Cloud point extraction of Cefixime drug by direct (UV-Vis) spectrophotometer and indirect (Flame Atomic Absorption) technique

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Abstract A new method for the determination of the Cefixime drug in some Pharmaceuticals using ultra violet-visible (UV-Vis) and indirect Flame Atomic Absorption Spectrophotometry (FAAS) by Cloud point Extraction by using Triton X-114 as surfactant, the method based to form chelating complex CEF – Pd (II) at 456nm, 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 chelating complex was (9). The best temperature on cloud-point extraction was 55°C at 20 min. then complex extracted with ethanol. The mole-ratio method has been used to determine the structure of chelate CEF – Pd (II) and found to be 1:1 L:M (Ligand : Metal). Beer’s Law was obeyed in the range 2.5-30 and 2.5-32.5 g/mL for UV-Vis and FAAS respectively. Limit of Detection and Limit of Quantitation LOD and LOQ values for these methods were (0.456592, 0.33374) g/mL (1.521976, 1.112471) g/mL respectively. The method was 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.

1. 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 of Cefixime 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 Bilary 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 Figure 1[4]

![Figure 1: The structure of Cefixime][4]

The cloud point procedure (CPE) is based on the following phenomenon: an aqueous solution of some surfactant becomes turbid and separation 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].

2. Experimental Parts
2.1. Materials and Methods:

**Apparatus**
- UV-Visible recording spectrophotometer (1986) Shimadzu Model (160A) (Japan) with a response time of 0.1s, was used for spectrophotometric determination. A quartz cell of 1 mL internal volume and 1 cm path length was used for absorbance measurements.
- Flame Atomic Absorption Spectrophotometer, GBC (933 plus)
- Hotplate Stirrer (Hotplate stirrer Model L-81 Labinco bv)
- 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).
2.2. Materials

- A pure grade of Cefixime was 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 250 g mL\(^{-1}\) or \(5.5132 \times 10^{-4}\)M for the drug Cefixime was prepared by dissolving 0.25g in minimum amount of water and diluted to mark with water in a 250 mL volumetric flask.
- A solution of 250 ppm of Pd \(^{2+}\) was prepared by dissolving 0.1041 gm of PdCl\(_2\) in small amount of water and complete the volume to 250 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 g 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 Ca\(_3\)(PO\(_4\))\(_2\) and CaCO\(_3\) 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 250 g mL\(^{-1}\) Pd\(^{2+}\) metal ion Then pH was adjusted by using 0.1M NaOH and 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 °C, 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 by 1mL of ethanol, the measurements of absorbance of the complex were followed by UV-Vis spectrophotometer with used 1.0 cm quartz cell to get max for CFX - Pd (II) complex against blank which was prepared in the same way but without drug.
3. Results and discussion by UV-VIS Method

3.1. Absorption Spectra

The absorption spectrum of the complex product CFX - Pd (II) formed was recorded against the corresponding blank between 220 to 900 nm before obtaining optimum conditions according to the recommended CPE procedure. Figure 2 show an absorbance at max 456nm. The molar absorptivity value is $1 \times 10^4 \text{Lmol}^{-1}\text{cm}^{-1}$. The value of molar absorptivity enables to carry out the quantitative analysis of cefixime in Pharmaceuticals directly.

![Absorption Spectra](image)

**Figure 2.** Absorption Spectra of (A) CEF Versus Distilled water, and (B) metal Versus Distilled water (C) Complex of the CEF - Pd(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-114 amount, equilibration temperature and incubation time.

3.2.1. Effect of metal ions concentration

The effect of palladium ion concentrations was studied by measuring the absorbance values according to the geranial procedure containing 1mL of 250 $\text{g mL}^{-1}$ Cefixim, 1mL of 10% (v/v) Triton X-114 of and varying volumes of the 250 $\text{g mL}^{-1}$ Pd (II) ranged from (0.2-1.8) mL. The optimum volume of the metal ions that gave maximum absorbance was 1.2 mL as shown in Figure 3 . this volume was used throughout this study.
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 2-14 were accomplished according to the described procedure. The maximum sensitivity and the best separation for the complexes drug- Pd (II) was obtained at pH 9. The results are shown in Figure 4 and Table 1.

**Table 1.** Data of absorbance to value of pH

| value of pH | Absorbance at max = 456 for Pd (II) |
|------------|-------------------------------------|
| 2          | 0.134                               |
| 3          | 0.137                               |
| 4          | 0.141                               |
| 5          | 0.169                               |
| 6          | 0.225                               |
| 7          | 0.229                               |
| 8          | 0.307                               |
| 9          | 0.453                               |
| 10         | 0.426                               |
| 11         | 0.439                               |
| 12         | 0.214                               |
| 13         | 0.26                                |

**Figure 4:** pH effect on the absorbance of CEF- Pd (II) complex
It was shown that the sensitivity increase at pH 9. At higher pH, the drug is deprotonated and it behaves like a hydrophilic molecule and easily gets solubilized in the micelles while at lower pH, the drug is protonated and its ionic characteristics increase and led to decrease in its solubilization in the hydrophobic micelles.

3.2.3. Effect of buffer solutions

The effect of buffer solutions tris (hydroxymethyl) aminomethane and Sodium tetra borate (borax) with acidic function 9 was studied on the intensity of complex formation CEF+Pd(II). The best intensity values of buffer Sodium tetra borate (borax) as shown in table 2.

| Preparation                | buffer pH 9 | Absorbance |
|----------------------------|-------------|------------|
| tris (hydroxymethyl) aminomethane |             | 0.066      |
| Sodium tetra borate (borax) |             | 0.494      |

3.2.4. Effect of Volumes buffer solutions

Figure (5) shows the value of absorbance intensity for the CEF- Pd$^{2+}$ complex against the value of volumes of Sodium tetraborate (borax) buffer solutions. It is evident that absorbance increase with increase the volume of buffer up 1.2 mL, but suddenly decrease the absorbance because the decomposition happen when increase basicity. 1.2 mL was selected for the subsequent

![Figure 5: buffer of pH effect on the absorbance of CEF- Pd (II) complex](image)

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, 1.2mL Pd, 1.2mL buffer pH 9] in 10mL volumetric flask and use different surfactant [Tween 20, Tween80, CTAP, SDS, Triton X-100, Triton X-114] at 50°C for 10 min incubation time then it centrifuged at 3000 rpm for 10 min, separated the surfactant-rich phase and dissolved in 1ml ethanol then measured by UV-Vis at max = 456nm for CEF–Pd(II) complex the results shown in Table 3.

Table 3. Data of absorbance of type of surfactant

| No | Surfactant       | Absorbance at max =456 nm for Pd (II) |
|----|------------------|---------------------------------------|
| 1  | Tween 20         | 0.593                                 |
| 2  | Tween80          | 0.57                                  |
| 3  | SDS              | 0.063                                 |
| 4  | CTAP             | 0.148                                 |
| 5  | Triton X-100     | 0.321                                 |
| 6  | Triton X-114     | 0.774                                 |

Figure 6: Effect of surfactant type on absorbance

It was observed that Triton X-114 which has maximum absorbance at 456 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 the cloud 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 (0.2-1.6 mL) for CEF–Pd(II) complex. The results are presented in Figure 7. It was noticed that the absorbance values of CEF drug continued to increase dramatically and reached maximum at 1.2mL 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 Figure 7.
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 (30 – 70)°C and (5 - 35) min, respectively, while keeping all other parameters constant. Excellent absorbance was found at temperature 55° C as shown in figure 8 and table 4, therefore choose 55° C, higher than 55° C is probably due to the decomposition of the complex.

| Temperature / °C | Absorbance at $\lambda_{\text{max}} = 456$ for Pd(II) |
|------------------|--------------------------------------------------|
| 30               | 0.60                                             |
| 35               | 0.626                                            |
| 40               | 0.63                                             |
| 45               | 0.795                                            |
| 50               | 0.807                                            |
| 55               | 0.810                                            |
| 60               | 0.808                                            |
| 65               | 0.806                                            |
| 70               | 0.802                                            |

Figure 8: Effect of temperature on the cloud point extraction of CEF- Pd (II) complex

Incubation time was also investigated in the range of (5-35) min figure 9 excellent absorbance found at 20 min the time for 20 min was selected to fulfill efficient separation conditions.
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. Figure 10 and Table 5 show that the best order of addition is the number 1 for target analytes due to giving a highest absorption signal among the others. It is noted that the best addition is the first order of complex CEF-Pd (II) because if it's another order gets lost in the intensity of color and this order fixed in subsequent experiment.

Table 5: Data of absorbance of order additions

| No | Order Additions | Absorbance at max =456 for Pd(II) |
|----|-----------------|-----------------------------------|
| 1  | D+ M+B+T        | 0.809                             |
| 2  | M+D+B+T         | 0.543                             |
| 3  | D+B+M+T         | 0.128                             |
| 4  | M+B+D+T         | 0.489                             |

Figure 10: Effect of order additions for CEF- Pd (II) complex

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 figure 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

| No | Solvents     | Absorbance at max = 456 for Pd ion |
|----|--------------|-----------------------------------|
| 1  | Water        | 0.805                             |
| 2  | Ethanol      | 0.811                             |
| 3  | Methanol     | 0.703                             |
| 4  | Acetonitril  | 0.132                             |
| 5  | chloroform   | 0.157                             |
| 6  | Acetyl acetone | 0.109                           |
| 7  | Dimethy formamide | 0.012                        |
| 8  | Dimethy phthalate | 0.165                       |
| 9  | Dimethy malonate | 0.234                        |

Figure 11: Effect of solvents. (A) For CEF- Pd (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- Pd (II) complex. The intensity of was developed follow the recommended procedure described earlier. It was observed from the table 6 and figure 12 were not interfering with the determination at levels found in complex form.

Table 7: Effect of Interference

| 100 g mL⁻¹ interference | Absorbance at max = 456 for Pd |
|-------------------------|--------------------------------|
| With out                | 0.813                          |
| Lactose                 | 0.05                           |
| Starch                  | 0.19                           |
| Arabic Gum              | 0.002                          |
| Talc                    | 0.073                          |
| Glucose                 | 0.178                          |
| Ca₃(PO₄)₂               | 0.046                          |
| CaCO₃                   | 0.155                          |

Figure 12: Effect of Interferences on the CEF-Pd (II) Complex
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 7 and were used in all subsequent experiments.

| Optimum Conditions | Concentrations | Range selected | Optimum quantities of complex (CEF-Pd$^{2+}$) |
|--------------------|----------------|----------------|---------------------------------------------|
| Effect of volume of metal ion required | 500ppm | 0.2-1.8 | 1.2mL |
| Effect of PH | 0.1M(NaOH) | 2-13 | 9 |
| Effect of volume of Buffer | Sodium tetraborate (borax) | 0.2-1.8 | 1.2mL |
| Effect of volume of Triton X-114 required | 10%(v/v) | 0.2-1.6 | 1.2mL |
| Effect of time heating | --- | 5-35min | 20min |
| CEF solution required | 500ppm | 2.5-30 | 1mL |

### Table 8: The optimum conditions for the determination of complex

**3.4. Preparation of Calibration Curve of CPE**
Amount of 10ml solution is prepared containing increasing concentration of drug Cefixime by taking (2.5-30) g mL$^{-1}$, 1.2mL Pd, 1.2mL buffer pH 9 and 1.2mL 10%(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 max = 456 nm for palladium, 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-palladium) as shown in Figure 13 .
Table 9: The absorbance measurements of standard solutions of complex (CEF-Pd)

| Conc. g mL⁻¹ | Mean Absorbance |
|--------------|-----------------|
| 2.5          | 0.026           |
| 5            | 0.088           |
| 7.5          | 0.202           |
| 10           | 0.275           |
| 12.5         | 0.359           |
| 15           | 0.465           |
| 17.5         | 0.52            |
| 20           | 0.609           |
| 22.5         | 0.711           |
| 25           | 0.813           |
| 27.5         | 0.867           |
| 30           | 0.981           |

3.5. 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 Pd (II) palladium (2×10⁻⁶–2×10⁻⁵)mol L⁻¹ metal. The absorbance of the solutions were measured by UV-Vis spectrophotometer versus blank at max 456 nm the stoichiometric ratio between 1:1 results are shown in the Table 10. Plotting the value of absorbance versus the CL / CM is shown in Figure 14.

CL: concentration of the ligand (Cefixime )
CM: concentration of the metal (palladium )

Table 10: The Mole - Ratio Method of the Cefixime - palladium

| CL     | CL / CM | Absorbance at 456 nm |
|--------|---------|----------------------|
| 2×10⁻⁶ | 0.2     | 0.003                |
| 4×10⁻⁶ | 0.4     | 0.047                |
| 6×10⁻⁶ | 0.6     | 0.111                |
| 8×10⁻⁶ | 0.8     | 0.198                |
| 1×10⁻⁵ | 1.0     | 0.284                |
| 1.2×10⁻⁵| 1.2     | 0.271                |
| 1.4×10⁻⁵| 1.4     | 0.268                |
| 1.6×10⁻⁵| 1.6     | 0.267                |
| 1.8×10⁻⁵| 1.8     | 0.258                |
| 2×10⁻⁴ | 2       | 0.256                |

Figure 13: (Cefixime+ Pd²⁺) Calibration Curve

Figure 14: Mole - Ratio plot of Cefixime and Palladium complex
3.6. Applications of the Cloud Point Extraction on Pharmaceuticals.

CPE has been applied on pharmaceutical Cefixime, 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 11.

Table 11: Data for Determination Cefix - Palladium in the Pharmaceutical Preparation Capsule (Cefixime) by CPE.

| Amount of Cefix / g mL⁻¹ | Mean absorbance | Relative standard deviation (RSD) | *Found Recovery % Average Recovery % | Erel % Average Erel % |
|-------------------------|-----------------|----------------------------------|---------------------------------------|-----------------------|
| 10                      | 0.289           | 1.38408                          | 10.3487                               | 103                   | 3.487                     | -5.2043                   |
| 20                      | 0.611           | 0.16366                          | 19.62                                 | 98                    | 100                       | -19                       | -5.2043                   |
| 30                      | 0.970           | 0.178562                         | 29.97                                 | 99                    | -0.1                      |                           |

[*]= Average of three

4-Results and discussion by (FAAS)Method

2- Indirect determination of antibiotics by Flame atomic absorption spectrophotometry (AAS)

Determination of drug CEF–Pd(II) 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 Pd(II) in the complex to detect the cefixime conc. as in figure 15. The complex CEF-Pd(II) was 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 palladium ion, it was found the best conc. of Pd(II) to give maximum absorbance 25 μg/mL of organic layer is enough to get higher absorbance for complex as in figure 16. 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 UV method.

4.1 Effect of metal ion concentration

Figure 15 show the effect of Palladium ion volume upon the absorbance values of the extracted complexes using (250 g/mL) of drug solution. The optimum volume of the metal ions that gave maximum absorbance was 1mL of Pd(II) for the complex, the absorbance is measured and the absorbance results are shown in table 12.
Table 12. Data of absorbance of optimum volume of metal ion.

| Volume of metal /mL | Absorbance for Pd (II) |
|---------------------|------------------------|
| 0.2                 | 0.058                  |
| 0.4                 | 0.19                   |
| 0.6                 | 0.198                  |
| 0.8                 | 0.233                  |
| 1                   | 0.257                  |
| 1.2                 | 0.207                  |
| 1.4                 | 0.204                  |
| 1.6                 | 0.169                  |

Figure 15: Effect of Optimum concentration Pd(II) ion conc. On absorbance of CEF-Pd(II) 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. The calibration curve was plotting the mean absorbance values of the cloud point versus the concentration (g mL⁻¹) of (CEF- palladium) as shown in Figure 16

Table 13: The absorbance measurements of standard solutions of complex (CEF-Pd)

| Conc. g mL⁻¹ | Mean Absorbance |
|--------------|-----------------|
| 2.5          | 0.054           |
| 5            | 0.119           |
| 7.5          | 0.171           |
| 10           | 0.216           |
| 12.5         | 0.268           |
| 15           | 0.315           |
| 17.5         | 0.361           |
| 20           | 0.396           |
| 22.5         | 0.444           |
| 25           | 0.497           |
| 27.5         | 0.552           |
| 30           | 0.625           |
| 32.5         | 0.681           |

Figure 16: (Cefixime- Pd) Calibration Curve by AAS Method
5. Comparison between the two methods of the proposed method

A simple comparison were make between the methods UV-Vis and AAS for determination of Complex and the calculation statistically parameter were illustrated in Table 14. The first and second 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 region and the best statistically calculation parameter.

Table 14: Comparison between the Two methods of the Proposed method to determination of Complex

| Parameter                        | Complex (cefixime-Pd) by UV-VIS Method | Complex (cefixime-Pd) by FAAS Method |
|----------------------------------|----------------------------------------|--------------------------------------|
| Concentration range (g mL⁻¹)     | 2.5-30                                 | 2.5-32.5                             |
| Regression equation              | y = 0.0347x - 0.070                    | y = 0.0201x + 0.0134                 |
| Correlation coefficient (r)      | 0.9999                                 | 0.9986                               |
| Correlation coefficient (r²)     | 0.9983                                 | 0.9974                               |
| Variation coefficient (%)        | 99.83                                  | 99.74                                |
| Limit of Detection (g mL⁻¹)      | 0.456592                               | 0.333741                             |
| Limit of Quantitation (g mL⁻¹)   | 1.521976                               | 1.112471                             |
| Slope (m)                        | 0.0347                                 | 0.0201                               |
| Intercept (C)                    | 0.0701                                 | 0.0134                               |

The proposed method was compared successfully with other literature methods and demonstrates which is the development of an excellent spectrophotometric method for 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 15. This method was successfully applied on pharmaceutical samples.

Table 15: Comparison of Cefixime determination in proposed method and other literature methods

| Analytical Method | Linear range μg.mL⁻¹ | max /nm | LOD/ μg.mL⁻¹ | Ref |
|-------------------|----------------------|---------|--------------|-----|
| UV-Vis Spectrometric | 4-24                 | 352     | 0.32         | 17  |
| UV-Vis Spectrometric | 8-16                 | 283     | 1.91         | 18  |
| Present method    | 2.5-30               | 456     | 0.456592     |     |
|                   | 2.5-32               | 456     | 0.333741     |     |
Conclusion
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 Pd (II ) in some Pharmaceuticals ,the method gives a very low limit of detection and green chemistry

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