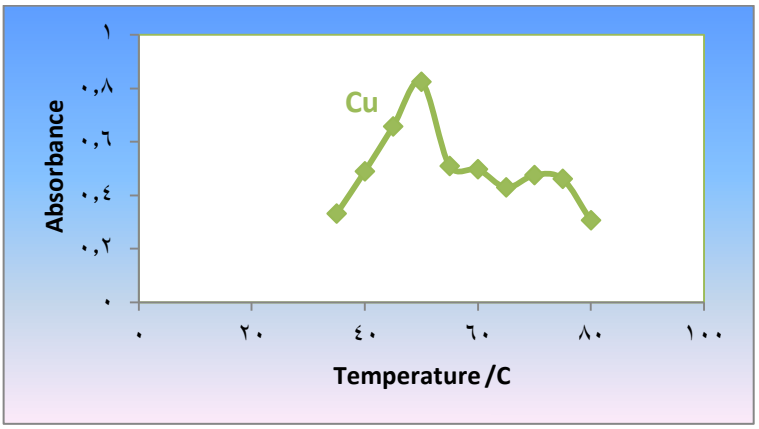

Figure8.Effect of temperature on the cloud point extraction ofCEF-(Cu II) complex

Incubation time was also investigated in the range of (5-50) min figure (9) excellent absorbance found at 20 min the time for 20 min was selected to fulfill efficient separation conditions.

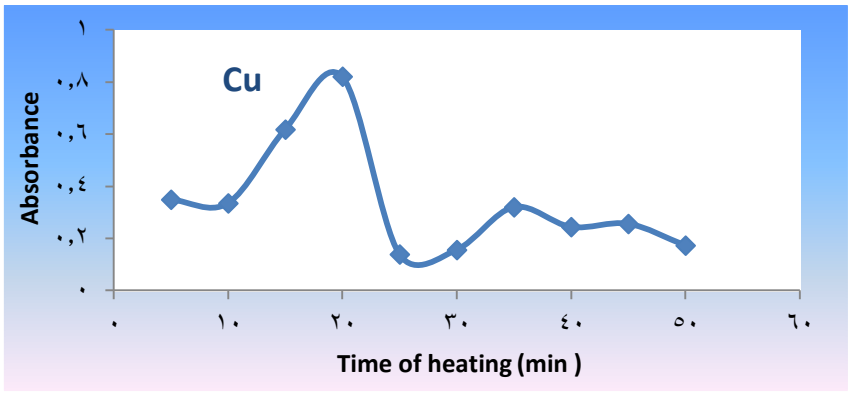

Figure 9: .Effect of time on the cloud point extraction ofCEF- Cu II complex

3.2. 8. Order of Additions

The effect of order for additions of the metal on the absorbance of each analyte by the general CPE was tested. Fig (10) and Table (5) show that the best order of addition is the number 1 for targetanalytes due to giving a highest absorption signal among the others.It is noted that the best addition is the first order of complex CEF- Cu (II) because if it's another order gets lost in the intensity of color and this order fixed in subsequent experiment

	Order Ad	Absorbance

		λmax = 827 for
	D+ M+B	0.788
	M+D+B	0.174
	D+B+M	0.087
	M+B+D	0.824

Table (5) Data of Absorbance of Order Additions

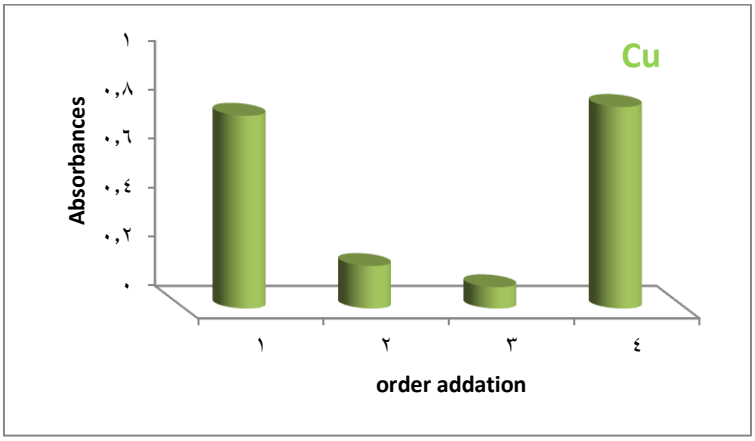

Figure 10 : Effect of Order Additions. For CEF- Cu IIcomplex

3.2. 9. Effect of organic solvents

Different organic solvents are examined to evaluate their effects on the intensity of the resulting complex and the data are shown in Table 6 and figurer 11.It has been shown that water is the optimum solvent, economically, sensitivity method, cheap price, to provide and nontoxic. This solvent is fixed in subsequent experiment

Table 6: Data of Absorbance to Solvents

	Solvent	Absorbar λmax = 827 fo ion
	Water	0.823
	Ethanol	0.795
	Methan	0.363
	Aceton	0.685
	H2O2	0.210
	chlorof	0.490
	Acetyl	0.203
	Dimeth mide	0.246
	Dimeth phthalate	0.043
	Dimeth ate	0.021

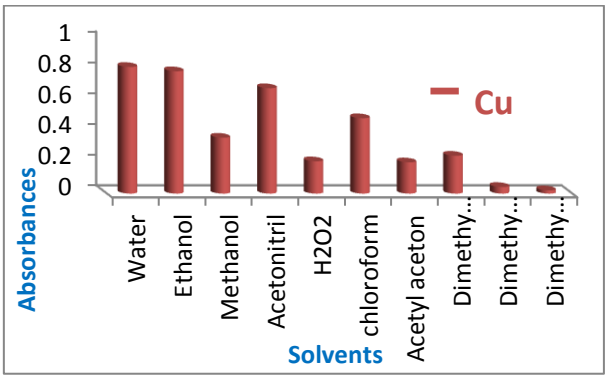

Figure 11 : Effect of Solvents . For CEF- (Cu II) complex

3.2.10 .Effect of Interference

The effect of some foreign organic compounds and Inorganic compounds which tabulated in table 7 were studied by adding 1ml of (100ppm) to the CEF- Cu II complex. The intensity of wasdeveloped follow the recommended proceduredescribed earlier. It was observed from the table7and figure12 were not interfering with the determination at levels found incomplexform.

Table 7: Effect of Interference

100µg ml-1 interference	Absorbance at λma for Cu
With out	0.822
Lactose	0.547
Starch	0.556
Arabic Gum	0.515
Talc	0.353
Glucose	0.385
Ca3(PO4)2	0.202
CaCO3	0.236

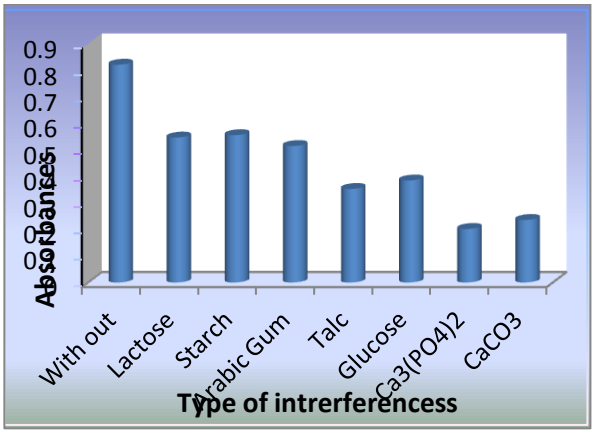

Figure 12: Effect of Interferences on the CEF-Cu IIComplex

3.3 .Selected Optimum Conditions

After the study of the effect of different optimum conditions on the absorbance intensity of the colored product,The optimum conditions for the proposed procedure were summarized in Table 8 and were used in all subsequent experiments.

Table 8: The optimum conditions for the determination of complex

Optimum	Concentrations	Range selected	Optimum quantities of complex (Cefxi- Cu)
ƛ max(nm)	----	190-1100	827
Effect of volume of metal ion required	1000 ppm	0.2 - 2 mL	1.8 mL
Effect of PH	0.1M(NaoH)	1-14	13

Buffer pH	----	----	potassiumbuffer solutions
Effect of volume of Buffer	----	0.2-1.4mL	0.8mL
Effect of volume of triton x114 required	10%(v/v)	0.2 -2.0mL	1.6 mL
Effect of time heating	----	5-50 min	20 min
Cefixime solution required	1000ppm	10 -130 ppm	1 mL

3.4. Preparation of Calibration Curve of CPE

Amount of 10ml solution is prepared containing increasing concentration of drug Cefixime by taking [1.4ml Cu ,0.8ml buffer pH 13 , (10-130) µg ml-1Cefixime and 1.6 ml10%(v/v)Triton X-114] then it is completed to the mark by distilled water, are mixed ,heated at optimum temperature in the thermostat water bath at optimum incubation time , to form cloud point then aqueous phase is separated by centrifugation at 3000 rpm for 20min ,1ml ethanol is added to the surfactant-rich phase to dissolve it then is measured by UV-Vis at λmax= 827 nm for copper , triplicate manner The absorbance measurements are illustrated in table 9

The calibration curve was .Plotting the mean absorbance values of the cloud point versus the concentration (ppm) of (CEF- Copper) as shown in Fig (13)

Table 9: The absorbance measurements of standard solutions of complex (CEF- Cu)

Conc. Ppm	Mean Absorbanc
10	0.155
20	0.219
30	0.286
40	0.345
50	0.417
60	0.497
70	0.582
80	0.661
90	0.742
100	0.823
110	0.897
120	0.986
130	1.034

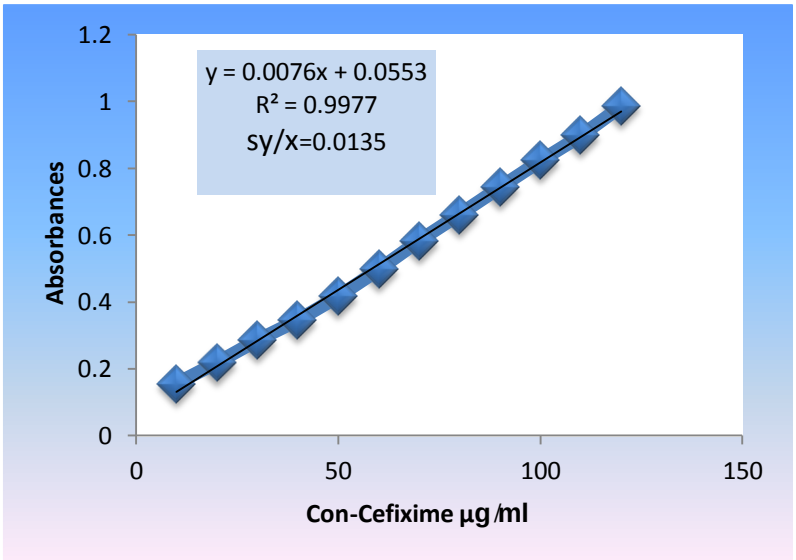

Figure 13:(Cefixime+ Cu) Calibration Curve

3.7. Stoichiometric Determination of Color complex :

3.7.1 Continuous Variation Method (Job`s method)

A series of (1, 2, 3, 4, 5, 6, 7, 8, 9) ml of (1×10 -4) mol L-1of the solution that contain Cefixime was pipette into each of 10ml volumetric flask then(9,8,7,6,5,4,3,2,1) ml of (1× 10-4) mol L-1of metal the absorbance

of the solution was measured by UV-Vis Spectrophotometer at λ max827nm the stoichiometric ratio between Cefixime with metal 1:1 results are shown in the Table (10)

Table10: The continuous variation method of Cefixime with metal (Copper) complex.

V I	V M	VD	Absorbar λ= 827
1	9	0.1	0.142
2	8	0.2	0.313
3	7	0.3	0.431
4	6	0.4	0.549
5	5	0.5	0.643
6	4	0.6	0.52
7	3	0.7	0.356
8	2	0.8	0.121
9	1	0.9	0.034

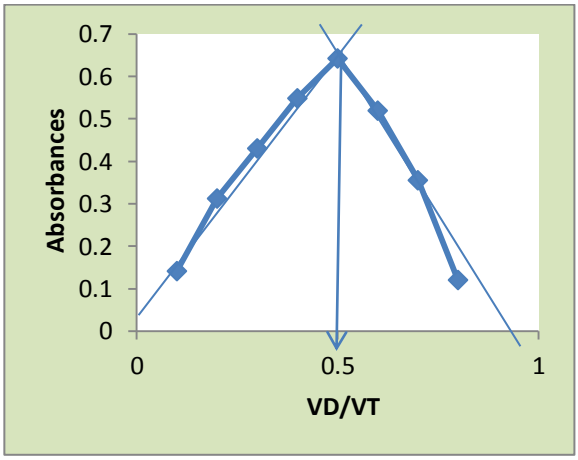

Figure 14 : Continuous variation method plot .

Plotting the value of absorbance versus the VD / VT is shown in Fig (14)

VD: values of the compound (Cefixime)

V M: The values of the metal (Copper).

VT: Total (V M+V D)

3.7.2. Mole – Ratio Method

Aliquots of 10 mL solution containing (1×10-4) molL-1 of (1mL) Cefixime and increasing concentrations (1×10-4) mol L-1 of (0.2,0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8) mL of (Cu) Copper (2×10-6--2×10-5)mol L-1 . The absorbance of the solutions were measured by UV-Vis spectrophotometer versus blank at λ max= 827 the stoichiometric ratio between 1:1 results are shown in the Table (11).

Table 11 : The Mole - Ratio Method of the Cefixime with Copper

CL	CL /	Absorbance 827 nm
2×10-(	0.2	0.032
4×10	0.4	0.094
6×10-(	0.6	0.121
8×10-(	0.8	0.153
1×10-5	1.0	0.201
1.2×10	1.2	0.194
1.4×10	1.4	0.199
1.6×10	1.6	0.195
1.8×10	1.8	0.199

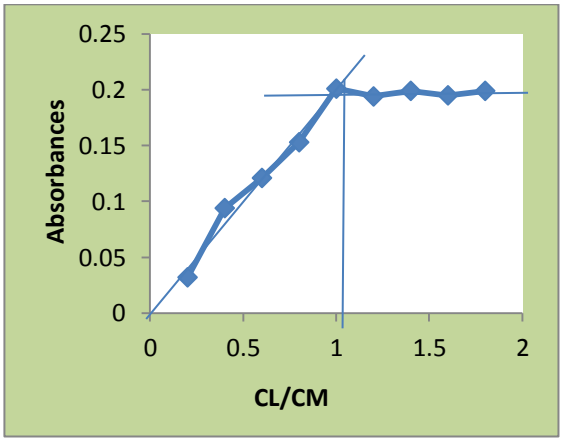

Figure 15: Mole - Ratio plot of Cefixime and Copper complex.

Plotting the value of absorbance versus the CL / CM is shown in Fig (15)

CL: concentration of the metal (Copper)

CM: concentration of the compound (Cefixime)

3.8.Applications of the Cloud Point Extraction on Pharmaceuticals.

CPE has been applied on pharmaceuticalCefixime, the manufacture company [Novartis] that contains (533.9mg) from Cefixime .The results are good and of high reliability in the analysis of samples in the pharmaceutical preparation. The results are summarized in the table (12) for Cefixi.

Table 12: Data for Determination Cefix with Copper in the Pharmaceutical Preparation Capsule (Cefixime) by CPE.

Am Cefix / µg	Mean absorbance	Relat stander devi (RSD	*Fo	Recov	Avera Recovery%	Ere	Average
30	0.263	0.380	27.3	91.0	90.8	-8.9	-9.03
60	0.487	0.410	56.8	94.6		-5.3	
90	0.651	0.153	78.3	87.0		-12	

[*]= Average of three

The proposed method is also applied on syrup Cefixime the manufacture company is [Novartis]. As each (5ml) from drug contains (100mg) Cefixime

4-Results and discussionby (AAS)Method

Amo Cefix / µg n	Mean absorbance	Relati stander devi (RSD	*Fo	Recove	Averag Recovery%	Er	Ave Erel%
30	0.270	0.370	28.2	94.1	93.8	-5	-6.0
60	0.479	0.361	55.7	92.9		-7	
90	0.702	0.376	85.0	94.5		-5	

2- Indirect determination of antibiotics byatomic absorption spectrophotometry (AAS)

Determination of drug CEF–CuII using Flame Atomic Absorption Spectrophotometer:

To be sure about the result obtained by UV-VIS, we used another technical method, Flame Atomic Absorption Spectrophotometer (FAAS) , by indirect measurement the absorbance of CuII in the complex to detect the Cefixime conc. as in figure (16) . The complex CEF-CuIIwas prepared by using optimum condition of pH , temperature , proper solvent etc . (The same conditions mentioned previously in U.V spectrophotometer) except changing the conc. of copperion, it was found the best conc. of CuII to give maximum absorbance 35 µg /ml of organic layer is enough to get higher absorbance for complex as in figure (17) .Also we measured the concentration of Cefixime in these pharmaceutical preparations using calibration curve of indirect (FAAS), we got the results close which obtained by U.V method

4.1Effect of metal ion concentration

Figure (16) show the effect of Cupper ion volume upon the absorbance values of the extracted complex using (1000µg/ml) of drug solution . The optimum volume of the metal ions that gave maximum absorbance was 35ppm of Cu(II)for the complex ,the absorbance is measured and the absorbance results are shown in table (14).

Table (14) Data of Absorbance of Optimum concentration of metal ion.

Concentra metal	Absorbanc Cu II)
5	0.006
10	0.013
15	0.019
20	0.020
25	0.031
30	0.035
35	0.047
40	0.043
45	0.039
50	0.025

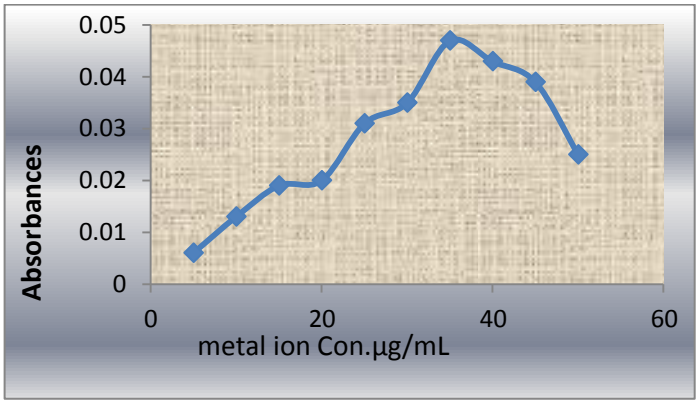

Figure 16: Effect of Optimum concentration (Cu II) ion conc. On absorbance of CEF-CuII complex by AAS method

4.2.Preparation of Calibration Curve for CEF

In order to test the linearity of the method and under the optimized conditions established by CPE procedure, Calibration graphs were established by plotting absorbance versus concentration of Cefixime . of The calibration curve was .Plotting the mean absorbance values of the cloud point versus the concentration (5-60µg ml-1) of (CEF-copper) as shown in Fig (17)

Table 15: The absorbance measurements of standard solutions of complex (CEF- Cu)

Conc. µg ml-1	Mean Absorbanc
5	0.067
10	0.095
15	0.12
20	0.146
25	0.175
30	0.201
35	0.232
40	0.258
45	0.284
50	0.302
55	0.326
60	0.351

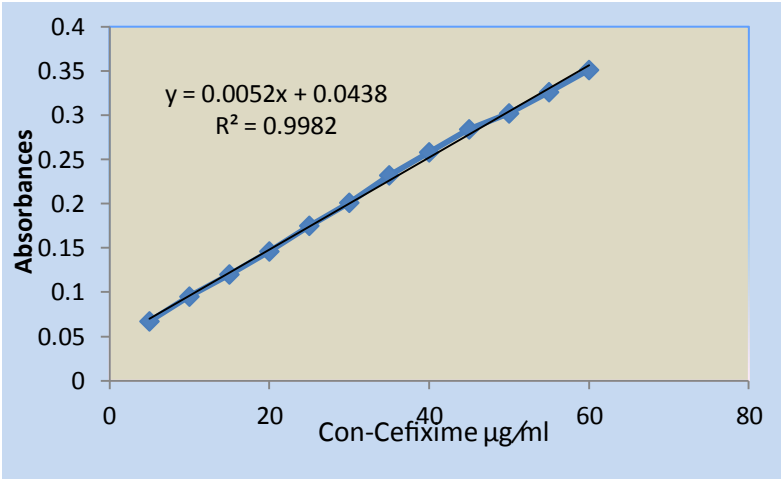

Figure 17 : (Cefixime- Cu) Calibration Curveby AAS Method

5.Comparison between the two methods of the proposed method

A simple comparison were make between the methodsUV-Vis and AAS for determination of Complex and the calculation statistically parameter were illustrated in Table (16).

The firstandsecond methods characterized by simplicity , highly economic accurate and apply the green chemistry requirement two method characterized by high selectivity economic and not used any harmful chemicals .From the opinion of scientist analyst ,The first method prefer it because the absence of any interferences which may appear in the UV-Vis regionand the best statistically calculation parameter.

Table 16: Comparison between the Two methods of the Proposed method to determination of Complex

Parameter	Complex (cefixime-Cu) by UV-VIS Method	Complex (cefixime-Cu FAAS Method
Concentration rang (µg ml-1)	(10-130 µg mL-1)	(5- 60 µg mL-1)
Regression equation	y =0.0076x +0.0553	y = 0.0052x + 0.0438
Correlation coefficient(r)	0.9988	0.9990
Correlation coefficient (r2)	0.9977	0.9982
Variation coefficient (%)	99.77	99.82
Limit of Detection (µg ml-1)	1.6906	0.6081
Limit of Quantitation(µg ml-1)	5.6355	2.0271
Slope (m)	0.0076	0.0052
Intercept (C)	0.0553	0.0438

The proposed method was compared successfully with other literature methods and demonstrates which is thedevelopment of an excellent spectrophotometric methodfor the determination of cefixime drug , rapid, precise, high selectivity, and sensitive than other spectroscopic methods in the literature for the complex product of cefixime as shown in table (17). This method was successfully applied on pharmaceutical samples.

Table 17: Comparison of Cefixime determination in proposed method and other literature methods

Analytical Me	Linear µg.mL-1	λmax	LOD/ µg.mL	Ref
UV-Vis Spectrometric	4-24	352	0.32	17
UV-Vis Spectrometric	8-16	283	1.91	18
	8-16	303	0.001105	
Present meth	10-130	827	1.6906	
	5-85	324	0.6081	

IV. CONCLUSIONS

The proposed method is simple, sensitive and free from drastic experimental conditions such as heating. It is also accurate, precise enough to be successfully adopted as an alternative to the existing spectrophotometric methods and evaluation of cefixime in an metal Using CPE and in pharmaceutical Preparation samples determination Cu (II) in some Pharmaceuticals ,the method gives a very low limit of detection and green chemistry

Reference

1. Nishant .AD , Uttam. PS , Rupak. KR , Singh .GN. Selection of appropriate analytical tools to determine the potency and bioactivity of antibiotics and antibiotic resistance, Journal of Pharmaceutical Analysis 6(2016)207–213
2. Elham. G , Behnaz. R , Samaneh. A , Alireza .V , Vahid R . Optimization of CefiximeNanosuspension to Improve Drug Dissolution,21 (2015) 136-144

3. Abdul AR , Hasna ML , Marw AD . UV-VIS spectrophotometric study for determination of cefixime in pure from and in pharmaceuticals through complexation with Cu (II) using acetat – NaOH buffer in water :methanol . International Journal of Pharmacy and Pharmaceutical Sciences. ISSN- 0975-1491. Vol 5, Issue 1, 2013.
4. Suddhasattya D , Prasanna KP , Upadhayay1 UM., Shreya S , Kuntal G . UV Spectrophotometric Determination of Cefixime in Bulk and its Dosage FormJournal of Pharmacy Research 2012,5(12),5419-5422.
5. Saadiyah AD , Sana RB :,. Cloud point extraction spectrophotometric determination of nickel, copper, cobalt and chromiumby 4- HBDA1, 5DPHPas reagent in wastewater of Iraq , ESAIJ, 10(4), 2015 [150-160].
6. Meng F , Chen X , Zeng Y . Sensitive liquid chromatography- tandem mass spectrometry method for the determination of cefixime in human plasma: application to a pharmacokinetic study, J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 819 (2005) 277–282.
7. Raj K A , Yada D , Yada D . Determination of cefiximetrihydrate and cefuroxime axetil in bulk drug and pharmaceutical dosage forms by HPLC, Int. J. ChemTech. Res. 2 (2010) 334–336.
8. Zendelovska D , Stafilov T , Milosevski P. High-performance liquid chromatographic method for determination of cefixime and cefotaximeinhuman plasma ,Bull. Chem. Technol. Macedonia 22 (2003)39–45.
9. Adam E H , Saeed A E ., Barakat I E. Development and validation of a high performance liquid chromatography method for determination of cefiximetrihydrate and its degraded pro- ducts formed under stress condition of UV light, Int. J. Pharm. Sci. Res. 3 (2012) 469–473.
10. Kathiresan K , Murugan R , Hameed M S . Analytical method development and validation of cefixime and dicloxacillin tablets by RP-HPLC, Rasayan J. Chem. 2 (2009) 588–592.
11. Deshpandea M M , Kastureb V S , Gosavib S A. Application of HPLC and HPTLC for the simultaneous determination of cefiximetrihydrate and ambroxol hydrochloride in pharmaceu- tical dosage form, Eurasian J. Anal. Chem. 5 (2010) 227–238.
12. Khandagle K S , Gandhi S V , Deshpande P B. High performance thin layer chromatographic determination of cefixime and ofloxacin in combined tablet dosage form, J. Chem. Pharm. Res. 2 (2010) 92–96.
13. Shah V , Raj H . Development and validation of derivative spectroscopic method for simultaneous estimation of cefiximetrihydrate and azithromycin dihydrate in combined dosage form, Int. J. Pharm. Sci. Res. 3 (2012) 1753–1760.
14. Jain R , Gupta VK , Jadon N , Voltammetric determination of cefixime in pharmaceuticals and biological fluids, Anal. Biochem. 407 (2010) 79–88.
15. Raj KA , Determination of cefiximetrihydrate and cefuroxime axetil in bulk drug and pharmaceutical dosage forms by electro- phoretic method, Int. J. Chem Tech. Res. 2 (2010) 337–340.
16. Saadiyah AD , Sana RB .Cloud Point Extraction Spectrophotometric Determination Of Copper ,Chromium and Cobalt by Salen as Reagent in wastewater of Iraq., Asian Journal of Chemistry, 26(24) (2014).

17. -Azmi SNH, Iqbal B, Mamari JK Al, Hattali KA Al, Hadhrami WN Al. Method Development and Validation for the Determination of Cefixime in Pure and Commercial Dosage Forms by Specrophotometry. Int J Chem Nucl Metall Mater Eng. 2014;8(6):561–7
18. Dey S. UV Spectrophotometric Determination of Cefixime in Bulk and its Dosage Form. J Pharm Res. 2012;5(12):5419–22.