View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Directory of Open Access Journals

Spectrophotometric Determination of Cefixime Following Simple Diazotization and Coupling with α-Naphthol

Samar A. Darweesh*,1

*Department of Chemistry, College of Education for Pure Science- Ibn Al-Haitham ,University of Baghdad,Baghdad,Iraq.

Abstract

Cefixime (CFX) was treated with sodium nitrite and hydrochloric acid for diazotization reaction followed by coupling with α-Naphthol in alkaline medium to form, a yellow colored azo dye compound which exhibits maximum absorption (λ_{max}) at 412 nm where the concentration of (CFX) was determined spectrophotometrically. The optimum reaction conditions and other analytical parameters were evaluated. Beer's law was obeyed in the concentration range of (1-20) µg.mL^{-1} with a molar absorptivity of 34870.5 L.mol^{-1}.cm^{-1}. The limit of detection was found to be 0.1090 µg.mL^{-1} and the Sandell's sensitivity value was 0.0130 µg.cm^{-2}. The proposed method could be successfully applied to the determination of (CFX) in pharmaceutical formulations.

Keywords: Spectrophotometric determination, Cefixime, Diazotization reaction, α-Naphthol, Coupling reaction.

التقدير الطيفي للسفكسيم بالأعتماد على الازوتة البسيطة والأقتران مع الفا نافثول

سمر احمد درويش *١

*قسم الكيمياء ، كلية التربية ابن الهيثم للعلوم الصرفة ، جامعة بغداد ، بغداد ، العراق .

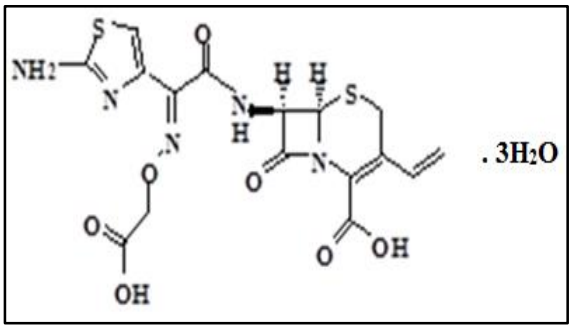
الخلاصة

عومل عقارالسفكسيم (CFX) مع نتريت الصوديوم وحامض الهيدروكلوريك لأزوتته ثم تبع ذلك اجراء تفاعل اقترانه مع الفا نافثول في وسط قلوي لتكوين صبغة الأزو ذات اللون الأصفر التي تظهر أعظم امتصاص (λ_{max}) عند٤١٢ نانوميتر ومن ثم تم تقديرتركيزالسفكسيم طيفياً. وقد تم تعيين الظروف الفضلى التي تؤثر على التفاعل والعوامل التحليلية الأخرى. تم التجاوب مع قانون بير على مدى من التراكيز الذي يتراوح بين (١-٢٠) مايكروغرام/مل وكانت قيمة معامل الامتصاص المولي مساوية لـ ٣٤٨٧,٥ لتر/مول/سم وكان حد الكشف يساوي ٠,١٠٩٠ مايكروغرام/مل ومعامل ساندل يساوي ٠,٠١٣٠ مايكروغرام/سم٢. لقد أمكن تطبيق الطريقة المقترحة بنجاح لتقدير السفكسيم في المستحضرات الصيدلانية.

الكلمات المفتاحية: التقدير الطيفي، سفكسيم ، تفاعل الأزوتة، الفا نافثول ، تفاعل الأقتران.

Introduction

Cefixime is a semisynthetic, cephalosporin antibacterial for oral administration (Scheme 1).



Scheme (1): The chemical structure of cefixime.

Chemically it is (6R,7R)-7-{(2-(2-Amino-1,3-thiazol-4-yl)-2-(Carboxy-methoxyimino)acetyl) amino } – 3 – ethenyl – 8 – oxo – 5 – thia – 1 - azabicyclo(4 . 2 . 0) oct – 2 – ene – 2 - carboxylic acid trihydrate. It is chemical formula is ($C_{16}H_{15}N_5O_7S_2$. $3H_2O$) and with molecular weight of (507.50) as the trihydrate. Its under the category of ß-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. It is helpful in acute urinary tract infections, biliary tract infections, sinusitis, acute otitis media, peptic ulcer and many more [1]. cefixime has been determined by the development of several analytical techniques such as flow injection analysis [2], HPLC [3-5], potentiometric method [6], voltametric method [7], spectrophotometric method [8-12].

[1]Corresponding author E-mail: s_a_1981@yahoo.com
Received: 1/6/2016
Accepted: 4/1/2017

The present study describes the use of α-naphthol as a chromogenic reagent in the development of simple, sensitive and a rapid spectrophotometric method for the estimation of CFX with reasonable precision, accuracy.

Experimental

Instruments

The absorption spectra and all spectrophotometric measurements were carried out on a double - beam (shimadzu 1800) spectrophotometer with 1cm matched quartz cells.

Materials and reagents

Pharmaceutical grade cefixime trihydrate received as a gift powder sample with a purity of pure form (99.99%) from The State Company for Drug Industries and Medical Appliances Samara-Iraq (SDI). All chemicals and reagents used were of analytical grade. Cefixime (400 mg capsules or 200 mg film coated tablets were purchased under the brand names (Suprax-caps-Al-Hikma-Jordon and Samaxim-S.D.I-Iraq) from the Iraqi pharmaceutical market.

Preparation of solutions

1- Sodium nitrite (1 % (wt/v)): was prepared by dissolving 1 g of $NaNO_2$ in 100 ml distilled water.

2- Hydrochloric acid (1 M): was prepared by taken 8.6 ml of concentrated HCl and diluted to 100 ml with distilled water.

3- Sulfamic acid (0.5 % (wt/v)): was prepared by dissolving 0.5 g of sulfamic acid in 100 ml of distilled water.

4- Sodium hydroxide (6 M): was prepared by dissolving 24 g of NaOH in 100 ml of distilled water.

5- α-Naphthol (2 % (wt/v)): was prepared by dissolving 2 g of α-Naphthol in l00 ml of 4 M NaOH.

Standard drug preparation (100 µg.ml^{-1})

Standard solution of CFX was prepared by dissolving accurately weighted amount of the pure drug equivalent to 10 mg in 1ml of concentrated HCl and further diluted to 100 ml with distilled water.

Preparation of drug solutions

Ten capsules of cefixime were weighed, and an accurately weighted portion of the powder equivalent to 200 and 400 mg of cefixime were dissolved in a 5 mL of concentrated HCl and mixed well and then filtered by using Whatman filter paper No.41. Then the volume was diluted to 100 ml with distilled water and analyzed as given under the assay procedures for bulk samples.

Procedure for assembling the calibration curve

To aliquots of the standard solution (l00 µg.mL^{-1}) containing (5-150 µg) of CFX were transferred into a series of 5 mL volumetric flasks and cooled in an ice bath, and then 0.5 mL of 0.5 % (w/v) sodium nitrite solution and 0.5 mL of 0.3 M HCl were added. Each solution was shaken thoroughly and left to stand for 2 min., then 1.0 mL of 0.1 % (w/v) sulfamic acid was added. The solutions were swirled and the resulting diazotized product was coupled with α-naphthol by the addition of 0.5 mL of 0.8 % (w/v) of this reagent in 1 M sodium hydroxide solution. The mixtures allowed to stand for 2 min., after that they were made up to the mark with distilled water. The absorbance of the yellow colored chomogen was measured at 412 nm against the reagent blank. The constructed calibration curve was used to compute the amount of CFX in the given samples.

Results and discussion

Absorption spectra and reaction scheme

In the method developed the presence of the aromatic amino group in cefixime, enable the use of diazotization of the drug with nitrous acid and coupling the resulting diazonium salt with α-naphthol to form colored azo-dye with a maximum absorption at 412 nm. The absorption spectra of the above dye are presented in Figure 1.

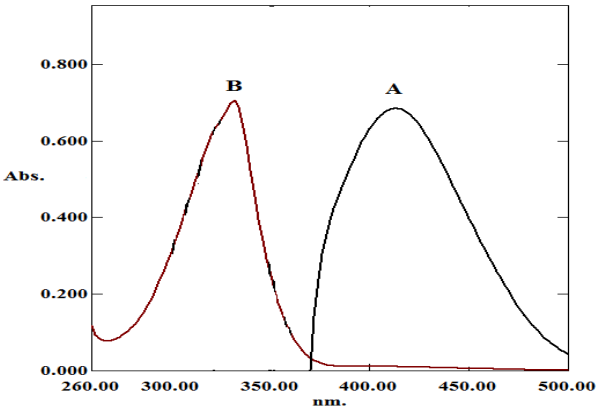
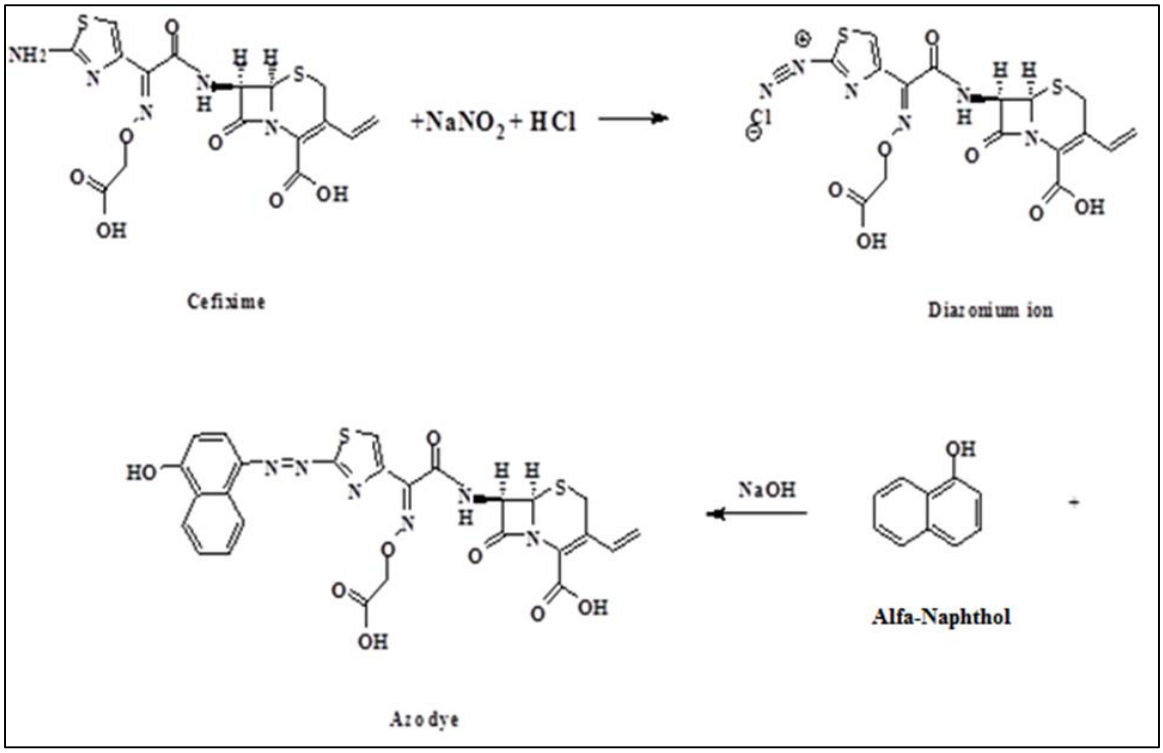


Figure (1): Absorption spectrum of (A) complex against (B) reagent blank solution.

Two steps are involved in the reaction that produces the colored dye. In the first step, cefixime is treated with nitrite solution in hydrochloric acid medium, undergoes diazotization to give diazonium ion. In the second step, the diazonium ion is coupled with the coupling agent α-naphthol, to form yellow colored azo-dye in an alkaline medium. The proposed chemical reactions are shown in Scheme 2.



Scheme (2): The suggested reaction mechanism for diazotization and reaction between cefixime and α-naphthol.

Optimization of reaction variables

Effect of sodium nitrite

The effect of adding various amounts of sodium nitrite solution on absorbance of 10 µg mL^{-1} cefixime was examined. The concentration of sodium nitrite was varied between 0.5 mL of (0.1-1%) sodium nitrite in water. The results showed that 0.5 mL of 0.5% sodium nitrite gave maximum absorbance (Figure 2). Below and above this concentration the absorbance was slightly decreased.

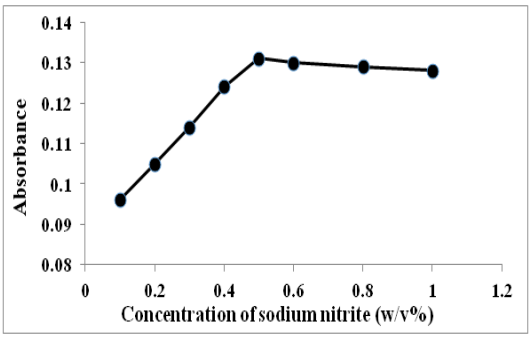


Figure (2): Effect of sodium nitrite concentration.

Effect of hydrochloric acid

Diazotization was carried out at 0-5 ˚C. The hydrochloric acid concentration was studied between (0.1-1.0) M and 0.3 M hydrochloric acid concentration was fixed for getting a stable diazonium ion, (Figure 3).

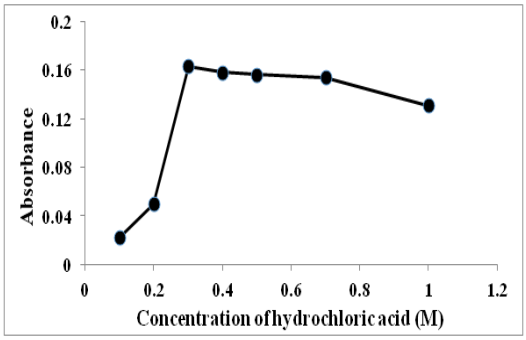


Figure (3): Effect of hydrochloric acid concentration.

Effect of diazotization reaction time

The optimum time for the diazotization of cefixime were established at 0-5 °C and 2 minutes, where longer times led to extremely low absorbance values. This implies that long time destroy the diazotized product as shown in Figure 4.

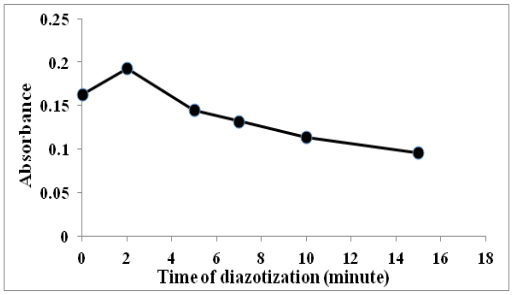


Figure (4): Effect of diazotization time.

Effect of sulfamic acid concentration

The excess of nitrite could be removed by the addition of 1 mL of 0.1% sulfamic acid. An excess of sulfamic acid decrease the color intensity of product, (Figure 5).

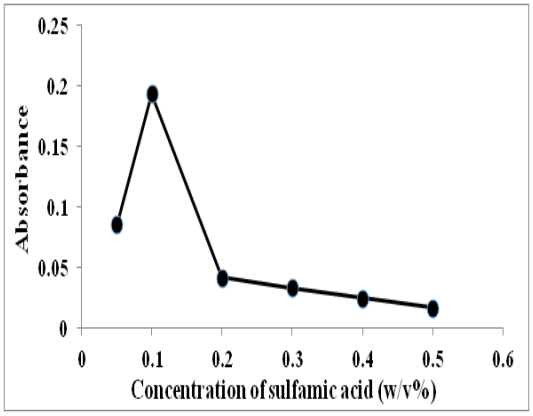


Figure (5): Effect of sulfamic acid concentration.

Effect of α-naphthol concentration

To optimize the concentration of coupling agent, 0.5 mL of different amounts (0.1-2%) α-naphthol were added to the mixture under study. It was found that 0.8% of α-naphthol solution was sufficient for maximum and stable color development. There was a decrease in absorbance at higher concentration of 0.8% α-naphthol, as shown in Figure 6.

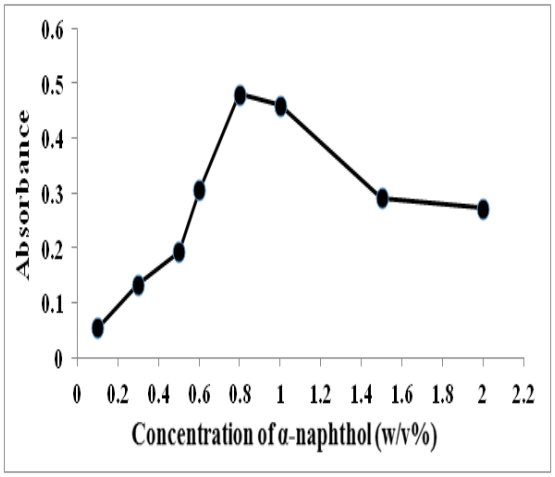


Figure (6): Effect of α-naphthol concentration.

Effect of alkalinity

The optimum concentration of sodium hydroxide leading to a maximum intensity of the azo dye was found to be 1 M. Higher concentrations of alkali may lead to partial decolorization of the dye. Figure 7 illustrates the results of the study.

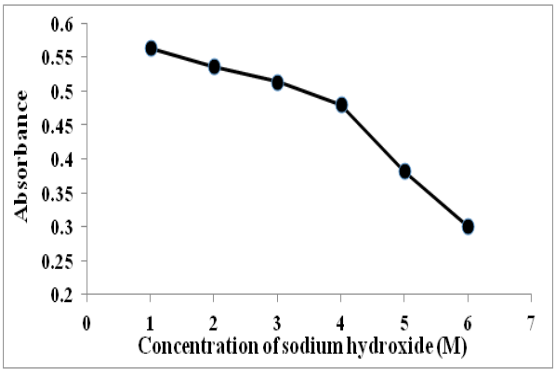


Figure (7): Effect of sodium hydroxide concentration.

Effect of coupling reaction time

It was found that maximum absorbance is attained after 2 min further increase of the reaction time results in a gradual decrease in the absorption intensity, therefore 2 min was chosen as the optimum reaction time, Figure 8.

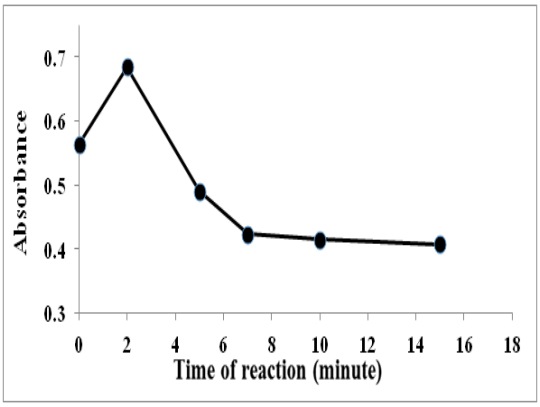


Figure (8): Effect of coupling reaction time.

Stability of the colored product

As shown in Figure 9, a slight decrease is observed upon leaving the colored product, after dilution, for a while of time. Therefore, it is advisable to measure the absorbance immediately after color development.

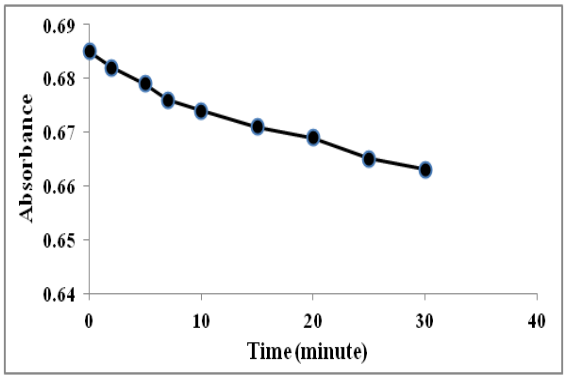


Figure (9): Stability of the colored product.

Calibration curves and analytical data

A calibration curve for cefixime drug was constructed and found to be linear over the concentration range of (1-20) µg.mL^{-1}. Figure 10 shows that the high value of the correlation coefficient for the regression equation, which indicates a good linearity over working concentration range. The statistical treatments of the analytical data are summarized in Table 1.

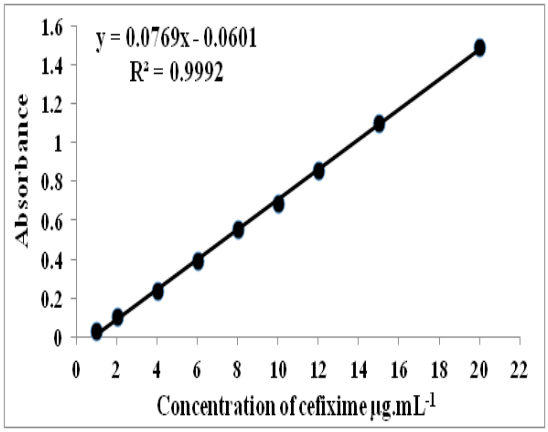


Figure (10): Calibration curve for the determination of cefixime.

Table (1): Optical characteristics and statistical data for the determination of cefixime.

Parameter	Value
λ_{max} (nm)	412
Color	Yellow
Linearity range (µg.ml^{-1})	1-20
Regression equation	A= 0.0769 (CFX. µg.mL-1) - 0.0601
Calibration sensitivity	0.0769
Correlation coefficient (R)	0.9996
Correlation of linearity (R2)	0.9992
Molar absorptivity (L.mol^{-1}.cm $^{-1}$)	34870.5
Sandell's sensitivity (µg.cm^{-2})	0.0130
Detection limit (µg.ml^{-1})	0.1090

Precision and accuracy

Cefixime was determined at four different concentrations in three replicates during the same day. The analytical results found after the investigation are briefed in Table 2 indicated good accuracy with reasonable precision of the proposed method.

Table (2): Accuracy and precision of the proposed method.

Sample	Conc. of CFX (µg.ml^{-1})		Relative Error %	standard deviation	Relative standard deviation %
	Taken	Found*			
Cefixime	5.00	5.10	+2.0	1.8470	0.0942
	10.00	9.86	-1.4	1.0375	0.1023
	15.00	15.15	+1.0	0.7551	0.1144

*****Average of three determinations

Application on pharmaceutical formulations

The suggested method was used for the quantification of cefixime in commercial tablets and capsules. The results, which are demonstrated in table 3, were satisfactory.

Table (3): Application of the proposed method to the cefixime concentration measurements in pharmaceutical formulations.

Sample	Labeled amount of CFX (mg)	*Found amount of CFX (mg)	Recovery %	standard deviation	* Relative standard deviation %
Suprax-caps Al-Hikma Jordon	200	204.92	102.46	0.8673	0.4232
	400	397.53	99.39	0.9542	0.2400
Samaxim S.D.I Iraq	200	198.06	99.03	0.7301	0.3686
	400	396.73	99.18	1.1420	0.2879

*****Average of three determinations.

Conclusions

Diazotization reaction of primary amine group followed by coupling with α-naphthol in alkaline medium was found to be a simple, sensitive, accurate and economic spectrophotometric method for quantitative determination of cefixime in pure form and pharmaceutical formulations. Different variables affecting the completion of the reaction were optimized. The proposed method offers good linearity and precision.

Acknowledgement

Thanks for everyone who helped me to accomplish this research.

References

1. Dey S, Pradhan P K, Upadhayay U M, Shah Sh, Goswami K, UV Spectrophotometric determination of cefixime in bulk and its dosage form. J. of Pharm. Res. 2012; 5(12): 5419-5422.

2. Al-Momani I F, Spectrophotometric determination of selected cephalosporins in drug formulations using flow injection analysis. J. of Pharm. and Biomed. Anal. 2001; 25: 751-757.

3. Bhingea S D, Malipatil Sh M, Development and validation of a stability-indicating method for thesimultaneous estimation of cefixime and dicloxacillin using theRP-HPLC method. J. of Taibah Uni. for Sci. 2016; 248: 1-11.

4. Bhinge S D, Malipatil Sh M, Sonawane L V, Chittapurkar H R, Simultaneous estimation of cefixime and dicloxacillin in bulk and tablet formulation by RP-HPLC method. FABAD J. Pharm. Sci. 2012; 37: 63-71.

5. Raj K A, Yada D, Yada D, Prabu C, Manikantan S, Determination of Cefixime Trihydrate and Cefuroxime Axetil in Bulk Drug and Pharmaceutical Dosage Forms by HPLC. Int. J. of ChemTech. Res. 2010; 2(1): 334-336.

6. Kulapina O I, Makarova N M, Kulapina E G, Potentiometric sensors for the determination of some cephalosporin antibiotics in biological fluids and medicinal preparations. J. of Ana. Chem. 2015; 70: 477-484.

7. Golcu A, Dogan B, Ozkan S A, Anodic voltammetric behavior and determination of cefixime in pharmaceutical dosage forms and biological fluids. Talanta 2005; 67: 703-712.

8. Ramadan A, Mandil H, Dahhan M, 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. Int. J. of Pharm. and Pharm. Sci. 2013; 5:428-433.

9. Ramadan A, Mandil H, Dahhan M, Novel formation three complexes of cefixime-copper using acetate–acetic acid buffer and determination of cefixime in pure and pharmaceutical dosage forms. Int. J. of Pharm. and Pharm. Sci. 2013; 5: 469-477.

10. Keskar M R and Jugade R M, Spectrophotometric determination of cefixime trihydrate in pharmaceutical formulations based on ion-pair reaction with bromophenol blue. Ana. Chem. Insig. 2015; 10: 11-16.

11. Ahmad N R, Spectrophotometric determination of cefixime through schiff's base system using vanillin reagents inpharmaceutical preparations. Iraqi Nat. J. of Chem. 2013; 49: 38-46.