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A NEW SPECTROSCOPY METHOD FOR THE QUANTITATIVE DETERMINATION OF IRON(III) BASED ON CURCUMIN REAGENT

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Abstract: The paper describes a simple, sensitive, and selective spectroscopy method for the determination of Fe^{3+} by curcumin reagent and iron(III). In acid media, a 1:2 complex was formed; its properties were identified by UV-VIS, FT-IR, Raman, and MS spectra. The maximum absorbance of UV-Vis spectra appeared at 518 nm. The parameters of the method for the determination of Fe^{3+} was validated. Beer's law was obeyed in the range 0.2×10^{-5} M to 2.0×10^{-4}mol/L of Fe^{3+}. The limited of detection (LOD) and limited of quantitation (LOQ) has been to be $0.5.0\times10^{-6}$ and 1.5×10^{-6} mol/L. This method was applied to determine the concentration of ferrous total in various samples.

Keywords: Curcumin, complex, spectroscopy, reagent

Introduction

Curcumin, an active ingredient of turmeric, is well-known for its medicinal properties. It exhibits antioxidant activity, anti-inflammatory, antimicrobial, anti-cancer, and anti-Alzheimer.[1] The β-diketo moiety of curcumin undergoes keto-enol tautomerism. Previous researches have

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reported that the symmetric structure of curcumin leads to a statistically even distribution of the enol proton between the two oxygen atoms.[2] This compound shows strongly in the chelating ability of diketones towards a significant number of metal ions.[3] Until now, the complex of curcumin with metal ions has attracted researchers' interest. Because of ketone functional groups' presence linked to metal ions, curcumin complexes show different properties compared to a free form of curcumin. The features and bioactivity of both curcumin and metal ions have been modified in the complex.[4] The 1:1 curcumin- Al^{3+} complex has been prepared and used to reduce the toxicity of Al^{3+} in Alzheimer's disease.[5] Curcumin-Au^{3+} complex was synthesized and investigated the anti-arthritic activity.[6] The toxicity of heavy metals like Hg^{2+}, Cd^{2+}, and Pb^{2+} has reduced through complexes formation.[7,8] The influence of curcumin and manganese complex of curcumin on cadmium-induced oxidative damage and trace elements status in mice tissues has been studied.[9] Curcumin-metal complexes are also being discovered as better antitumor agents than curcumin itself.[10] Zinc(II)-curcumin complex has showed the effects of antidepressants in rodent models of gastric ulcers.[11] Mechanisms and pharmacological implications of Zn(II), Cu(II)-curcumin complexes in the Neuroprotective effects have been studied.[12] The supporting of this complex in the fibrillization and aggregation of amyloid-beta (A_β) peptide have been studied.[13] Differential Pulse Voltammetry and UV-Vis Spectrophotometry were also used to study the Cr-curcumin complex.[14] Antibacterial activity, antitumor activity of the complexes of curcumin with Cr(III), Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with were tested.[15,16] Recently, the DNA-binding and in vitro cytotoxic activity of Pd(II)-curcumin- caffeine complex have been examined.[17]

Several studies on iron -curcumin complexes have also been published and applied in the therapy. The chelation of curcumin treats iron overload neoplastic transformation,[18] and iron overload disorders[4] The 3:1 (ligand: metal) complex of curcumin with Fe^{3+} has tested cytotoxicity on four cancer cell lines.[19] The spectroscopic, polarographic, potentiometric,[3] and formation constants[20,21] of Cur-Fe(III) were investigated. In our previous works, the synthesis and biological activity of Curcumin complex with iron (III) ions have also been reported.[16,22]

However, up to now, the research of Curcumin for the quantitative analysis of iron(III) has not been reported. Therefore, we focus on studying the optimal conditions related to the complex formation in solution. Selectivity, recovery, and limit of detection were investigated. The recommended method has been applied to analyzing synthetic and actual samples. The results showed that Curcumin could completely act as a selective reagent for Fe (III) detection.

Materials and methods

Chemicals

All used chemicals and solvents were in analytical grade and were used without further purification unless otherwise mentioned. Double distilled and degasified water was used in this study. Curcumin was purchased from Sigma–Aldrich Pty Ltd.

Equipment

The UV-VIS absorption spectra were measured on Lambda 25 UV visible recording spectrophotometer (USA). The IR of curcumin complexes was recorded on the FTIR-8400S-Shimadzu

spectrometer using KBr pellets. The MS spectra were recorded on a Bruker microtof–Q 10187 spectrometer.

Procedure to form complex solution

Appropriate volumes (from 0.1 mL to 1.0 mL) of Fe(III) standard solutions (10^{-3}M) were added 2 ml of Cur 10^{-3}M solution in EtOH. The resulting solution was then added 5 mL CH_3COONa/CH_3COOH buffer solution to keep the pH in the range of 1÷3 and adjusted with a mixed solution of EtOH-H_2O (1:1) to 100 mL. Afterward, a portion of the solution was transferred into a 1- cm quartz cell, and variations of absorption spectral were recorded from 300 to 700 nm of wavelength to figure out the λ_{max}. For further experiments, the absorbance is measured at the optimal wavelength.

Determination of the composition and stability constant of the complex

The ratio of the complex was determined by using the Job's method of continuous variation. A series of solutions with different metal ion and Cur concentrations were prepared by maintaining the total Cur and metal ion concentration constant. The absorbance was measured at the optimum wavelength and was plotted against the mole fraction of the ligand.[23]

The stability constants were estimated by monitoring the reduction in the intensity of the absorbance at the peak with the data reduction being effected using Benesi-Hildebrand plots.[24–26]

Method Validation

Linearity

A series of reference standard solutions of Fe^{3+} were prepared in the range of concentrations of 0.2×10^{-5} to 20×10^{-4} mol/L. Based on the

absorbance value obtained versus the level of Fe^{3+}, the calibration curves equation was calculated.

Determination of LOD and LOQ

Limit of detection (LOD) and limit of quantification (LOQ) are calculated by the formula: LOD = 3SD and LOQ = 3LOD. Where: SD is the standard deviation of the absorbance of the blank solution (n = 7).

Recovery and Precision

For examining the recovery, precision, the experiment was carried out with synthetic samples, which was spiked analytic ion Fe^{3+} with the concentration of 60, 90, and 120 μg/L. At each level, the test was measured seven times for calculating SD, R%, RSD%.

Real sample preparation

The collected samples were decomposed by the wet digestion method for the determination of iron metal. Briefly, 10 g of each sample (fish, meat, vegetable) was transferred into the digestion flask. 20 mL of sulphuric acid and 2 mL of perchloric acid were added to it. The digestion flask was heated for 30 min. After the flocculation was settled, the flask was heated on high flame. After digestion, hydrogen peroxide was added dropwise until a clear solution was obtained. The content of the flask was filtered into a 50 mL volumetric flash and made up to the mark with distilled water.

Results and discussion

UV-Vis, FT-IR, and Raman spectra

The absorption spectra of the Cur and Cur-Fe(III) complex are presented in Figure 1. The curve ‘a’ and ‘b’ are the spectra of Cur and Cur–Fe(III) complex against ethanol blank. The UV spectra of reagent Cur

exhibits a weak absorption in the UV region, usually ascribed to the phenolic moiety and a more structured absorption in the visible region, with a maximum at 424 nm and a shoulder at lower wavelengths. The first regional bands at 220 – 300 nm correspond to a π to π*transition, whereas the bands existing at 310 – 470 nm region can be attributed to an n to π* transitions type. This phenomenon is typical for Curcumin in a polar solvent. It is generally referred to as the keto-enol moiety, following characteristic spectra observed by other authors. Whereas the intensity of Cur-Fe(III) spectra at 424 nm decreases, a new conspicuous absorption peak at 518 nm appears (Figure 1b).

Along with Fe(III) 's incremental addition in a particular range, the peak at 424 nm trailed off, and the peak at 518 nm boosted up. For seeing more clearly, the complex's absorption spectra (curve ‘c’) were measured with a blank sample of the Curcumin solution at the same concentration as the complex. As can be seen, the maximum of the reagent's absorption peak lies at 424 nm, whereas the absorption peak of the complex is dissimilar to it. The remarkable thing to note is that the addition of Fe(III) induced the change from yellow to red, and the new absorption peak at 518 nm has appeared. The complex color was changed from yellow to red only 10s after Fe(III) was added to the Curcumin stock solution. After 2.0 min., the equilibrium was attained. The clean region around 600 nm provides that the system is free of phenolate species upon the addition of Fe (III) ion.

The appearance of medium-intensity bands at region 460 cm^{-1} (Cur-Fe) in IR spectra, assignable to ν_{M-O}, indicated that the carbonyl groups formed the bonding with the metal ion.[7] The Raman spectrum shows that new oscillations appear at positions 393 cm^{-1}, which can be attributed to the valence variations of M-O bonds.

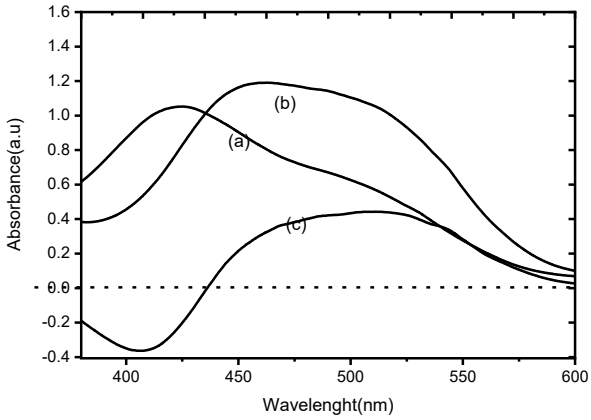

Figure 1. Absorption spectra of Cur and its Fe(III) complex at pH 2.5. Conditions: (a) the solution containing 2.0×10^{-5} mol/L of Cur against water blank; (b) the solution containing 2.0×10^{-5} mol/L of Cur and 1.0×10^{-5} mol/L of Fe^{3+} against water blank; (c) the solution containing 2.0×10^{-5} mol/L of Cur and 1.0×10^{-5} mol/L of Fe^{3+} against as Cur blank.

Optimation of condition for the complexation

Composition of complex

For determination of the stoichiometric ratio between ligand and metal ion, the Job's plot experiment was carried out by varying the concentration of both Cur and Fe^{3+} ion. Figure 2 displays typical Job's plots of metal complexation. Job's plot plotting experiment of Cur-Fe(III) was conducted at 518 nm, where complex showed maximum intensity. The maximum point at the mole fraction ($C_{Fe(III)}/(C_{Fe(III)}+ C_{Cur}$) was about 0.33, which refers to a ligand–metal complex ratio of 1:2.

The ESI-MS of Cur-Fe(III) was recorded in the solution. The ion fragment 880 of m/z has appeared, and this information confirmed that the ratio of iron(III) with Cur in complexes is 1:2. These results are also entirely consistent with the data of previously published documents.[22, 27,28]

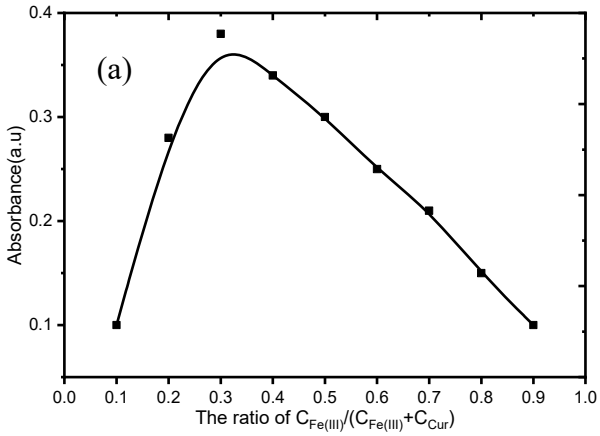

Figure 2. Job's continuous variation plots for Cur- Fe(III) at 518nm

Effect of pH on the absorbance of the complex at 518 nm

The absorbance of the absorption spectra of the Cur-Fe(III) complex was investigated in the pH range 0.5 – 6.0. The effect of pH on the absorbance of the complex at 518 nm is shown in Figure 3. Various pH values were adjusted by acetate buffer solution and confirmed by a digital pH-meter. As shown in Figure 3, in the tested pH range, different acidities display a prominent effect on the absorption peak intensity. The absorbance at 518 nm increase with acidity increment first, then reaches the peak point and decreases last. The absorbance of the complex has reached a maximum in the pH range of 1.5÷2.5. So the pH condition of 2.0 was selected for the following experiments.

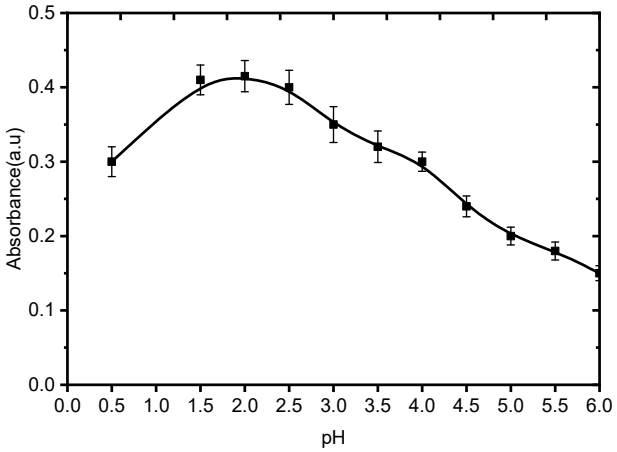

Figure 3. Effect of pH conditions on the complex's absorbance at 518 nm (2.0×10^{-5} mol/L of Cur and 1.0×10^{-5} mol/L of Fe^{3+}).

Effect of metal ion concentration in the absorption spectrum

Figure 4A exhibits the continuous change in color from yellow of the reagent to the deep orange color of the complex. This phenomenon shows that the color intensity (absorbance) of the system has a linear relationship with the iron concentration added. It could be explained that the complex has formed with the appearance of iron(III). The Cur's ketone groups joined to bonding formation, resulting in a change of bonding system of reagent. For having a further insight into the chromogenic behavior of ligand, the absorption profile as a function of metal ion concentration was checked. This experiment has been carried out at pH 1.5÷2.5 with the Cur solution as blank. As can be seen from Figures 4A, the absorption spectra of the complex at 518 nm showed a continuous rise in intensity along with the augment of the iron (III) concentration in the range of $0.1\times10^{-6} \div 20.0\times10^{-5}$ mol/L, in which a plateau is reached until the iron (III) ion concentration increased to 6.0×10^{-5} mol/L. The linear relation between the absorbance and the level of analyte ion were conspicuous in the range of 0.5×10^{-6} to 4.0×10^{-5} mol/L of iron(III). The linear regression equation was determined to be as follows: absorbance $A = 0.001\times C + 0.2379$, $r = 0.998$, and $n = 6$.

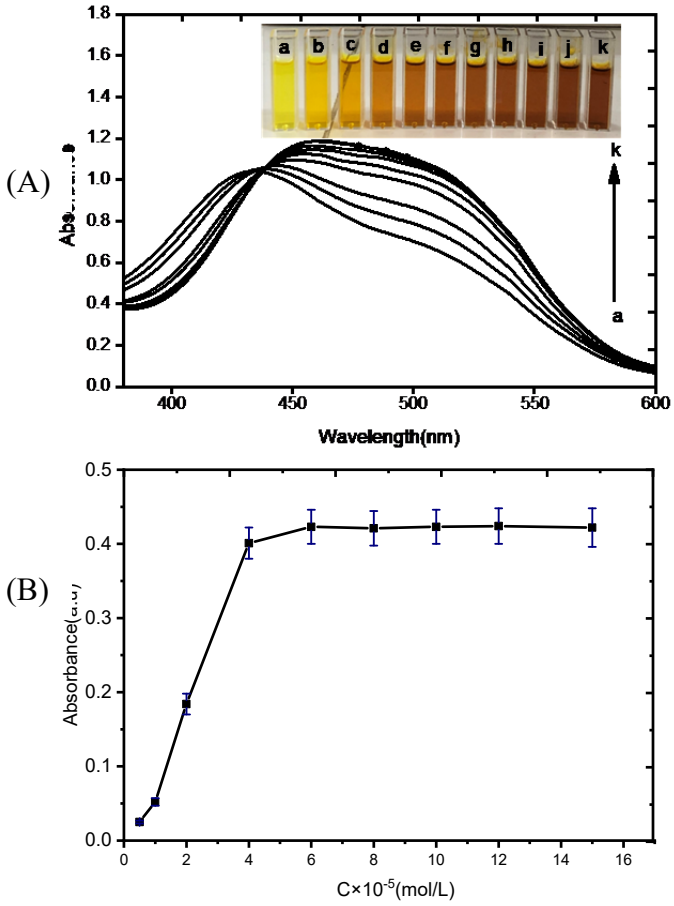

Figure 4. (A)Absorption spectra of Cur (a) and Cur-Fe(III) (b to k) against water blank, condition: 2.0×10^{-5} mol/L of Cur and 0.1×10^{-5} to 10.0×10^{-5} mol/L of Fe(III) at pH = 2.0. (B) Effect of Cur reagent concentration on the change in the absorbance of the complex.

Effect of reagent on absorbance

The effects of Cur concentration on the absorbance of the complex were conducted with 2.0×10^{-5} mol/L of concentration of metal ions, 2.0 of pH value, and in the range of 0.2×10^{-5} to 16.0×10^{-5} mol/L of Cur concentration. The absorbance of the complex was measured at 518 nm. As shown in Figure 4B, the increasing Cur concentration caused an increase in

the absorbance. However, when the Cur concentration increased to higher than 4.0×10^{-5}mol/L, complexes' absorbance did not change.

Calculations of the complex formation constant of the curcumin-Fe(III)

The stability constant was estimated by monitoring the decrease in the absorbance intensity at the peak with the data reduction being affected using Benesi-Hildebrand plots,[24–26] and the stability constant (*K*) was calculated to be 6.03×10^{4} (mol^{-2}/L). The $\varepsilon_{complex}$ was estimated to be 3.5×10^{4} (mol/L.cm).

Method validated

Linearity, LOD, LOQ

The calibration curve is linear over the range of 0.2×10^{-5} to 2.0×10^{-4} mol/L. The mean correlation coefficient is 0.9989. LOD, LOQ of the validated method are 6.4 and 19.3 μg/L, respectively. Therefore, the developed method was suitable for the direct analysis of Fe(III) in samples.

The effect of interfering ions

The tolerance limit of each foreign ion on the absorbance was tested. The solution of the sample containing 100 μg/L of iron was added amount of tested ion. It is considered to cause interference when the absorbance of the mixture sample is higher than 5%.[26] Table 1 indicates that most of the cations and anions did not show any significant absorbance interference at a ratio greater than 200. Among the cations, the presence of Mn^{2+}, Hg^{2+}, Al^{3+}, and borate at ten times higher has caused analyte ion interference. However, the content of these elements in the real sample is often lower than the content of iron. Therefore, we could apply the method for directly quantitative analyzing iron in the sample without masking.

Table 1. Effect of diverse ion the determination of 100 µg/L of iron.

Foreign ions	Tolerance limit (µg/L)
Na^+, K^+, Li^+	20.000
NO_3^-, CH_3COO^-, Cl^-, ClO_4^-	20.000
Ca^{2+}, Ba^{2+}, Mg^{2+}	10.000
Ni^{2+}, Co^{2+}, Ni^{2+}, Cd^{2+}	5.000
Hg^{2+}	1000
Mn^{2+}	1000
Al^{3+}	1000
Borate	1000

Table 2. Recovery and repeatability of the proposed method at three concentrations of iron (III).

	Added concentration (µg/L)	Recovery (R%)	Repeatability (RSD%)
Fe^{2+}, Cu^{2+}, Zn^{2+}, Ni^{2+} 2000	30	109.24	7.29
(µg/L); Al^{3+}, Cr^{3+} 900	60	92.14	4.35
(µg/L)	90	117.43	5.87

The precision of the determination of iron(III) was evaluated under the optimum conditions mentioned above. For this purpose, we used three model sample solutions with the known concentration of iron (III) as follows: 30, 60, and 90 µg/L, respectively. As presented in Table 2, it was found that the recovery of the method is 92.14÷117.43%. Thus, the process in this work has a high recovery efficiency and can be applied to real sample analysis. A comparison with the previously published methods for iron (III) determination is given in Table 3. The developed method provides sensitivity in comparison with published procedures. The sensitivity of the

technique is similar to some of the reagents. It is quite a quantitative analysis of iron (III).

Table 3. The comparison of the proposed method with previously published methods for the iron (III) determination.

Reagent	λ_{max} (nm)	$\varepsilon(\times 10^4$ mol/L.cm)	References
Ferrozine	562	2.79	[29]
2,4,6-Tri(2-pyridyl)-1,3,5-triazine	595	2.15	[30]
2-(5-Bromo-2-pyridylazo)-5-diethylaminophenol	558	7.10	[31]
Azid-tetrahydrofuran	396	1.53	[32]
Thiocyanate-benzyltriethylammonium	476	2.79	[33]
Pyrocatechol violet-CTAB	595	6.55	[34]
2,4,6-Tris(2-pyridyl)-1,3,5-triazine picrate	600	22.0	[35]
Morin-Triton X-100	418	6.15	[36]
1-Nitroso-2-naphthol-Tween 80 446 1.69	446	1.69	[37]
Curcumin	518	3.5	This work

Application analyses of real sample

A volume of 2.0 mL of the sample solutions was transferred into a 25 mL volumetric flask and added 2 mL of Cur 10^{-3} mol/L solution in EtOH. The resulting solution was then added 5 mL acetate buffer solution to keep the pH in the range of 1-3, and adjusted with a mixed solution of EtOH-H_2O (1:1). Afterward, a portion of the solution was transferred into a 1-cm quartz cell. Absorbance was recorded at 518 nm against Cur as blank. The collected data is calculated based on the linear regression equation. The

analysis results of three different types of samples are presented in Table 4. The iron content of these samples is entirely consistent with the declaration of their nutritional composition. Besides, to evaluate the accuracy of the validated method, the ICP-MS method was also used for comparing. Table 4 also shows that the proposed method also shows similar results with modern ICP-MS techniques.

Table 4. The content of iron in some samples (mg/kg).

Samples	Proposed method	ICP-MS
Beef 01	28.7 ± 1.6	27.6 ± 1.1
Beef 02	26.5 ± 1.8	25.2 ± 1.1
Beef 03	30.7 ± 2.1	29.3 ± 1.4
Mackerel 01	18.2 ± 0.8	19.1 ± 0.2
Mackerel 02	16.9 ± 0.9	17.4 ± 0.8
Mackerel 03	21.3 ± 1.1	23.2 ± 0.8
Spinach 01	25.4 ± 1.2	24.2 ± 1.2
Spinach 02	28.3 ± 1.8	29.2 ± 1.2
Spinach 03	32.4 ± 1.5	33.2 ± 1.5

Note: Each value is expressed as mean ± SD (n=3.)

Conclusion

In this work, we have studied the formation of iron and curcumin complexes. Factors affecting the complexing such as pH, reagent residue, complex ratio, other metal ions, and complex forming constants have been thoroughly studied. Based on the complexity, the spectrophotometric method has been developed and evaluated. Selectivity, recovery, and precision have been checked. The technique has been applied for the determination of iron in the spike and real samples with low cost, short time,

convenience, and high accuracy. This study clearly shows the potential and versatility of this method for determining this iron from food samples.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' Contribution

The authors have contributed equally to this work.

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