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Development of an Eco-Friendly Method for Iron Extraction and Determination in Pharmaceuticals Using Ciprofloxacin Drug as Chelating agent

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Abstract:

A method is developed for the determination of iron (III) in pharmaceutical preparations by coupling cloud point extraction (CPE) and UV-Vis spectrophotometry. The method is based on the reaction of Fe(III) with excess drug ciprofloxacin (CIPRO) in dilute H_2SO_4, forming a hydrophobic Fe(III)- CIPRO complex which can be extracted into a non-ionic surfactant Triton X-114, and iron ions are determined spectrophotometrically at absorption maximum of 437 nm. Several variables which impact on the extraction and determination of Fe (III) are optimized in order to maximize the extraction efficiency and improve the sensitivity of the method. The interferences study is also considered to check the accuracy of the procedure. The results have shown that the preconcentration factor of 71 fold leading to obtain a limit of detection of 2.67 ng mL^{-1} with linear calibration range of 5-150 ng mL^{-1} (r=0.9998) and a superb sensitivity in terms of molar absorptivity of $1.13x10^6$ $L.mol^{-1}.cm^{-1}$. The mean percent recovery of 99.78±0.53% and the precision (RSD %) ranged from 1.96 to 0.76 are achieved. The developed method is applied to the determination of iron in four selected pharmaceutical drugs. The experimental values agree statistically with the quoted values stated by the manufacturer' companies.

Key words: Iron (III), Ciprofloxacin Drug, Hydrophobic Complex, Cloud Point Extraction, Molecular Spectrophotometry

Introduction:

Iron (Fe) as a transition metal is a very important biological mineral that exists in all cells of the human body and plays several vital functions. It is the bulk of the hemoglobin in red blood cells which carries O_2 from the lungs to all parts of the body, facilitates the use and storage of O_2 in muscle [1] and it is necessary for the natural growth and development of cellular function, and the synthesis of certain hormones and connective tissue [2-3]. Disorders of iron metabolism are among the most common diseases in humans. For instance, iron deficiency causes anaemia and other pathological changes in the body which remain an important public health problem, while an excess of iron

(iron overload) in the body causes several diseases such as cirrhosis, cancer, heart attack, diabetes mellitus, osteoarthritis, osteoporosis, metabolic syndrome, hypothyroidism, hypogonadism, numerous symptoms and in some cases premature death [4]. In order to prevent and treat iron deficiency, some iron containing pharmaceutical products are used which may be oral iron containing vitamins and dietary supplements or injectable iron containing pharmaceuticals[5]. Therefore, the U.S. Recommended Daily Allowance (USRDA) for iron is 18 mg for male and 1.0 mg for female between the ages of 19-50 years[6]. Thus in all cases ,the determination of iron is very important from the point of view of biochemical and nutritional studies .

Recently, Several methods have been reported in chemical literature regarding the determination iron in biological specimens and/or pharmaceutical formulations including flow injection analysis (FIA) , isotope dilution analysis with high-resolution (IDA) , inductively coupled plasma-mass spectrometry (ICP-MS) , atomic absorption spectrometry (AAS), high-performance liquid chromatography(HPLC), and cathodic stripping voltammetry (CSV) [7]. However, most of these techniques involve expensivee instrumental set up, lengthy treatments and hence lack the simplicity needed for routine analysis. But the majority of methods used involve the employing of UV-Vis spectrophometry for the assay of iron in different matrices and pharmaceuticals in particular, because it is relatively cheap, rapid, simple and available in many laboratories. The presence of metal ions at very low concentration levels in such complex matrices as natural, river, wastewaters, biological fluids, pharmaceuticals, foods and environmental samples etc. require a pre-treatment process to release metal ions from these matrices and to extract and enrich them prior to their determination [8].

The cloud point extraction (CPE) combined with any instrumentation can achieve the above-exigent demands and permit to design extraction systems and analyses. Consequently, several methods have been reported for the determination of iron including; CPE, for instance, coupled with flow injection- flame atomic absorption (CPE-FI-FAAS) [9-11], flame atomic absorption(CPE-FAAS) [12-14], graphite furnace atomic absorption(CPE-GFAAS) [15] , capillary zone electrophoresis (CPE-CEZ) [16], and Uv-Vis spectrophotometry [17-18]. In all the above-mentioned methods, CPE is based on using commercial organic reagents to form chelate (hydrophobic) with iron at specific pH, apt to interact with surfactant in solution.

As a result of previously published papers [19-21], it becomes clear that there are some medicines that have chemical structures capable of forming a complex hydrophobic compounds with some metal ions possibly exploited rather than commercial chemical reagents due to the easy availability and cheapness and thereby it can be used in complexation of metal ions.

In the present work , An eco-friendly procedure is designed for the determination of iron in pharmaceutical formulations using the combined CPE with visible spectrophotmetry. The developed method is based on the reaction of Fe(III) with drug ciprofloxacin in dilute H_2SO_4, forming a hydrophobic Fe(III)- Cipro complex which can be extracted into a non-ionic surfactant Triton X-114, and iron ions are determined spectrophotometrically at absorption maximum of 437 nm.

Materials and Methods:

Apparatus

A Shimadzu double-beam UV-Vis Spectrophotometer model UV-1800 (Kyoto, Japan) equipped with 10 mm optical path cell is used for the absorption spectra and absorbance measurements of analyte. Iron residue in aqueous solution is measured by a double-beam Atomic Absorption Spectrophotometer AA-6300(Shimadzu, Japan) equipped with a burner unit made of titanium (10 cm slot) air-cooled premixed for air/acetylene flame. The solution pH is measured by a portable pH-meter microprocessor (HANNA, Germany). Thermostatic water bath (WNB7-45) Experts (England) is used for CPE experiments.

Materials and Reagents

All chemicals used in this work are of analytical reagent grade and Doubly distilled water used for preparation and dilution of the reagents. A pure grade ciprofloxacin-HCl (99.4%) is supplied by the Drug Industries and Midical Appliance (SID) Samarra/ Iraq. A stock solution of ciprofloxacin hydrochloride ($1x10^{-3}$ M) is prepared by dissolving 0.0368 g in 100 mL distilled water and the diluted solutions are daily prepared by appropriate dilutions in water. A stock solution (1000 μg mL^{-1}) of iron (III) is prepared by dissolving 0.8634 g of pre-dried $NH_4Fe(SO_4)_2$ (BDH) in 0.050M H_2SO_4 (BDH) in 100 mL volumetric flask .This solution is only used after at least 24 h, to guarantee complete dissolution. A surfactant type Triton X-114 (99.6%) is obtained from ACROSORGANICS (New Jersey, USA) from which 10% v/v is prepared by diluting 10 mL in 100 mL water. A 0.1 M sulphuric acid (1M) solution was prepared by diluted 5.43 mL of 98%H_2SO_4 (1.84 g/mL, BDH) with distilled water in 1L calibrated flask.

Recommended CPE Procedure

In 10 mL volumetric flask , a known amount Iron (III) standard or sample solution is mixed with 1 mL of 5.0×10^{-4} mol L^{-1} CIPRO , $5x10^{-4}$ M of H_2SO_4, 0.6 mL of Triton X-114 (10%) diluted to mark with distilled water. The content of the flask is transferred into a 10 mL centrifugal tube and then subjected to heating in a water bath at 75 ºC for 20 min to from cloudy solution. The phases separation is accelerated by centrifuging at 6000 rpm for 20 min followed by cooling in ice bath until viscous surfactant-rich phase formed. Then, the aqueous phase could be separated by using a syringe. Subsequently, 2 mL of ethanol was added to the surfactant-rich phase in order to decrease its viscosity and make the final volume feasible to transfer into the optical cell of 10-mm for the measurement of iron ion spectrophotometrically at the respective absorption maxima against a reagent blank prepared under similar conditions without metal ion.

Preparation of the Pharmaceutical Samples

Four drug formulations containing iron are purchased from local drugstores**.** Iron Dextran (50 mg/mL) injection produced by USP Parma Roth Wiesbaden (Germany),Iron Dextran (100 mg /2 mL) produced by Cox-pharmaceutical Ltd. ,G.B, England (100mg/2ml), tot'héma Iron gluconate (50mg/10mL)solution produced by laboratories' Innotech International (FRANCE) and Ironorm Syrup Wallace manufacturing chemists LTD Iron (250mg/5ml)England. Each sample is analyzed for iron after appropriate dilution with water matched with the calibration range of Fe(III) following the recommended CPE procedure and iron content is determined spectrophotometrically at λ_{max} of 437.

Measurement of Residual iron (III)

A flame atomic absorption spectrophotometer is used to detect the remaining iron in aqueous solution after extraction by CPE. The experiments are conducted by taking 10 mL containing $7x10^{-5}$ M of CIPRO, 50 ng mL^{-1} iron and 0.6 mL of Triton X-114 following the general CPE procedure. The aqueous phase separated from surfactant-rich phase which contains a residual of iron is analyzed by previously calibrated FAAS for iron at the central organization for standardization and quality control (COSQC) / Baghdad and iron is determined at 248 nm.

Results and Discussion:

Spectroscopic Study

Figure 1 shows the absorption spectra for all reaction constituents i.e. between iron (III) and CIPRO drug in acidic medium to form Fe(III)-CIPRO complex. As can be seen, the drug CIPRO solution gives two absorption maxima at 271 and 273 nm , while Fe(III) solution displays one absorption band at λ_{max} of 300 nm. With regard to Fe(III)-CIPRO complex , its absorption spectrum is conducted according to the recommended CPE procedure at the established optimum conditions versus the blank solution scanned at the same wavelength range (190-600 nm). It is shown that absorption spectrum of this complex gives a remarkable absorption bands with shoulder occurred at 437 nm, indicating the formation of complex between Fe(II) ion and the drug CIPRO.

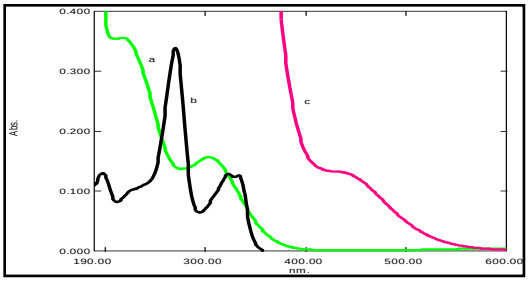

Fig.(1): Absorption Spectra (a) Fe (III) (b) Reagent Ciprofloxacin HCl and (c) Fe (III)-CIPRO Complex by CPE.

A preliminary study shows that the changing of order of additions of the reagents gives no significant shift in wavelength maximum of the complex. Thus, the absorption maxima of 437 nm for Fe-CIPRO complex is adopted throughout this study.

Optimization of CPE Procedure

In order to achieve the best sensitivity of the method and to enhance the extraction efficiency of CPE, effect of most important parameters is optimized via the classical optimization method. The parameters including, H_2SO_4 concentration, CIPRO concentration, Triton X-114 amount, equilibration temperature and incubation time. As reported by Suliman and Sultan**[22]** , H_2SO_4 concentration plays a significant role in the reaction between Fe(III) and CIPRO and responsible for the composition ratio of the reactants to form a hydrophobic complex, the effect of H_2SO_4 concentration in the range of $1x10^{-4}$ -0.025 M H_2SO_4 is conducted by recording the absorbance signals of the Fe(III)-CIPRO complex at λ_{max} of 437 nm for solution containing 50 ng Fe (III) mL^{-1} , 5 x 10^{-4} M of CIPRO and 1mL of 10 % (v/v) Triton X-114, according to recommend CPE procedure as shown in Figure 2. It appears that the absorbance increases sharply with increasing H_2SO_4 concentration and reaches a maximum at $5x10^{-4}$ M H_2SO_4 and suddenly decreases thereafter at high concentration which may result in dissociation of complex and in incomplete extraction in micelle. Thus a concentration of $5x10^{-4}$ M H_2SO_4 which corresponds to ionic strength of $1.5x10^{-3}$ M is chosen as the optimal in the subsequent experiments. The influence of the CIPRO concentration is studied by measuring the absorbance signals for the solution containing 50 ng mL^{-1} Fe(III) , $5x10^{-4}$ M H_2SO_4 , 1 mL of 10% (v/v) of Triton X-114 and varying volume of $5x10^{-4}$ M CIPRO in the

range of 0.1-1.6 mL according to the recommended CPE procedure.

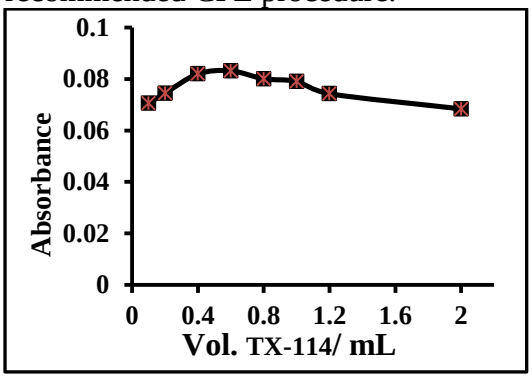

Fig .(2): Effect of H_2SO_4 Concentration on the Extraction of Fe (III)-CIPRO Complex by CPE

Figure 3 reveals that the analytical responses increase rapidly as the concentration of the drug increases, then decreases slightly with further increasing in the chelating agent. Any excess of CIPRO concentration may lead to the deviation of the equilibrium toward the backward reaction because of the law of mass action.

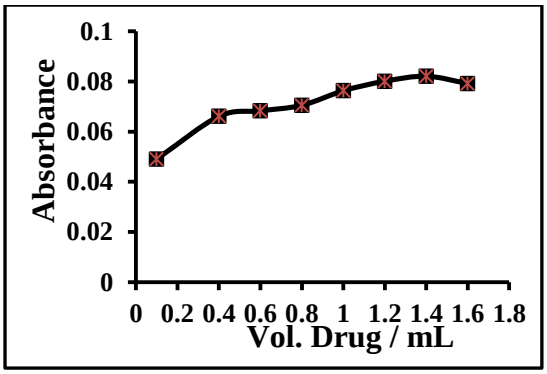

Fig. (3):Effect of CIPRO Concentration on the Extraction of Fe (III)-CIPRO Complex by CPE

Consequently, 1.4 mL of $5x10^{-4}$ mol L^{-1} of CIPRO is chosen as optimum for Fe (III). The slight difference in the concentration of chelating agent with Fe (III) may be attributed to the differences in the stability constants of complex formation in the micellar medium. Figure 4, depicts the effect of variation of Triton X-114 amount on the absorbance signal for the determination of Fe (III) ion. Different volumes of Triton X-114 (10% v/v) ranging from 0.1- 2 mL are used in this study at previously optimum conditions. It can be noticed that the responses of the complex increase with increasing Triton X-114 volume up to 0.6 mL of 10% (v/v) and then suddenly decrease at higher amounts.

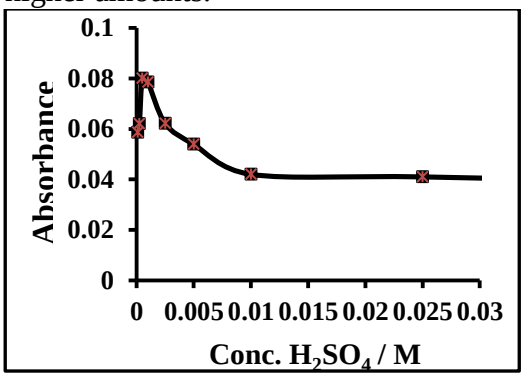

Fig. (4): Effect of Triton X-114 Amount on the Extraction of Fe (III)-CIPRO Complex by CPE

Thus 0.6 mL of 10% (v/v) Triton X-114 is used as the optimal.

The effect of the equilibrium temperature and incubation time are examined due to their importance for the reaction completion and efficient separation of the phases, which reflect certainly the magnitude of preconcentration factor of an analyte. Consequently, a study is carried out to choose the range of temperature that enhances higher absorbance signals for Fe (III) ion. The temperature varies from 25 ^{o}C to 85 ^{o}C in a search of optimum value. It can be seen from Figure 5 that the highest absorbance signals were achieved when the temperature at 75 ^{o}C. It was not also observed that the incubation time of 30 min is sufficient for the maximum absorbance (Figure 6). Thus, the temperature of 75^{o}C for 30 min was selected to fulfill efficient separation conditions. It was also noted that the centrifugation speed and time of 20 min at 6000 rpm at 20 min were sufficient to separate two phases.

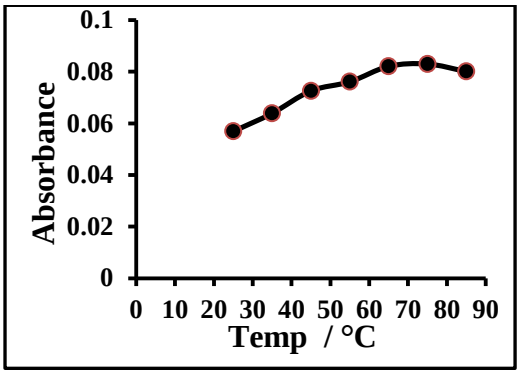

Fig. (5): Effect of Temperature on the Extraction of Fe(III)-CIPRO Complex

At optimum reaction conditions, the composition of Fe (III)-CIPRO complex was investigated by using mole ratio and continuous variation

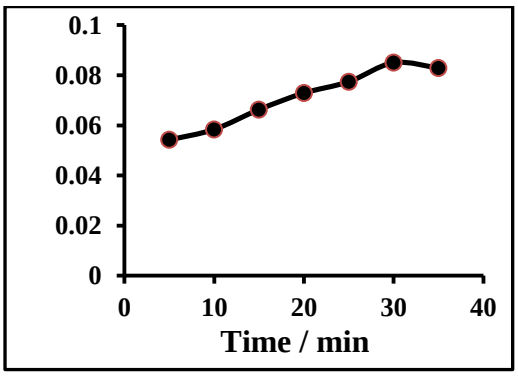

Fig. (6): Effect of Incubation Time on the Extraction of Fe (III)-CIPRO Complex

methods as reported in details in our previous published paper [19]. Our findings indicated that expected ratio Fe: CIPRO in the complex was of 1:2 by the two methods (Figures not shown here; see ref.19) and this was in harmony with results obtained by Suliman and Sultan [22] and Al-Momani et al [23], but it was inconsistent with the results reported by other study of Sultan and Suliman [24] where a 1:1 complex was found at acidic medium higher than 0.025 M H_2SO_4. The calculation of The stability constant (K_f) of Fe(III)-CIPRO complex was also conducted via the Job's plot and found to be of 5×10^{11} $(L\ mol^{-1})^2$ at 437 nm from which the standard free energy $\Delta G°$ for the complexation reaction was computed by using the equation ($\Delta G° = -2.303\ RT\ \log K_f$) and found to be equal to (-18.63) kcal mol^{-1}, indicative the spontaneously of the reaction.

Calibration graph for iron(III)

Under the established optimized conditions, Ten standard solutions were prepared by pipetting (0.05-1.5 mL) of 1.0 µg mL^{-1} iron standard solution into 10 mL volumetric flasks , then 1.4 mL of 5.0 x 10^{-4} mol L^{-1} CIPRO reagent solution, $5x10^{-4}$ M H_2SO_4 concentration., 0.6 ml of Triton X-114 (10%) were added to each flask and diluted to mark with water. These standard solutions are corresponding to (5-150 ng mL^{-1}) for Iron (III). The content of each flask was transferred into a 10 mL centrifuging tube and subjected to the recommended CPE procedure and an aliquot was transferred into the optical cell of 10-mm for the measurement of Fe ions spectrophotometrically at absorption maximum of 437 nm against a reagent blank prepared under similar conditions without metal ion. The standard calibration graph was constructed by plotting absorbance signals versus metal concentration from which the content of Fe (III) ion in sample solutions was determined by regression as showed in Figure 7.

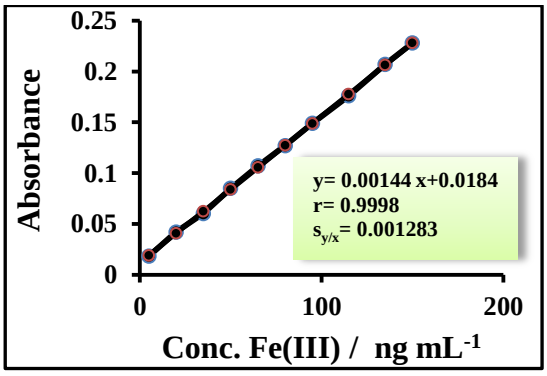

Fig. (7): Iron Calibration Line Fit Plot by CPE Procedure

To check on the validity of the simple regression line for Fe(III)

concentration vs. absorbance above , the normal probability plot reveals that an ideal linear trend indicative of the normality of absorbance response is being acceptable as shown in Figure 8.

However, the Fe (III) concentration residual plot (Figure 9) does not fall into any obvious pattern though low Fe (III) concentration, there appears to be a downward trend in the residual. There is a suggestion, though not very strong, of a quadratic trend and that inclusion of a quadratic term in Fe (III) concentration could improve the model to fit further.

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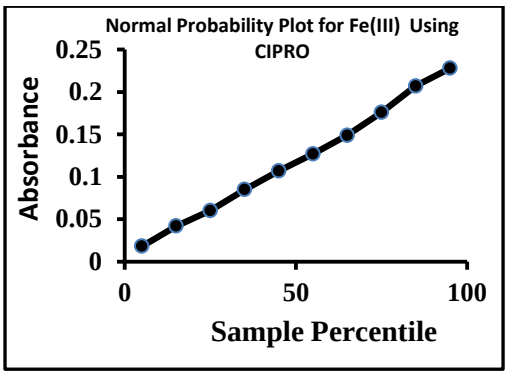

Fig. (8): Normal Probability Plot of Absorbance Data for Analysis of Fe(III) Using CIPRO as Chelating Agent.

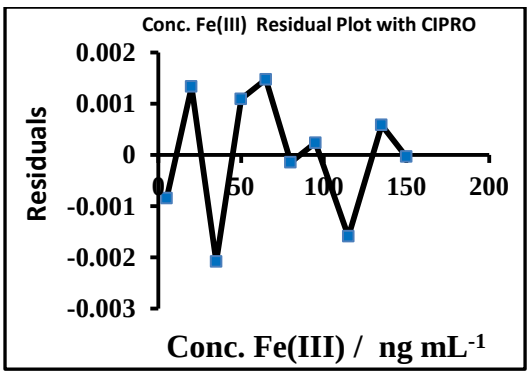

Fig. (9): Fe (III) Residual Plot

The statistical analytical figures of merit of the proposed method are summarized in Table 1. As can be shown, the calibration curve for Fe (III) determination by CPE-Spectrophtometry using CIPRO drug a ligand is linear over the concentration range of 5-150 ng mL^{-1} (10 pair points). The pre-concentration factor obtained is 71 fold leading to achieve limit of detection (LOD) and limit of quantitation (LOQ) of 2.67 and 8.90 ng mL^{-1}, respectively. Regarding the limit of detection , the proposed method is much better than with most results obtained by other authors as reported in Table 5. Also, the proposed method gives unprecedented sensitivity via the achieving a molar absorpitivity of $1.13x10^{6}$ L mol^{-1} cm^{-1} or Sandell's sensitivity of $6.98x10^{-4}$ mg cm^{-2}/0.001A.U.

Accuracy and Precision

Seven replicate analyses of 50, 100 ng mL^{-1} iron solutions following the recommended CPE procedure give repeatability in term of relative standard deviation (RSD) of 2.54%, 1.52% (Table 1). Because the commercial certified reference material for iron in drug formulations is not available and in order to investigate if of recovery percent is studied by spiking of 30, 50 and 70 ng mL^{-1} standard Fe(III) solutions to the drug containing iron namely Iron gluconate produced by Labortoire InnoTech International/ France) and containing 50 mgFe /10ml, thereafter the same steps are followed with the recommended CPE procedure. The results are tabulated in Table 2, indicating that there is no highly significant systematic error in case of the presence of other constituents in iron drug matrix.

Table (1): spectrophotometric determination of Fe (III) using CPE methodology.

Parameter	value
λ_{max} (nm)	437
Regression equation	y=0.00141x+0.011
Std. deviation of regression line	0.001283
Correlation coefficient(r)	0.9998
Coefficient of determination	99.97%
C.L. for slope (b± tsb) at 95%	0.001441±0.00002
C.L. for intercept (a± tsa) at 95%	0.01184±0.00178
Concentration range (ng mL^{-1})	5-150
Limit of Detection (ng mL^{-1})	2.67
Limit of Quantitation (ng mL^{-1})	8.90
Sandell's sensitivity (mg cm^{-2}/0.001A.U)	$6.98x10^{-4}$
Molar absorptivity ($L.mol^{-1}.cm^{-1}$)	$1.13x10^{6}$
Composition of complex (Fe-CIPRO)*	1:2
RSD% (n=7) at 50 ng mL^{-1}	2.54
RSD% (n=7) at 100 ng mL^{-}	1.52
Preconcentration factor**	71
Extraction efficiency(%E)***	99

*by mole ratio and Job methods(see ref.19)
****** Preconcentration factor calculates as the ratio of the original sample volume to that of extracted volume (of surfactant-rich phase) *** Extraction efficiency is calculated according to the following formula,

$$\%\boldsymbol{E} = [(\mathbf{1} - \boldsymbol{Cw}|(\boldsymbol{Rv} + \mathbf{1})\boldsymbol{CSRP}]\boldsymbol{x}\mathbf{100}$$

where R_v is the volume ratio of surfactant-rich phase(SRP) to aqueous phase. C_w is the concentration of analyte in aqueous phase (original solution before CPE), and C_{SRP} is the concentration of target analyte in SRP, which was quantified using calibration curve obtained

Table (2): Accuracy of the proposed method.

Amount Fe taken (ng mL^{-1})	Amount Fe found (ng mL^{-1})	Recovery (%)	E_{rel} (%)	Mean Rec.±t.s/√n (%)
30	29.86	99.53	-0.46	99.78±0.53
50	49.95	99.90	-0.1	
70	69.93	99.90	-0.1	

Table (3): Effect of excipients on the absorbance Fe (III) ions (80 ng mL^{-1} and 0.127 absorbance unit) by CPE-Spectrophotometry.

Interferent species	Interfernt/ Fe (III) ratio	A	ΔA	$\%E_{rel}$
Cu(II) as chloride	100	0.132	0.005	3.93
	1000	0.132	0.005	3.93
	10000	0.133	0.006	4.70
Mn(II) as Chloride	100	0.126	-0.001	-0.79
	1000	0.125	-0.002	-1.57
	10000	0.128	0.001	0.79
Ca (III) Stearte	100	0.131	0.004	3.14
	1000	0.129	0.002	1.57
	10000	0.130	0.003	2.36
Ca(II) as Gluconate	100	0.130	0.003	2.36
	1000	0.132	0.005	3.93
	10000	0.132	0.005	3.93
Dextran	100	0.125	-0.002	-1.57
	1000	0.127	0.000	0.00
	10000	0.124	-0.003	-2.36
Sodium Glycerophosphate	100	0.139	0.012	9.40
	1000	0.143	0.016	12.50
	10000	0.165	0.038	29.92
Nicotinamide	100	0.145	0.018	14.17
	1000	0.152	0.025	19.60
	10000	0.179	0.052	40.94
Potassium Nitrate	100	0.130	0.003	2.36
	1000	0.130	0.003	2.36
	10000	0.132	0.005	3.93

Interference Study

The selectivity of CPE for iron as Fe (III) ion is conducted by studying the effect of some metal ions and salts that expected to be present in iron drug formulations such as copper sulphate, manganese chloride, calcium stearate, calcium gluconate, dextran, disodium glycerophosphate, nicotinamide and potassium nitrate. For each experiment, 80 ng ml^{-1} of Fe (III) standard solution is taken and from 100 to 10000 times concentration of each interfering species are added. Each solution is subjected to the recommended CPE procedure and the absorbance is measured for Fe-CIPRO complex. The results are summed up in Tables 3. It is agreed that an extraneous ion is deemed to interfere seriously when it gives a relative error percent of more than ± 5 % [25] . It can be seen from Table 3 that there is no effect of most additives of the drug formulations in the determination of iron, except of sodium glycerophosphate and nicotinamide which causes severe interferences on the absorbance of iron. Therefore, these two interfering species should be removed or masked before determination of iron or added to standard Fe (III) solutions before the construction of calibration curve.

Table (4): Analysis of Fe in pharmaceutical samples by the Proposed method

Sample	Quoted value	Found by Proposed method	$t=(x-\mu)\sqrt{n}/s_d$ proposed method vs. Quoted value at(α=0.05)	% mean Recovery% at(α=0.05)
1	50 mg/ mL	49.80 49.94 49.59 **Ave:** 49.78±0.25	t=2.17 2.17<4.303	99.50± 0.89
2	100 mg/ 2 mL	99.25 98.55 99.70 Ave: 99.17±1.44	t=2.48 2.48<4.303	99.16±1.44
3	50 mg/ 10 mL	49.50 49.74 49.73 Ave: 49.74±0.46	t=2.43 2.43<4.303	99.49±0.87
4	250 mg/ 5 mL	268.87 264.38 268.44 Ave: 267.23±6.16	t=12.03 12.03>4.303	106.89±2.46

1) Iron Dextran injection(USP pharma- roth Wiesbaden, Germany)
2) Iron Dextran Cox Pharmaceutical LTD, G.B
3) Tot-Hema®Iron gluconate solution buvable laboratoire innotech international (FRANCE) Ironorm Syrup Wallace manufacturing chemists LTD Iron (250mg/5ml) Englan

Determination of Iron in Pharmaceutical Formulations

The established method is applied for the detection of iron in four medicaments containing iron as an active ingredient. The results are presented in Table 4. It was shown that the t-values calculated for iron determination are less than t-tabulated (4.303) at 95% confidence interval and (n-1) degrees of freedom, thus the null hypothesis H_o is maintained and concluding that there is no evidence for systematic and random errors at 95% confidence level and indicative the acceptance of manufacturer's claims. However, the latter medicament, which contains 250 mg/ 5 mL of iron may deviate from the norm as the calculated t is higher than the critical value at 95% confidence level, so the null hypothesis (H_o) should be rejected and accepting the alternative hypothesis (H_1), indicating that there is evidence for the occurrence of systematic error due to the potential interferences caused by the presence of some additives in the drug formulation.

Table (5): Comparison of the proposed method with reported methods

Method	Reagent used	Linear range (ng mL^{-1})	Limit of Detection (ng mL^{-1})	Ref.
CPE-FI-FAAS	APDC	Up to 350	19	9
CPE-FI-FAAS and spectrophoto-metry	APDC for ,total Fe and ferrozine for Fe(ll)	50-160 Up to 100	7 3	10
CPE-FI-AAS	tetra-*n*-butylammonium chloride	5-150	1.7	11
CPE- FAAS	8-HQ	2.5-4500	0.105	12
CPE- FAAS	Ferron	10-400	0.4	13
CPE- FAAS	Eriochrome Cyanine R	1.5- 25	0.33	14
CPE- GFAAS	Me-8-QH	6.5 -265	1.9	15
CPE- Electrophoresis -UV detection	5-Br-PADAP	Up 500	0.48	16
CPE-Spectrophotometry	Bromopyrogallol red	0.05- 43.0	0.02	17
CPE- Spectrophotometry	5-Br-PADAP	5-112 µg/L	0.8	18
CPE- Spectrophotometry	Ciprofloxacin HCl	5-150	2.67	This work

APDC: ammonium pyrrolidine dithiocarbamate; **Ferron**: 7-iodo-8-hydroxyquinolin-5 sulphonic acid**; 5-Br-PADAP:** 2-(5-bromo-2 pyridylazo)-5-diethylaminophenol**; Me-8-QH:** 2-methyl-8-quinolinol**; 8-HQ:** 8-hydroxyquinoline**; FAAS**: flame atomic absorption spectrometry**; GFAAS:** Graphite furnace atomic absorption spectrometry; FI: flow injection

Conclusions:

In the present work, the CPE-Visible spectrometry is designed for the determination of iron using the drug CIPRO as chelating agent for the first time. The proposed method is simple, rapid, cheap, highly sensitive and accurate. Regarding the limit of detection and linearity, the established method is much better than with some other results obtained by other authors as reported in Table 5.

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تطوير طريقة صديقة للبيئة لاستخلاص وتقدير الحديد في المستحضرات الصيدلانية باستعمال دواء السيبروفلوكسين ككاشف تعقيد

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الخلاصة:

جرى تطوير طريقة لتقدير الحديد في المستحضرات الصيدلانية باقتران تقنية الاستخلاص بنقطة الغيمة والمطيافية الجزيئية . اعتمدت الطريقة على تفاعل الحديد الثلاثي مع زيادة من تركيز دواء السبروفلوكساسين في محيط حامض الكبرتيك المخفف لتكوين معقد هيدروفوبي (Fe(III)- CIPRO) الذي يمكن استخلاصة بالمادة السطحية اللايونية من نوع (Triton X-114) وتقدير ايون الحديد طيفيا عند الامتصاص الاعظم (437) نانوميتر. كما تم دراسة المتغيرات العديدة التي تؤثر على استخلاص وتعيين أيون الحديد الثلاثي للحصول على الظروف الفضلى من اجل تعظيم كفاءة الاستخلاص وتحسين حساسية هذه الطريقة فضلا عن دراسة التداخلات للتحقق من ضبط الطريقة . وقد اظهرت النتائج ان عامل التركيز المسبق كان بمقدار 71 مرة مما ادى الى الحصول على حد كشف بمقدار 2.67 نانوغرام مل$^{-1}$ مع مدى معايرة خطي 5-150 نانوغرام مل$^{-1}$ (بمعلمل الارتباط 0.9998) وامتصاصية مولارية ممتازة وبمقدار($1.13x10^6$) لتر مول$^{-1}$ سم$^{-1}$. تراوح معدل الاسترداد بالمئة 99.78±0.53 % وكانت الدقة بين 1.96 الى 0.76 % محسوبة على اساس الانحراف القياسي المئوي. تم تطبيق الطريقة المستحدثة في تقدير الحديد في العقاقير الدوائية المحددة وتبين ان القيم التجريبية متفقة احصائيا من القيم المصرح بها من قبل الشركات المصنعة .

الكلمات المفتاحية : الحديد الثلاثي ، دواء السبروفلوكساسين، معقد هيدروفوبي ، الاستخلاص بنقطة الغيمة ، المطيافية الجزيئية