ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

New Spectrophotometric Determination Cefdinir Coupling with Bisphenol A via Various Analytical Methods

Nisreen Kais Abood[1], Mohammed Jasim M Hassan[1], Muneer. A. Al-Daamy[2]

1. *Department of Chemistry, College of Science, Mustansiriyah University, Baghdad, Iraq.*
2. *Department of Chemistry, College of Education for pure Science, Kerbala University, Kerbala Iraq.*

Abstract

A new three spectrophotometric methods are developed for determination of cefdinir. The first method including conversion the of amine functional group in cefdinir to diazonium ion followed by reaction with reagent Bisphenol A in alkaline medium. Produced azo dye has a Reddish- Orange with absorption intensity at λ_{max} 495 nm. The concentration ranges 1-50 µg/ mL, Beer's law is obeyed, correlation coefficient was 0.9996, molar absorptivity was 0.613×10^4L.mol^{-1}.cm^{-1} and the detection limit was 0.194 µg/mL. The Second method was cloud point extraction (CPE) of a trace amount in aqueous solution that product of diazotization followed by measuring with a UV-visible spectrophotometer at λ_{max} 505, purple color. The concentration range obeyed the Beer's law was 0.25-6 µg / mL, correlation coefficient was 0.9995, molar absorptivity was 0.727×10^5L.mol^{-1}.cm^{-1}, detection limit was 0.036 µg/mL, Pre-concentration factor was 25 and Distribution coefficient(D) was 394.13. Flow injection analysis third methods it is simple for setimation the cefdinir based on the measurement of absorption signal for product resulting from diazotization, all experimental parameters chemical and physical were studied to development and stability the colored of product. Flow injection of 1.5mL/min was pumped and active material was detecting at λ_{max} 495nm. In this the proposed methods were successfully, applied to the estimation Cefdinir in pharmaceutical formulation. The three opposed methods have been applied successfully to the Cefdinir drug in the pharmaceutical formulation.

Keywords: *Cefdinir, Diazotization, Cloud point extraction, Bisphenol A, Flow Injection Analysis.*

Introduction

Cefdinir (CFD) is an antibiotic fitting to the third-generation broad spectrum of the family Cephalosporin, which matches to the beta-lactam class and has the molecular formula $C_{14}H_{13}N_5O_5S_2$ and its molecular weight 395.416 g/mol, a partial -artificial antibiotic, its scientific name under IUPAC is: (6R,7R)-7-[[(2Z)-(2-Amino-4-thiazolyl) (hydroxyimino) acetyl] amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid [1] (Fig. 1).

As with other cephalosporin's, bactericidal activity of CFD results from the inhibition of cell wall synthesis [2].Greatly effective versus many grams positive and gram negative bacteria and established effective for common bacterial infections of the ear, sinus, throat and skin and it is utilized to treat otitis media, delicate tissue diseases, and respiratory tract contaminations, including sinusitis [3, 4].In the literature. the CFD has been analyzed in numerous methods, including RP-HPLC [5, 6], spectrophotometric [7, 8], voltammetry [9], spectrofluorometric [10], LC–MS/MS[2], and colorimetric[11].In this research, the proposed method was based on the reaction of (azo-coupling), where the drug containing the amine group was diazotized in acidic medium and then coupled with the reagent in an alkaline medium to form a Reddish - Orange -colored product (azo dye) and Automation with FIA.

The CFD will be studied in the visible spectrophotometric method using the UV-visible spectrophotometer. In aqueous solutions for the surfactant micellar systems, the temperature at which the solution becomes turbid before separation into two phases (a surfactant-rich phase and an aqueous phase) known as the cloud point [12, 13].The CPE method has generated widespread interest as an alternative to conventional extraction [14, 15].

As for the trace concentrations, they can be measured by pre-concentration through cloud point extraction and using a non-ionic surfactant (Triton X-114) and a cationic surfactant (CTAB) to increase the size of the surfactant-rich phase and increase the enrichment factor [16].

These methods have several advantages including low cost, sensitivity, accuracy, rapidity, Low toxicity and less dangerous and simplicity of procedure. Have been applied to pharmaceuticals and have proven successful in estimating the effective ingredient [17].

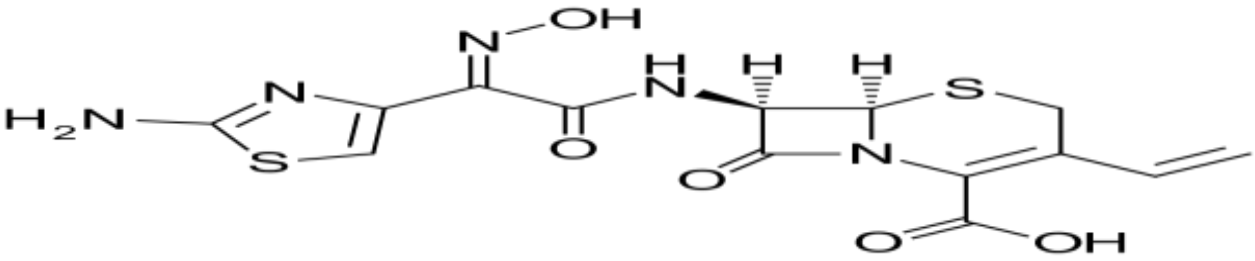

Fig.1: Structure of Cefdinir

Experimental

Instrumentation

A spectral and absorbance measurement were carried out in single beam UV. Visible spectrophotometer 160. Equipped with 1cm and 0.5 cm quarts' cell. An Ultrasonic and thermostatic water bath from Elma Hans Schmidbauer Gmbh and Co.KG coupled with Extraction of samples. Atomation Flow injection configuration a three channel manifold Fig.2, was employed for (FIA). Peristaltic pump (ALITEA, C4, made in Sweden) with polyvinyl chloride tube (0.8) mm internal diameter.

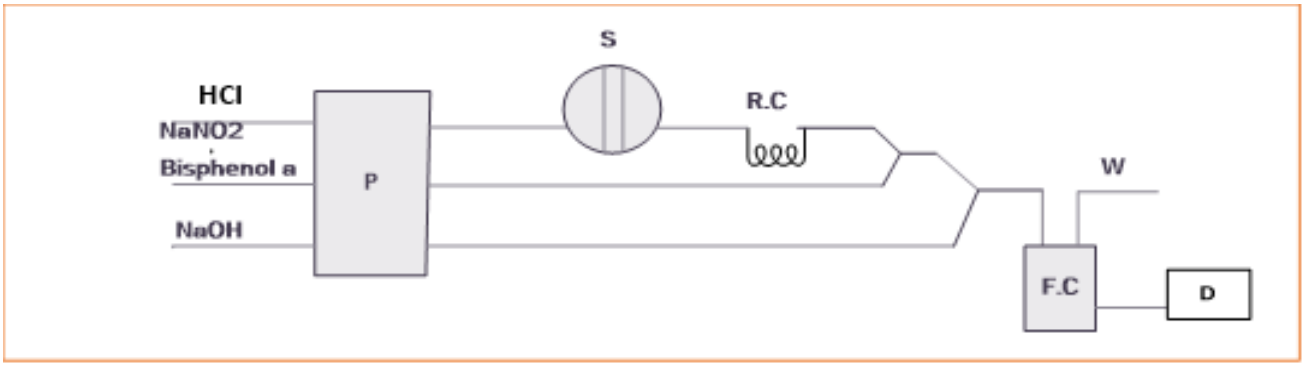

Fig. 2: Scheme of employed flow system, P: peristaltic pump, R.C: reaction coil, S: sample injection, W: waste, FC: flow cell

Chemicals and Reagents

All chemicals were analytical quality and were bought from Merck Ltd. (Jordan). However, cefdinir was purchased from the quality control laboratory (the general company for the manufacture of medicines and medical supplies - Samarra).

Preparation of Standard Solution

Reagents

All Chemicals were analytical grade. stock solutions (1000 $\mu g.m^{-1}$) Cefdinir was prepared by dissolving 0.1 mg of Cefdinir(CFD) in distilled water and dilution to the mark in 100ml volumetric flask. Stock solution of Bis phenol A (1000 µg/mL) was prepared by dissolving 0.1 mg of 2-aminothiazole in distilled water and dilution to the mark in 100ml volumetric flask.-preparation 25% NaOH (6.25 M),1%$NaNO_2$ (0.144M), 4% Urea ,10% Triton X-114,0.01M of HTBA (0.3644g in 100 ml in distilled water) and 5% w/v Na_2SO_4.

The Standard Solutions of Pharmaceutical Formulation

Cefdinir Capsules: 10 capsules were accurately weighed from cefdinir for the commercial drugs (sefarin®) and (Azord®) 300 mg each capsule separately, and then the mean weight of the capsule was extracted. Then aliquot amounts of both drugs; Azord® and sefarin were dissolved in distilled water with of 1M NaOH (0.6 ml) and made up to 100 ml, after which the solutions were filtered to move insoluble solute.

General Procedure for Preparing the Calibration Curve for the Diazotization Method

The excellent method was developed to prepared Azo Coupling by adding accurately (1ml 1000µg.ml^{-1}) Cefdinir in 20 ml volumetric flask immersed in ice bath 0-5ºC, add 0.5mLof (1:1) HCl , add gradually 0.5 mL of 1% $NaNO_2$, wait 10 mint for the Cefdinir. Followed by add 1 mL of (1000) µg/mL from Bisphenol A, then add 1.5 mL of 25% NaOH for Cefdinir finally brought to 20 mL with distilled water. The Azo-dye formed the absorbance reddish-orange, colored that gave absorbance at λ_{max} 495 nm against a reagent blank. For Cefdinir.

General Procedure of the Cloud Point Extraction (CPE)

After selecting the best experimental conditions, the calibration curve was prepared from several concentrations ranging from 0.25-6 µg/mL of the azo dye CFD and transferred to 15 mL centrifuge tubes, then 1 ml of Triton X- 114 10% v/v was added followed by addition of 2 mL of 0.01 M (CTAB), 2mL of 5% w/v Na_2SO_4, then distilled water was added to make total solution volume to12.5 mL. The solutions were Solutions were placed under ultrasonic for 2 minutes at room temperature followed by further ultra-sonication at 60 ° C for 50 mint. The resultant solutions were centrifuged for 5 minutes at 4000 rpm, and then cooled in ice bath for 10 minutes to stabilize the micelle layer at the bottom of the centrifuge tube.

The supernatant was removed and 0.5 ml of ethanol was added to dissolve the micelle layer. An absorption measurement was made on the prepared dye at λmax 505 nm against a reagent blank in UV-Vis spectrophotometer (a shift of the absorption peak due to the change of solvent), using a quartz cell (1 cm, 1 mL), blank was similarly prepared and measured.

General Procedure of Flow Injection of CFD

A 100 µl of drugs CFD injected into carrier stream that product by mixing three channel, the first channel used to carrier the (5.99×10^{-3}) M phenyl hydrazine, second channel including carrier acid and sodium nitrite using T-shaped, this reaction was carry out via mixed well in 50 cm reaction coil after that the mixture allow to pass through injector and the result product reacted with a stream of 1.5 M NaOH and the absorbance of the resulting Reddish-Orange measured at λmax 495nm.

Results and Discussion

Part I. the Diazotization Method

The idea is based on converting the CFD to an azo dye by the diazotization method by coupling with Bisphenol A reagent in an alkaline medium to form a Reddish-Orange with the highest absorption intensity at λmax 495 nm for CFD. The absorption intensity of the dye formed Indicates the concentration of the CFD under the beer's law. Fig. 3 shows the absorption spectra of the resulting azo dye.

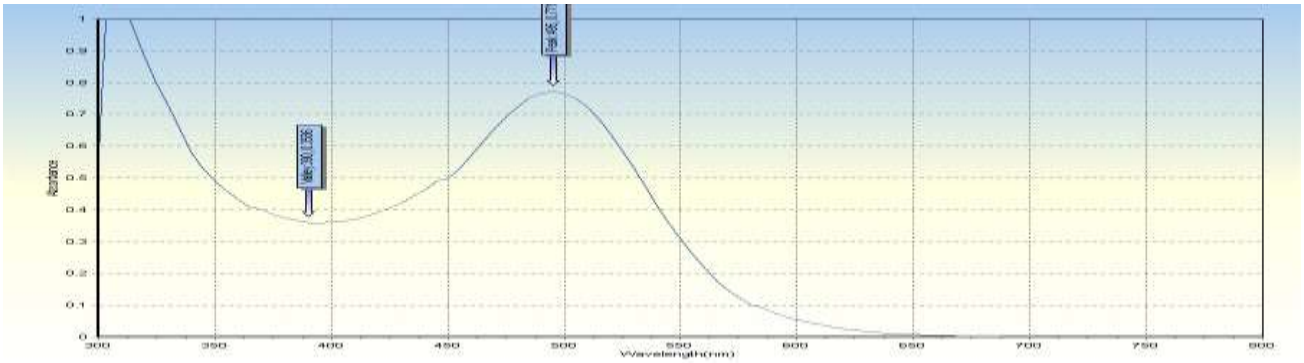

Fig. 3: Absorption spectrum for 50 µg/mL Cfdinir with the reagent against the reagent blank under optimum conditions

Optimization Experimental Conditions

The effect of the different variables on the absorption intensity has been studied to determine the optimum conditions required to determine the CFD concentration in the samples.

The concentration of the CFD studied was 50 µg / mL (1 mL of stock solution). The effect of acid type was studied by several (1:1) dilute acids (HCl, H_2SO_4, HNO_3, CH_3CO_2H) were tested in the process of diazotization, and the highest absorption was observed when HCl was used, as shown in Table 1.

Table 1: Effect type of acids on absorbance

Type of acid	Cefdinir λ max 495 nm
HCl	**0.633**
H_2SO_4	0.521
HNO_3	0.459
CH_3COOH	0.336

Various volumes (0.25-2.5 mL) of HCl were studied in the diazotization process and the highest absorption intensity was reached when using 0.5mL for CFD because the diazotization process was done in alkaline medium and the increase in amount of acid used, reduced absorption as shown in Figure 4. The effect of the amount of $NaNO_2$ was studied by varying the volumes of (0.144M (1% w/v) $NaNO_2$) used from 0.5-2.5ml in the diazotization process and it was found that 0.5 mL gave the best absorption intensity as shown in Fig 5.

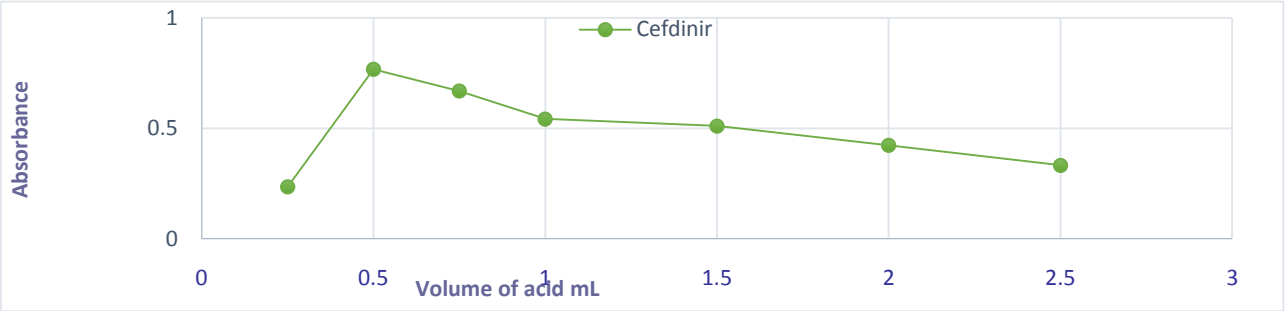

Fig.4: Effect volume of acid

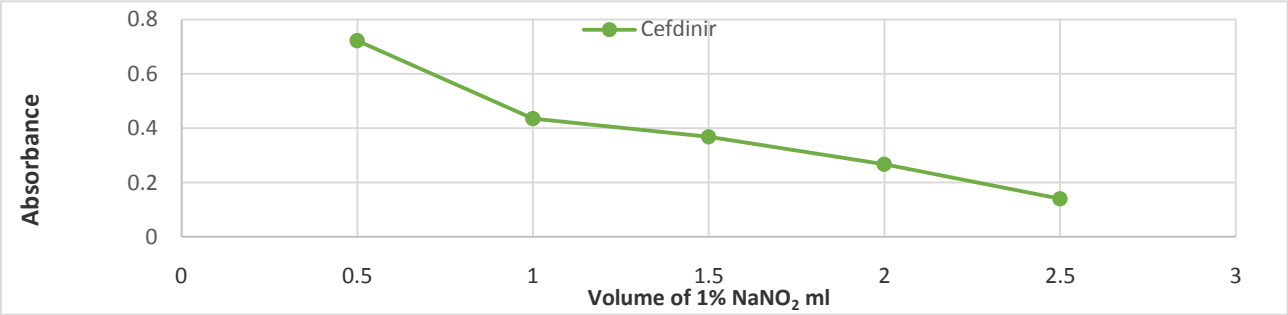

Fig. 5: Effect volume of NaNO2

The waiting time effect was studied by using different range of times (0-40) min, the time required to complete the interaction diazotization for the drugs was 10 min for the Cefdinir. Best waiting time that give the highest absorbance intensity at the λ_{max} 495 nm. Show in Fig. 6 this waiting time is therefore used in subsequent studies. Nitrite acid is also formed due to excess amount of sodium nitrite which leads to side reactions.

The alkali medium type has an important effect on the absorption intensity. The effect of four types of base (KOH, NaOH, Na_2CO_3 and NH_4OH) was studied. It was found that NaOH gives the highest absorption intensity in this reaction. Therefore, the effect of different volumes of 6.25 M NaOH (0.5-3.5 mL) was studied. The addition of 1.5 mL was the best volume to obtain the highest absorption intensity as shown in Fig.7.

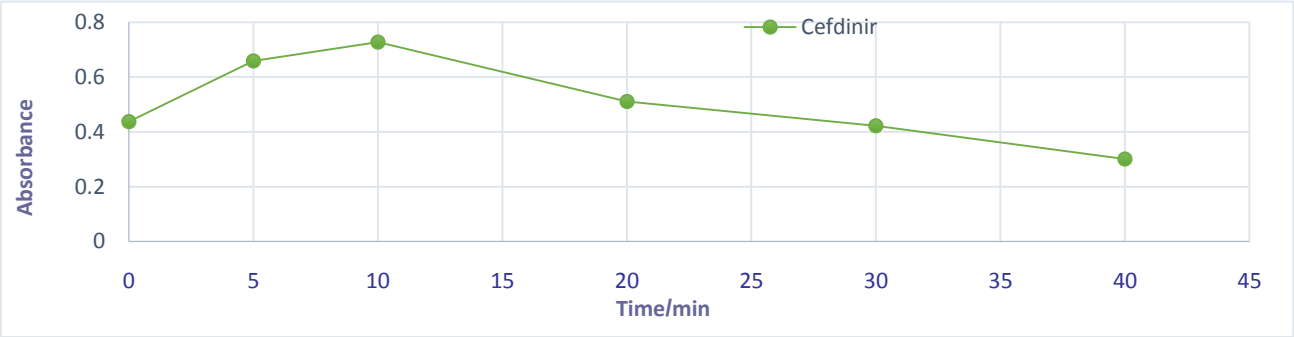

Fig. 6: Effect time/min

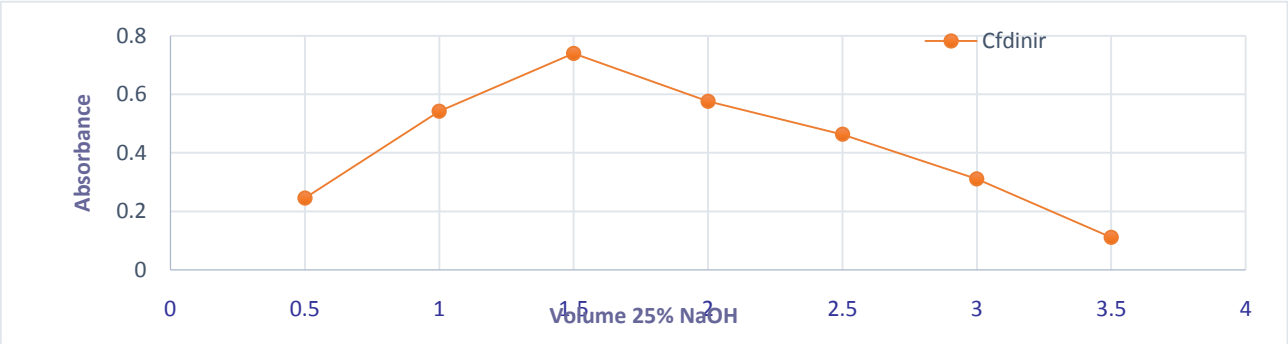

Fig.7: Effect volume of NaOH

Study the Effect of the Reagent Volume and the Nature of the Colored Pigment

The Bisphenol A reagent solution was prepared at a concentration equal to the CFD concentration. So to ensure the same molar ratio is used between the drug and the reagent. Several volumes (0.2-1.4 mL) of 0.252×10^{-2} M Bisphenol A were studied. The best absorption of 1 mL (50 µg / mL) of the drug was at 1 mL of the reagent. That is, the ratio in the resulting colored dye is (1: 1) as shown in Fig 8.

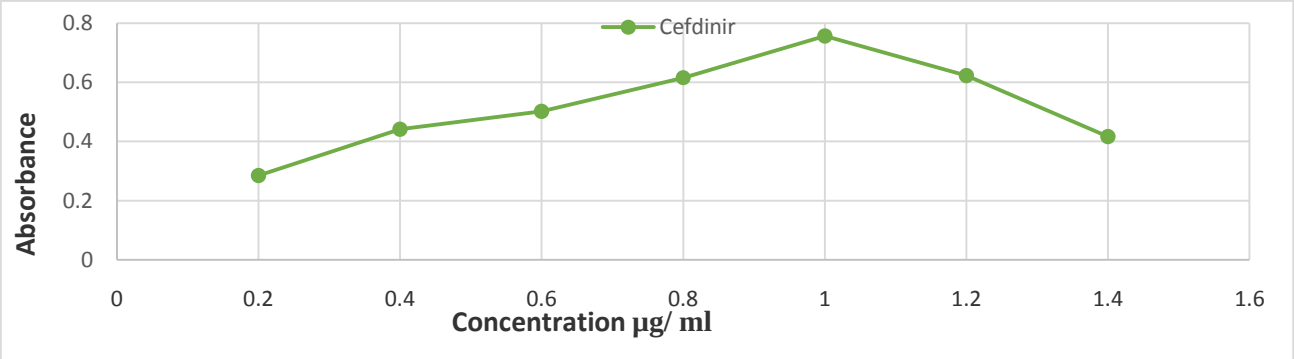

Fig.8: Effect volume of reagent

The effect order of addition on the absorbance of the Diazotization was studied under the optimum experimental conditions, and the results indicated that the best sequence contained the following for the amine drugs Cefdinir and Cefixime the best sequence was (salt+ reagent+ base).The result shown in Table 2.

Table 2: Order addition of amine drug

Order addition	Abs. Cefdinir λ max 495 nm
Salt + reagent+ base	**0.752**
Salt+(reagent +base)	0.721
Salt+ base + reagent	0.326

The Possible Reaction Path May be Written as Follows

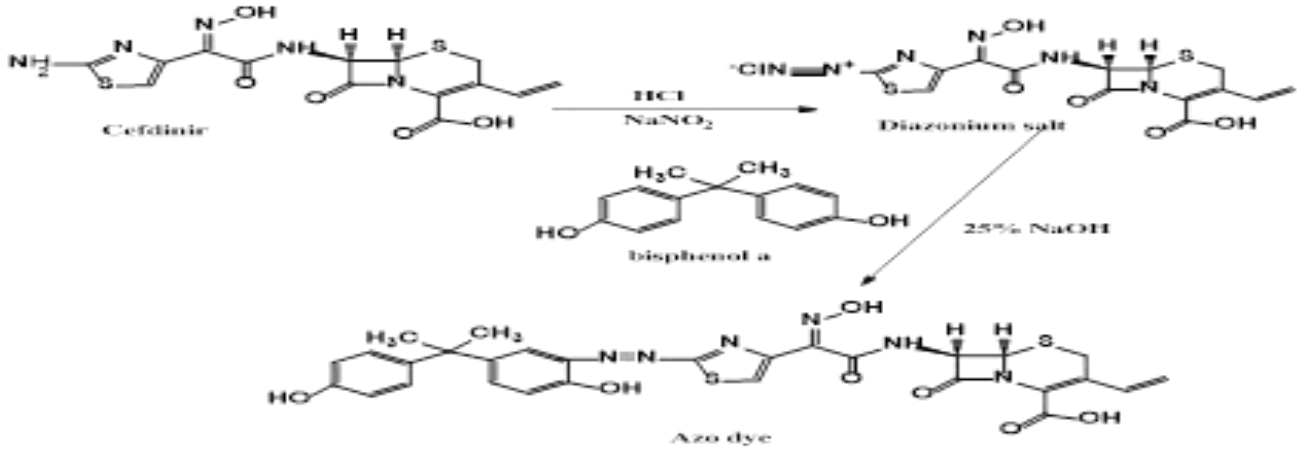

Fig.9: The suggest mechanism of reaction Cefdinir drug with bisphenol A colored step

Analytical Data

Under the optimized conditions, the absorbance of (amine drug increase the linearly as the concentration of amine drugs increase, the calibration graph through the series of standard solution of Cefdinir was conducted and the linearly regression equation, correlation to determination (R), slop (a) and intercept (b).

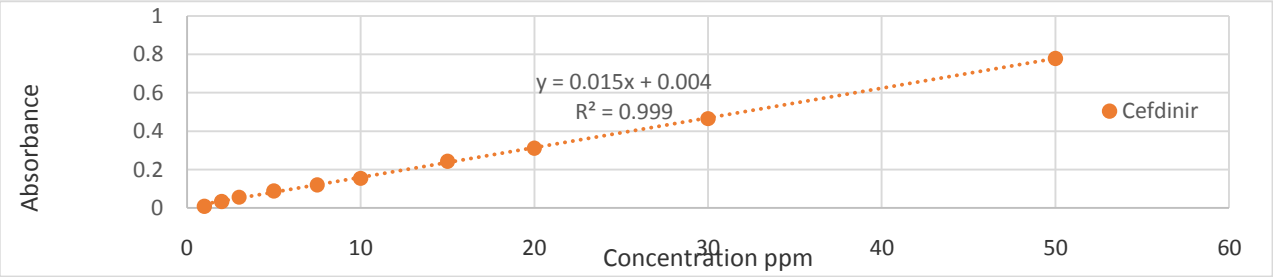

Figure 10: Calibration graph of Cefdinir in diazotization method

Table 3: Characteristic parameter for the regression equation of the proposed diazotization method for Cefdinir

Parameter	Cefdinir
λ max(nm)	495
color	Reddish-Orange
linearity rangeμg/mL	1-50
Molar absorptivity ($L.mol^{-1}\ cm^{-1}$)	0.613×10^4
Sandell's sensitivity μg/cm²	0.064
Correlation coefficient ®	0.9996
Regression equation	Y=0.0155x+0.0041
Slope(b)	0.0155
Intercept(a)	0.0041
Analytical sensitivity μg/mL	0.065
Limit of detection μg/mL	0.194
Limit quantification μg/mL	0.639
C.L. for the slope ($b\pm ts_b$)at 95%	0.0155±0.00104
C.L. for the intercept ($a\pm ts_a$ at 95%	0.0041±0.021384
Standard error for regression line (Sy/x)	0.00605

Accuracy and Precision

The accuracy and precision were studied for the proposed method, under optimum conditions using three different concentrations and measured absorbance at a minimum for five readings per concentration. The accuracy estimated by determination the relative error, percentage and Recovery .Precision estimate determination for the percentage relative standard deviation RSD%, as shown Table 4&5.

Table 4: Data the accuracy and precision of proposed method for estimation of pure samples

Type of Drug	Amount of drugs μg /ml		Relative Error %	Recovery %	Average Recovery%	RSD% (n=5)
	Taken	Found				
Cefdinir	10	9.870	-1.3	98.70	99.52	0.09
	20	19.89	-0.55	99.45		0.18
	30	30.12	0.4	100.4		0.12

Table 5: The accuracy and precision of proposed method for estimation of commercial pharmaceuticals

Type of Drugs	Amount of drugs mg		Relative Error %	Recovery %	Average Recovery %	RSD% (n=5)
	Taken	Found				
Cefdinir (sefarin® capsules300mg/ Product by pharma international Co. Amman-Jordan	300.12		0.04	100.04	99.89	0.06
	300	299.88	-0.04	99.96		0.05
		298.99	-0.34	99.66		0.35
Cefdinir(Azord® capsules300mg/ Product by DAR AL DAWA DEVELOPMENT&NVESTMENT CO.LTD (Na'ur-Jordan)	299.45		-0.18	99.82	99.88	0.94
	300	298.87	-0.38	99.62		0.15
		300.65	0.22	100.22		0.25

Effect of Interferences

We have been studying effect of interference expected present in drug Cfdinir to the proposed method by add 1g from each interference to 50 μg the drugs, then complete addition under the optimum conditions and dilution with distilled water in 20 ml volumetric flask after that measured the absorbance, the results shown in Table 6.

Table 6: Effect of interference compound on pure drug

Interference compound	Recovery %Of Cefdinir
Sucrose	99.88
Lactose	100.32
Maltose	100.21
Fructose	99.78
Sodium Benzoate	100.12
Starch	99.98

Part II. Cloud Point Extraction Method

The trace concentration of the CFD in the azo dye is estimated by the UV-visible spectrophotometer to be inaccurate due to several factors: detector sensitivity, amplitude efficiency and interference. Therefore, the pre-concentration of trace concentrations by cloud-point extraction (CPE) will increase the enrichment factor and eliminate interference effect, thus increasing accuracy in estimation and increasing the detection limit.

Optimal experimental conditions for the CPE. Surfactant concentration is important in determining the value of the pre-concentration factor, so the appropriate surfactant concentration should be selected until the analyte is fully extracted. Several volumes (0.25-2mL) were tested for 10% w/v Triton X-114, and found that 1 mL gave the highest extraction efficiency as shown in Fig 11. To increase the hydrophilic characteristic of the micellar phase, cationic surfactant molecules (CTAB) was added. CTAB was incorporated into the non-ionic micelles and leads to the changing of the surface charge and increasing repulsion between micelles, thus increasing the cloud point. Therefore, the effect of a different volumes (0-3 mL) of (0.01M) CTAB was studied on the extraction efficiency. It was found that 2 mL gave the highest distribution ratio and the highest absorption as shown in Fig.12. The addition of electrolyte with a suitable concentration in an aqueous solution of the surfactant micellar system accelerates phase separation and enhances micellar concentration in the surfactant-rich phase due to the salting-out phenomenon. Therefore, the volume of surfactant-rich phase will decrease due to the addition of salt, leading to an increase in the pre-concentration factor, but the surfactant-rich phase will become more viscous.

For the selection of salt and the appropriate concentration, several electrolytes (KCl, HCl, Na_2SO_4, and CH_3COOH) were studied at a concentration of 5% w / v of each salt and found that 2.5 mL of Na_2SO_4 was the best electrolyte and 2 mL the optimum volume required to obtain the highest extraction efficiency and highest distribution ratio as shown in Fig13.The temperature of the equilibrium and the incubation time have an important role in the efficiency of separation and completion of the reaction. Therefore, different temperatures (25-75) ˚C and several incubation times (30-90 minutes) were studied. At 60°C and 50 mint .At the highest extraction efficiency and absorption signal as shown in Figs.14.

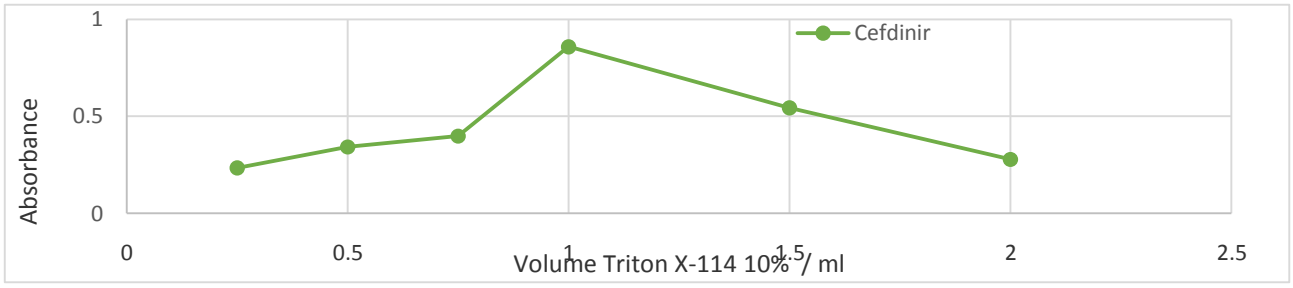

Fig.11: Effect volume of TritonX-114

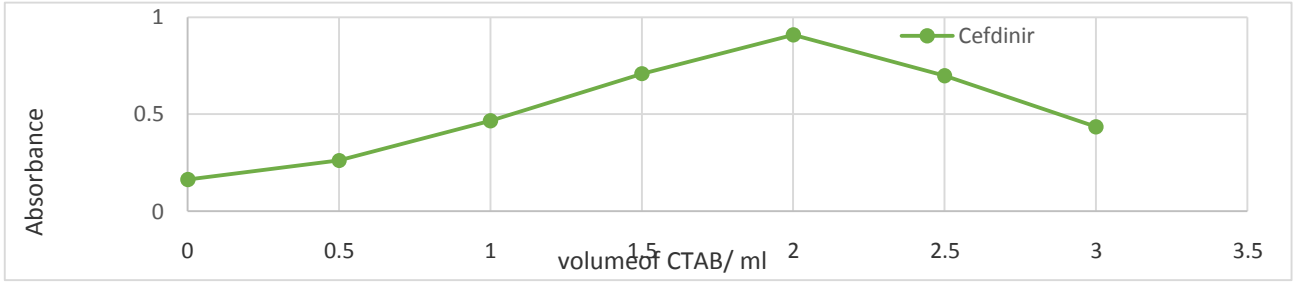

Figure 12: Effect volume of CTAB

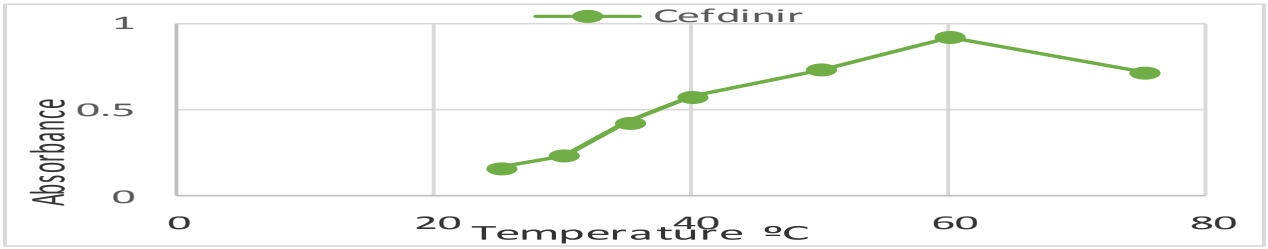

Fig. 13: Effect volume of Na2SO4

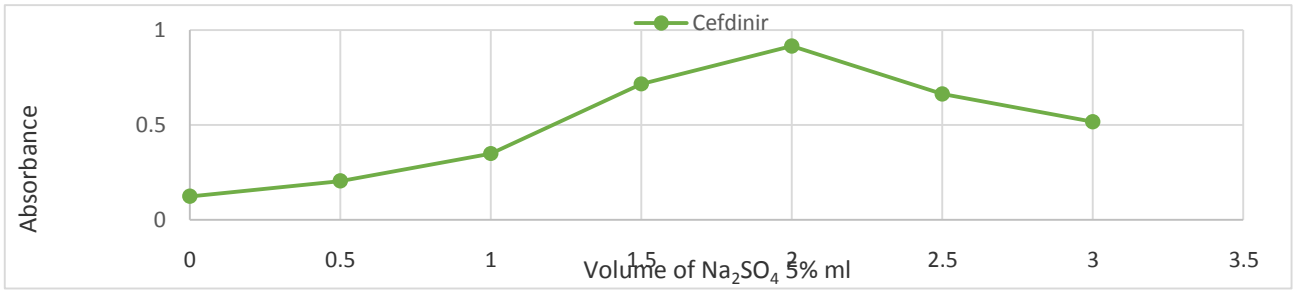

Fig. 14: Effect of temperature

Analytical Data

Under the optimized conditions, the absorbance of (amine drug increase the linearly as the concentration of amine drugs increase, the calibration graph through the series of standard solution of Cefdinir was conducted and the linearly regression equation, correlation to determination (R), slop (a) and intercept (b).Shown Fig.15.

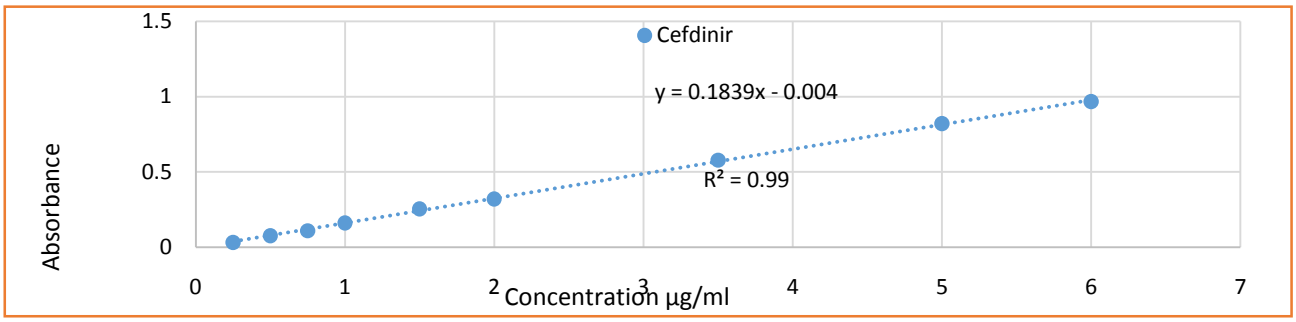

Fig. 15: Calibration graph of Cefdinir by cloud point extraction

Table7: Characteristic parameter for the regression equation of the proposed diazotization method for CFD

Parameter	Cefdinir
λ max(nm)	505
color	Purple
linearity rangeµg/mL	(0.25-6)
Molar absorptivity (L.mol^{-1}.cm^{-1})	0.727×10^5
Sandell's sensitivity (µg/ cm^2)	0.0054
Correlation coefficient r	0.9995
Regression equation	Y=0.1839x-0.004
Slope(b)	0.1839
Intercept(a)	-0.004
Analytical sensitivity µg/mL	0.539
Limit of detection µg/mL	0.036
Limit quantification µg/mL	0.109
Enrichment Factor(EF)	11.86
Pre-concentration factor(PF)	25
Distribution coefficient(D)	394.13
C.L. for the slope(b±ts$_b$)at 95%	0.1839±0.012327
C.L. for the intercept(a±ts$_a$) at 95%	-0.004±0.037072
Standard error for regression line (S$_{y/x}$)	0.010371

Accuracy and Precision

The accuracy and precision were studied for the proposed method, under optimum conditions using three different concentrations and measured absorbance at a minimum for five readings per concentration. The accuracy estimated by determination the relative error, percentage and Recovery .Precision estimate determination for the percentage relative standard deviation RSD%, as shown Table 8&9.

Table 8: Data the accuracy and precision of proposed method for estimation of pure samples

Type of Drugs	Amount of drugs µg /mL		Relative Error %	Recovery%	Average Recovery%	RSD% (n=5)
	Taken	Found				
Cefdinir	2	2.02	1.00	101.0	100.29	0.14
	5	4.96	-0.8	99.2		0.83
	6	6.04	0.66	100.66		0.99

Table 9: The accuracy and precision of proposed method for estimation of commercial pharmaceuticals

Type of Drugs	Amount of drugs gm		Relative Error %	Recovery %	Average Recovery %	RSD% (n=5)
	Taken	Found				
Cefdinir (sefarin® capsules300mg/ Product by pharma international Co. Amman-Jordan	300	298.7	-0.43	99.56	99.86	0.78
		300.3	0.1	100.1		0.92
		299.8	-0.06	99.93		0.52
Cefdinir(Azord® capsules300mg/ Product by DAR AL DAWA DEVELOPMENT&NVESTMENT CO.LTD (Na'ur-Jordan)	300	300.7	0.23	100.23	100.04	1.06
		301.8	0.6	100.6		0.94
		297.9	-0.7	99.3		0.08

The Optimum Reaction Conditions of Flow Injection Analysis Method

An optimization conditions chemical parameters comprising the concentration of reagent, sodium nitrate and sodium hydroxide concentration. Several concentration of Bisphenol A (4.999×10^{-4}-7.99×10^{-3}) M µg/mL, the absorbance increase with increasing the concentration for Bisphenol A up to (5.99×10^{-3}M), later than that with increasing the concentration decreases the absorbance as in Fig. 16. Sundry concentration of acids HCl was applied to obtain the highest absorption on the flow injection for CFD, the concentration of Acids was HCl (0.8) M. The expanse of sodium nitrite has an active role in this reaction use appropriate concentration lead to the speed and completeness of the reaction, the various concentration of $NaNO_2$ was used to find highest concentration for CFD in flow injection, the results shown in Fig. 17.

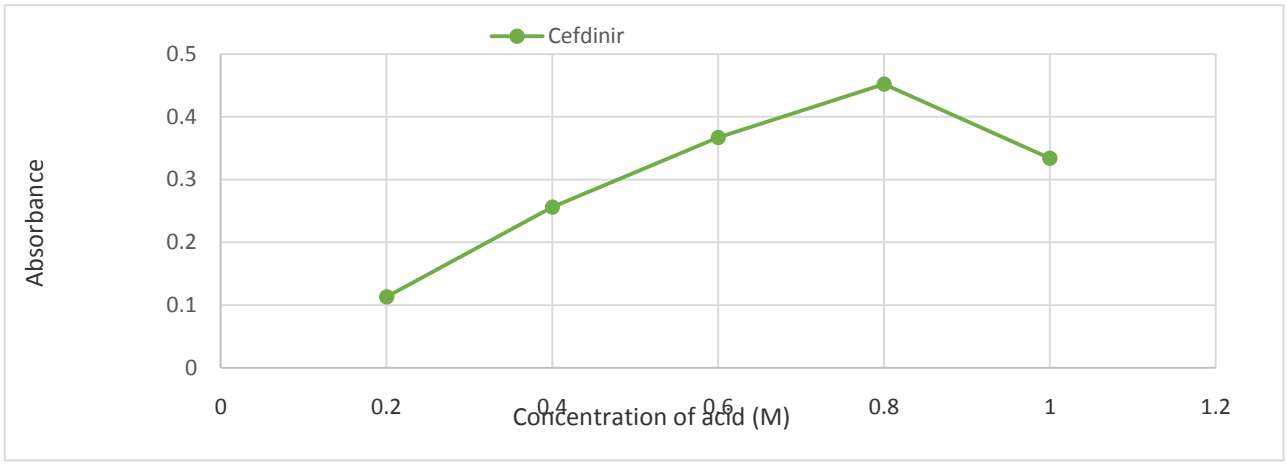

Fig. 16: Effect concentration of reagent

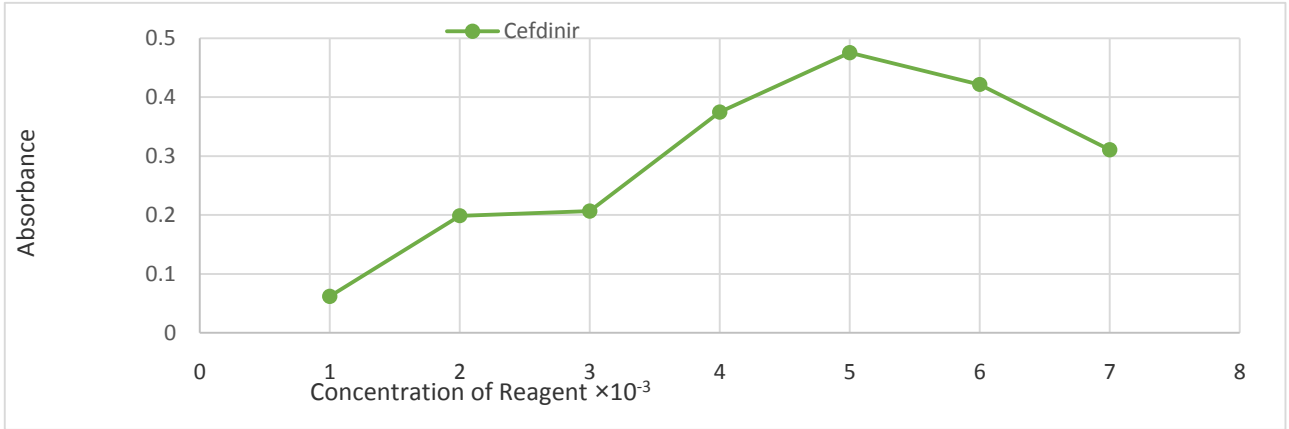

Fig.17: Effect concentration of acid

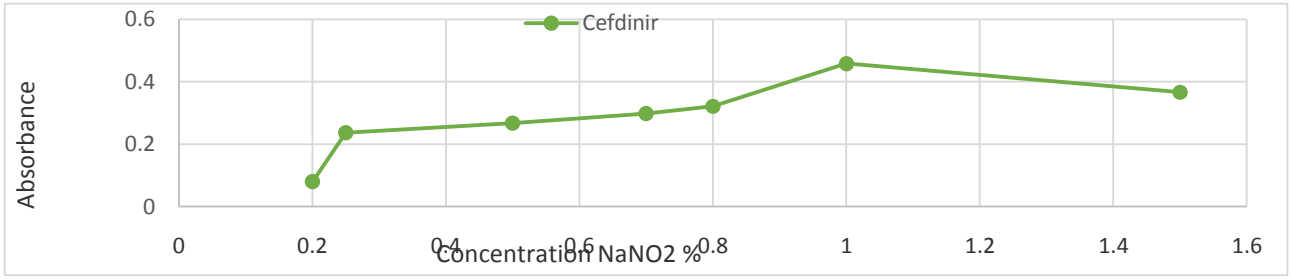

Fig.18: Effect concentration of NaNO2

Study Optimization of Manifold Parameters

Study several physical parameters such as reaction coil, length of the reaction coil range (30-230) cm, 50 cm the was best reaction coil gave high best absorbance at λ_{max} 495nm for CFD Fig.19.The total flow rate (1-5) mL/ min was studied, the flow rate gave highest absorbance was 2.5 mL/ min. and use fixed in all subsequent experiments show the result in Fig.20. The different volume (50-200) µL of the injection sample studied, 100 µl volumes was the best volume that give highest absorbance and was use fixed in all subsequent experiments, the results in Fig.21.

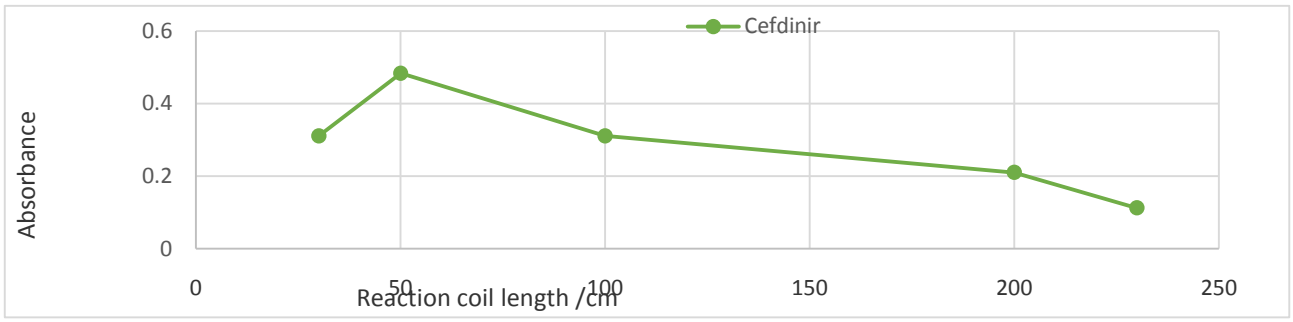

Fig.19: Effect of Length Reaction Coil /cm

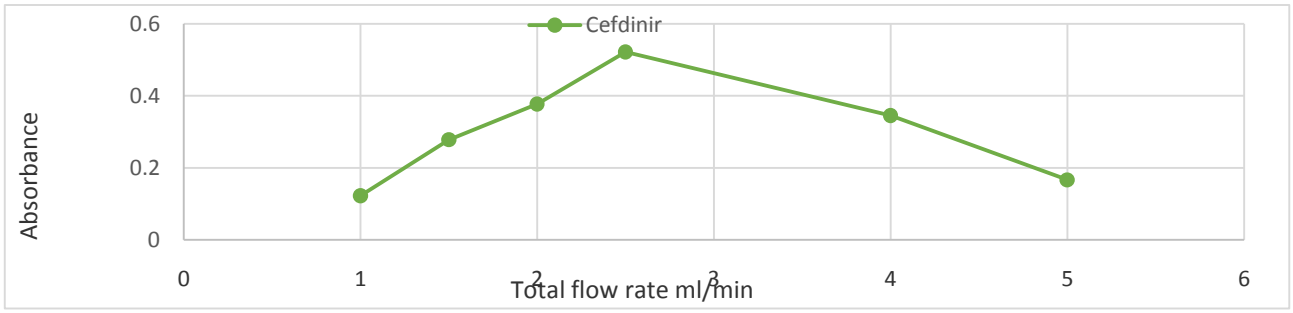

Fig.20: Effect of Total rate mL/min

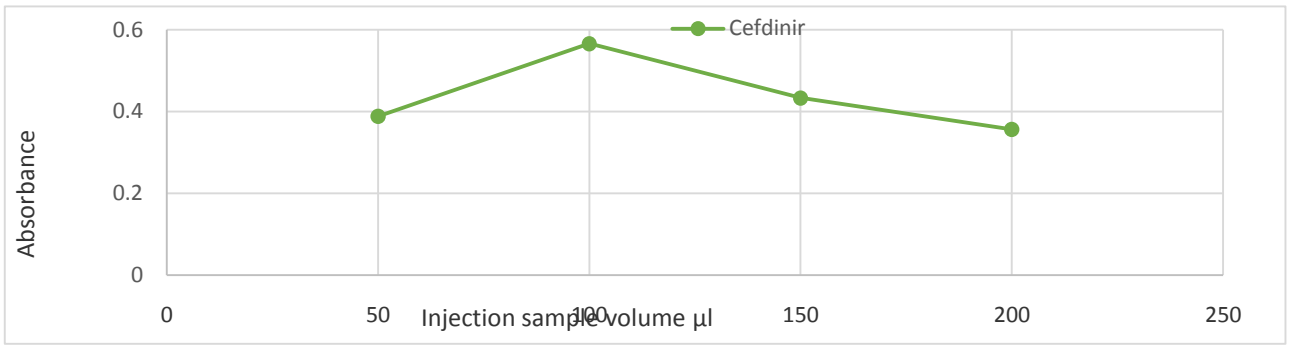

Fig.21: Effect Injection Sample Volume

Calibration Graph of Flow Injection for CFD Drug

Under optimal conditions, flow injection prepared the curve of FIA by a plotting absorbance various concentration of CFD 1-150 µg/ mL, Fig.22. Tables 10 show the parameter Characteristic for the regression equation FIA method.

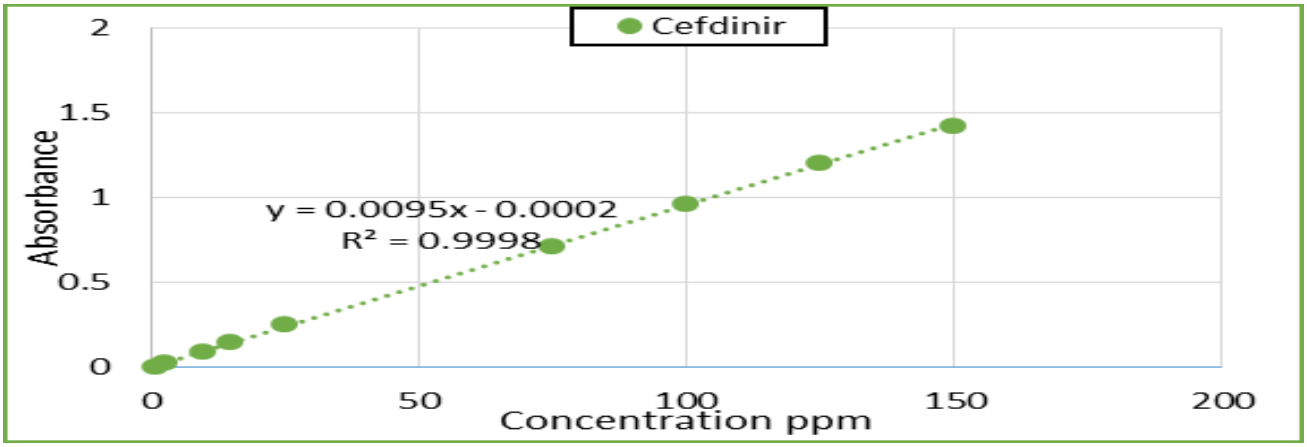

Fig.22: Calibration graph for Cefdinir by Flow Injection Analysis

Table10: Analytical data for the regression equation of the Flow Injection Analysis

Parameter	Cefdinir
λ max(nm)	495
color	Reddish-Orange
linearity range µg/mL	1-150
Molar absorptivity (L.mol^{-1} cm^{-1})	0.376×10^{4}
Sandell's sensitivity (µg/ cm^{2})	0.105
Correlation coefficient ®	0.9998
Regression equation	Y=0.0095x-0.0002
Slope(b)	0.0095
Intercept(a)	-0.0002
Analytical sensitivity µg/mL	0.017
Limit of detection µg/mL	0.032
Limit quantification µg/mL	0.104
C.L. for the slope (b±ts$_b$)at 95%	0.0095±0.000371
C.L. for the intercept (a±ts$_a$ at 95%	-0.0002±0.02912
Standard error for regression line (Sy/x)	0.008692

Accuracy and Precision

The accuracy and precision for the proposed method were studied, under optimal conditions using three different concentrations and measured absorbance at a minimum for five readings per concentration. The accuracy estimated to determination relative error, percentage and Recovery. Precision estimate determination for the percentage relative standard deviation RSD%, as shown Table 11&12.Table 13 confirmed the calculated t-values and F-values for CFD Estimation in various pharmaceuticals Formulation are a smaller amount than t-tabulated and F-tabulated at 95% confidence interval and (n-1) degrees of freedom.

Table 11: accuracy and precision of proposed method for estimation of pure samples

Type of Drug	Amount of drugs µg /mL		Relative Error %	Recovery %	Average Recovery%	RSD% (n=5)
	Taken	Found				
Cefdinir	10	10.06	0.6	100.60	100.03	0.82
	30	29.88	-0.4	99.60		0.74
	50	49.95	-0.1	99.90		0.53

Table 12: The accuracy and precision of proposed method for estimation of commercial pharmaceuticals

Type of Drugs	Amount of drugs mg		Relative Error %	Recovery %	Average Recovery %	RSD% (n=5)
	Taken	Found				
Cefdinir (sefarin® capsules300mg/ Product by pharma international Co. Amman-Jordan	300	300.25	0.08	100.08	99.90	1.06
		298.99	-0.34	99.66		0.98
		299.88	-0.04	99.96		1.00
Cefdinir(Azord® capsules300mg/ Product by DAR AL DAWA DEVELOPMENT&NVESTMENT CO.LTD (Na'ur-Jordan)	300	299.47	-0.18	99.83	99.98	0.09
		298.69	-0.44	99.56		0.15
		301.66	0.55	100.55		1.02

Table 13: Comparison the proposed method with stander method using t and F- Statistical test at 95% confidence level

Pharmaceutical preparation	Proposed methods						Standard method[18]
	Rec% Batch method	Value		Rec% FIA method	Value		Rec %
		t	F		t	F	
Pure Cefdinir	100.33	0.246 (2.131)	1.84 (19.00)	99.22	1.403 (2.131)	1.395 (19.00)	99.11
Cefdinir (sefarin® capsules300mg/ Product by pharma international Co. Amman-Jordan	99.89			99.90			99.00
Cefdinir(Azord® capsules300mg/ Product by DAR AL DAWA DEVELOPMENT&NVESTMENT CO.LTD (Na'ur-Jordan)	99.88			99.98			99.66

Conclusions

Batch, Cloud point extraction and flow-injection spectrophotometric methods were developed for the Estimation of CFD.A simple, sensitive and fast CFD with Bisphenol A. The method involving convention CFD to the colored product (Azo-dye) then reasonable by UV. Visible Spectrophotometric. Preconcentration of colored azo-dye by CPE and Automation the batch method with FIA technique. It is very simple and sensitive to Estimation the CFD in pharmaceutical formulation.

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