



Synthesis, spectrophotometric, spectroscopic, microbial studies and analytical applications of Cu(II) and Zn(II) complexes of chalcone ligand

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Abstract

The ligation behavior of the chalcone ligand namely (E)-3-(4-hydroxy-3-methoxyphenyl) acrylic acid (ferulic acid) (FA) toward the Cu(II) and Zn(II) ions was determined. The structure of the isolated solid complexes was elucidated by elemental analyses, spectral techniques (IR, UV–Vis, ¹³C- and ¹H-NMR spectra) as well as the conductance measurements and thermal analyses. UV–Vis spectra and magnetic moments had suggested square planar and tetrahedral stereochemistry for Cu(II) and Zn(II) complexes, respectively. The kinetic and thermodynamic parameters for some selected decomposition steps have been calculated. Two precise and sensitive spectrophotometric methods were utilized to determine Zn(II) and Cu(II) complexes with ferulic acid using a micellar media of cetylpyridinium bromide (CPB) and sodium lauryl sulfate (SLS) with an absorption maxima of 430 and 465 nm for Zn(II) and Cu(II), respectively. Various analytical conditions, for example, the concentration of the reagent, temperature, the sequence and timing of addition were also looked into. Under optimum conditions, the complexes exhibited good linearity in concentration range of 2.0–70.0 and 4.0–140.0 µg mL⁻¹; molar absorptivities 1.3161 × 10⁴ and 8.826 × 10³ L mol⁻¹ cm⁻¹; and Sandell's sensitivity 0.00496 and 0.00719 µg cm⁻² for the proposed methods of Zn(II) and Cu(II), respectively. The complexes ratio was found to be 1:2 [Zn(II):FA or Cu(II):FA] and the stability constants were 2.771 × 10⁵ and 2.826 × 10⁵, respectively. Finally, the newly synthesized complexes were shown potent antimicrobial activity.

Keywords Spectrophotometry · Chalcones · Biological activity · Metal · Analytical

Introduction

Polyphenols are a diverse class of natural compounds defined by the presence of an aromatic ring containing one or more hydroxyl groups in their chemical skeleton. Polyphenols are divided into many sub-classes depending on their structure including flavonoids, phenolic acids and phenolic alcohols (Genova et al. 2012). Ferulic acid (4-hydroxy-3-methoxycinnamic acid, FA) is a phenolic acid which widely spread in the cell walls of fruits, vegetables and grain plants (Wang et al. 2020). It has a broad range of potential therapeutic

effects beneficial in the treatments of lung, diabetes, cancer and cardiovascular diseases, as well as hepatic, neuro and photoprotective effects and anti-inflammatory and antimicrobial activities (Paiva et al. 2013). Ferulic acid (Fig. 1) is a free radical scavenger, but also an inhibitor of enzymes that catalyze free radical generation and an enhancer of scavenger enzyme activity (Zdunska et al. 2018).

Copper is a biologically active element, whose compounds have a strong effect on the vital activities of organisms. Copper also plays an important role in biological operations including metabolism, hemoglobin synthesis, nerve function and bone development (Veitia et al. 2009; Horstkotte et al. 2012; Kannan and Arumugham 2013). It has an effective role in industry as it enter in coin making, wire making, fashioning metal products, alloys, thermal conductivity and transportation industry. The accumulation of copper in human body and the environment through many industrial sources causes serious problems to public health (Alharthi and Al-Saidi 2020; Ahmed and Zannat 2012). In

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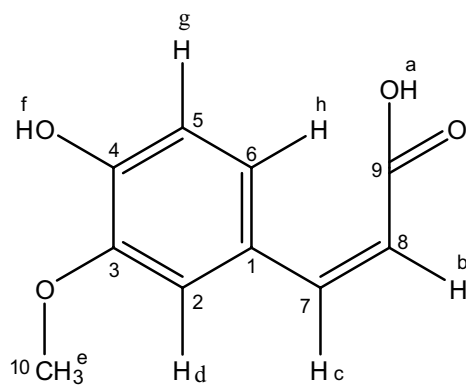


Fig. 1 Ferulic acid chemical structure with atoms numbering

the human body, zinc is the second most abundant transition element. Zinc is found in various foods such as cereals, liver, meat, rice, oysters, cheeses nuts; in several enzymes and DNA-binding proteins. It plays a huge physiological role in human beings like gene transcription, mammalian reproduction, brain function, immune function and pathology (Reddy et al. 2016; Frederickson et al. 2005). Many spectrophotometric methods were reported for the determination of Cu(II) and Zn(II) using different analytical reagents (Alharthi and Al-Saidi 2020; Souza et al. 2016; Babayeva et al. 2017; Jiaa et al. 2020; Rahmani et al. 2015; Reddy et al. 2016; Najim et al. 2020). Among the various analytical techniques suitable for the quantification of Cu(II) and Zn(II), spectrophotometry is the most widely employed one. In this study, Cu(II) and Zn(II) chelates of FA had been prepared in solution as well as isolated as solid. The isolated solid complexes were characterized utilizing elemental, thermal, spectroscopic, spectrophotometric, and antimicrobial methods. Moreover, the developed spectrophotometric methods were applied for the determination of Cu(II) and Zn(II) in various analytical implementations.

Experimental

Equipments

The spectrophotometric experiments were made by using a T80 UV/Vis double beam spectrophotometer with a spectral bandwidth of 2.0 and 10.0 mm matched quartz cells, manufactured by PG Instruments Ltd. in the United Kingdom. The pH readings were taken with a pH meter (Adwa pH meter, Model AD 1030, Romania). The apparatus and its templates used to classify the chemical structures of the synthetic complexes are summarized in Table 1.

Synthesis of (E)-3-(4-hydroxy-3-methoxyphenyl) acrylic acid (FA)

Ferulic acid was prepared by the condensation reaction of vanillin with malonic acid using benzylamine as the catalytic

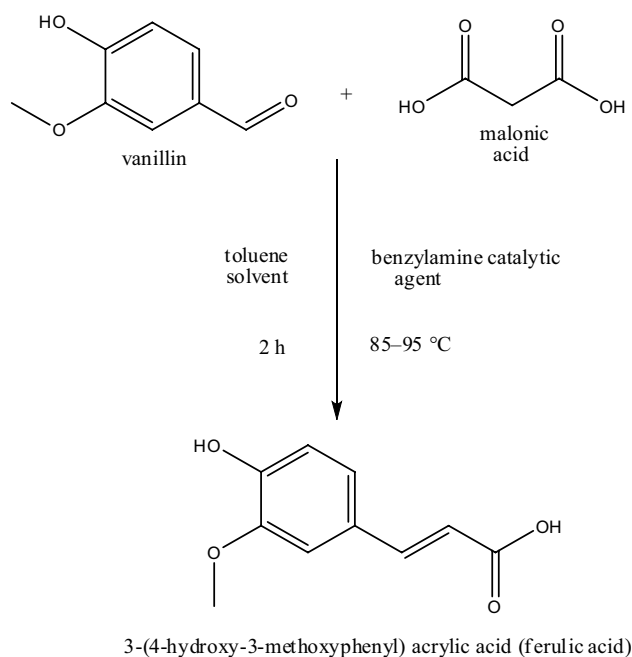


Fig. 2 Preparation of ferulic acid (FA)

Table 1 The apparatus and its templates

Type of analysis	Models
Elemental analyses	Perkin Elmer CHN 2400
Molar conductivities	CONSORT K410
FT-IR spectra	FT-IR 460 PLUS (KBr disks) in the range from 4000 to 400 cm^{-1}
Magnetic moment	Sherwood scientific magnetic balance using Gouy balance using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as calibrant
^1H NMR spectra	A Varian Mercury VX-300 NMR spectrometer
TGA-DTG	TGA-50H Shimadzu

agent, toluene as the solvent and a reaction temperature of 85–95 °C for about 2.0 h (Fig. 2) according to reported method (Shiyi and Kwok 2004). Appearance: white solid; Mp: 169–171 °C; MF: C₁₀H₁₀O₄; MWt: 194.18 (Fig. S1); ¹HNMR (300 MHz, *d*₆-DMSO): 12.13 (*s*, 1H), 9.56 (*s*, 1H), 7.48 (*d*, *J* = 15.9 Hz, 1H), 7.28 (*d*, *J* = 1.8 Hz, 1H), 7.08 (*dd*, *J* = 1.8 Hz, 6.3 Hz, 1H), 6.78 (*d*, *J* = 8.1 Hz, 1H), 6.36 (*d*, *J* = 15.9 Hz, 1H), 3.81 (*s*, 3H); ¹³C NMR (300 MHz, *d*₆-DMSO): 167.98, 149.02, 147.86, 144.49, 125.73, 122.79, 115.57, 115.47, 111.06, 55.61; LC MS (*m/z*): [M⁺H⁺]⁺—194.19.

Synthesis of complexes

The [Cu(FA)₂]SO₄·3H₂O solid complex was prepared by adding 1.0 mmol (0.2499 g) of CuSO₄·5H₂O in 20.0 mL acetone drop-wise to a stirred solution of 1.0 mmol (0.194 g) ferulic acid (FA) in 50.0 mL acetone. The reaction mixture was refluxed for 6.0 h; the formed olive green precipitate was filtered off, washed several times with acetone and dried under vacuum over anhydrous CaCl₂. The yellowish-white solid complexes, [Zn(FA)₂]SO₄·H₂O, were prepared similarly at 1:2 molar ratio (M:FA).

Materials and solutions

Commercially available chemicals were purchased from commercial suppliers (Sigma Aldrich Chemical Company (St. Louis, MO, USA)) and used as received, without further purification. A standard solution was formed by combining 0.01951 g, (99.50%) of ferulic acid in dimethyl formamide (DMF) and diluting to 100.0 mL in volumetric flask to obtain the final concentration of (1.0 × 10⁻³ M). A (1.0 × 10⁻³ M) of Zn(II) standard solution was elaborated by blending 0.01616 g of anhydrous ZnSO₄ (99.90%, M. wt. 161.47 g mol⁻¹) in deionized water and diluting to the mark in 100.0 mL volumetric flask. A (1.0 × 10⁻³ M) of Cu(II) standard solution was drawn up by thawing 0.02499 g of CuSO₄·5H₂O (99.90%, M. wt. 249.68 g mol⁻¹) in deionized water and diluting to the mark in 100.0 mL volumetric flask. Series of different surfactants including anionic surfactants [sodium lauryl sulfate (SLS), dioctyl sodium sulfosuccinate (aerosol GPG-E)], nonionic surfactants [triton X-100, tween 80] and cationic surfactants [cetyltrimethyl ammonium bromide (CTAB), cetylpyridinium bromide (CPB)] were prepared at concentration (1.0 × 10⁻² M) by dissolving the suitable amount of each surfactant in deionized water and diluting to the mark in 100.0 mL volumetric flask. They were applied with no additional purifying. A set of buffer solutions including borate, phosphate and universal buffers in the pH range from 7.0 to 12.0 were prepared by standard methods (Britton 1952; Bower and Bates 1955; Lurie 1978).

Procedures

Spectrophotometric procedures

Aliquots solutions of ZnSO₄ (10.0–1000.0 μg mL⁻¹) and CuSO₄·5H₂O (10.0–1800.0 μg mL⁻¹) were poured into a set of 10.0 mL volumetric vials. A concentration of 2.0 mL (1.0 × 10⁻³ M) of ferulic acid reagent was applied. Following that, for Zn(II) assays, 5.0 mL borate buffer pH = 10.0 was used, and for Cu(II) samples, 4.5 mL phosphate buffer pH = 8.0 was used. Then, 1.2 mL of CPB and 1.0 mL of SLS surfactants were added to Zn(II) and Cu(II) samples, respectively. The mixtures were diluted to 10.0 mL with deionized water, mixed well, and kept at room temperature for 15.0 min. The absorbance of this solution was measured at 430 and 465 nm in comparison to each blank solution made in the identical way with all additions except metal ion for Zn(II) and Cu(II) complexes, respectively (Elgendy et al. 2020a, b; Abd El-Wahaab et al. 2020; Elgendy et al. 2020a, b).

Applications

Determination of zinc and copper in brass alloy

A brass sample weighing 0.2 g was dissolved in 10.0 mL concentrated HNO₃ and 5.0 mL concentrated H₂SO₄ with heating until practically dry. The residual was re-dissolved in 5.0 mL concentrated HNO₃ and diluted with 10.0 mL deionized water after 30.0 min at 80 °C. A solution was frigid to room temperature and blended with deionized water to a constant volume appropriate for the concentration limits. The total concentration of zinc and copper was determined by the general procedures described above. Copper was masked by sodium thiosulfate (Fabre and Reynes 2010); then, the concentration of zinc was determined as described above. The obtained results were compared by the data obtained from the recommended method (Fabre and Reynes 2010).

Determination of zinc and copper in vegetables by digestion method [Spinach and Broccoli]

A dried vegetables weighing 0.5 g were mixed and stirred with 0.5 mL concentrated sulfuric acid, 1.0 mL perchloric acid, and 5.0 mL concentrated nitric acid and heated gently for few minutes by constantly raising the temperature. The blend was digested for 15.0 min on hot until white vapors emerged. The subsequent combination temperature was lowered to 25 °C then adding 10.0 mL of deionized water and the temperature was raised to 70 °C again for another 20.0 min. As previously, the solution was cooled, diluted, and examined.

Determination of zinc and copper in sea water, waste water and tap water

A 1000.0 mL of water sample was concentrated to 20.0 mL by heating for 5.0 h on a hot plate. Then, 5.0 mL of concentrated HNO_3 and 2.0 mL of 30% hydrogen peroxide were added to this solution and evaporated to near dryness. The leavings were dissolved in 5.0 mL of hydrochloric acid (5.0%) and 10.0 mL deionized water at 80 °C for 30.0 min. The resulting solution was cooled, diluted and analyzed according to the abovementioned method.

Determination of zinc and copper in blood

A specific volume of blood (10.0 mL) was taken from an adult human body. A 5.0 mL portion of this sample was centrifuged using a tube containing sodium citrate as an anticoagulant to separate plasma, and the remaining 5.0 mL was centrifuged to separate serum. A 0.5 mL serum sample was placed into a beaker containing a (1:3) concentrated ($\text{HClO}_4\text{:HNO}_3$). The combination was gradually heated until the solution was transparent, then cooled and analyzed as previously stated.

Antibacterial potency

The antibacterial activity was assessed utilizing the diffusion process (Beecher and Wong 1994) against *Escherichia coli*, *Citrobacter* and *Salmonella Typhi* as Gram -ve bacteria, *Staphylococcus aureus*, *Bacillus cereus* and *Listeria monocytogenes* as Gram + ve bacteria. Amoxicillin/clavulanic calibration disks were used as positive controls for antibacterial efficacy, whereas DMSO was used as a negative control. Müller–Hinton agar was prepared which was then cooled to

47 °C and planted with checked microorganisms. During solidification, 5.0 mm diameter holes were drilled with a sterile cork-borer. The tested compounds were introduced in holes (only 100.0 μL) after being dissolved in DMSO at 1.0×10^{-3} M. These culture plates were then incubated at 37 °C for 20.0 h. Then, the diameters of the inhibition zones have been recorded.

Results and discussion

The new synthesized chelates of Cu(II) and Zn(II) with ferulic acid (FA) were stable, colored and non-hygroscopic in nature. The Cu(II) and Zn(II) complexes were dissolved in Dimethyl formamide and dimethyl sulfoxide. The results of analytical data for the FA ligand and its prepared complexes are listed in Table 2. The chemical analysis demonstrated the existence of SO_4^{2-} anions outside the coordination sphere. The molar conductivity for freshly prepared DMSO solutions (1.0×10^{-3} M) of the complexes was measured at room temperature. The data showed the molar conductance value of the complexes Cu(II) and Zn(II) around 95.40 and 99.36 $\text{S cm}^2 \text{mol}^{-1}$, respectively, indicating these complexes as 1:1 electrolytes, (Geary 1971). The measurements demonstrate that the metal complexes were electrolyte in contrast with FA ligand. The complexes were characterized through their elemental analysis, magnetic properties, melting points, molar conductance, FT-IR, UV–Vis as well as thermogravimetric analyses. The results enable us to characterize the complexes and make an appreciation of the bonding and structure inherent in them. The magnetic susceptibility tests showed that Zn(II) chelate was diamagnetic but Cu(II) complex was paramagnetic (1.65 B.M), which indicated one unpaired electron per Cu(II) ion.

Table 2 Elemental analysis and physico-analytical data for FA and its metal complexes

Compounds M.Wt. M.F	Yield%	Mp/°C	Color	Found (Calcd.) (%)				μ_{eff} (B.M)	Λ ($\text{S cm}^2 \text{mol}^{-1}$)
				C	H	S	M		
FA 194.18, $\text{C}_{10}\text{H}_{10}\text{O}_4$	98	169–171	Yellowish	61.66 (61.85)	5.00 (5.19)	–	–	Diamagnetic	–
$[\text{Cu}(\text{C}_{10}\text{H}_9\text{O}_4)_2]$ $\text{SO}_4 \cdot 3\text{H}_2\text{O}$ 599.10, $\text{CuC}_{20}\text{H}_{24}\text{O}_{15}\text{S}$	85	240	Olive green	40.00 (40.04)	3.90 (4.03)	5.24 (5.34)	10.42 (10.59)	1.65	95.40
$[\text{Zn}(\text{C}_{10}\text{H}_9\text{O}_4)_2]$ $\text{SO}_4 \cdot \text{H}_2\text{O}$ 565.84, $\text{ZnC}_{20}\text{H}_{20}\text{O}_{13}\text{S}$	93	235	Yellowish-white	41.88 (42.45)	3.44 (3.56)	5.47 (5.67)	11.21 (11.56)	Diamagnetic	99.36

Spectroscopic analysis

FT-IR spectra

The IR spectrum of ferulic acid ligand exhibits a distinct peak of the carbonyl group $\nu(\text{C}=\text{O})_{\text{COOH}}$ and the hydroxyl

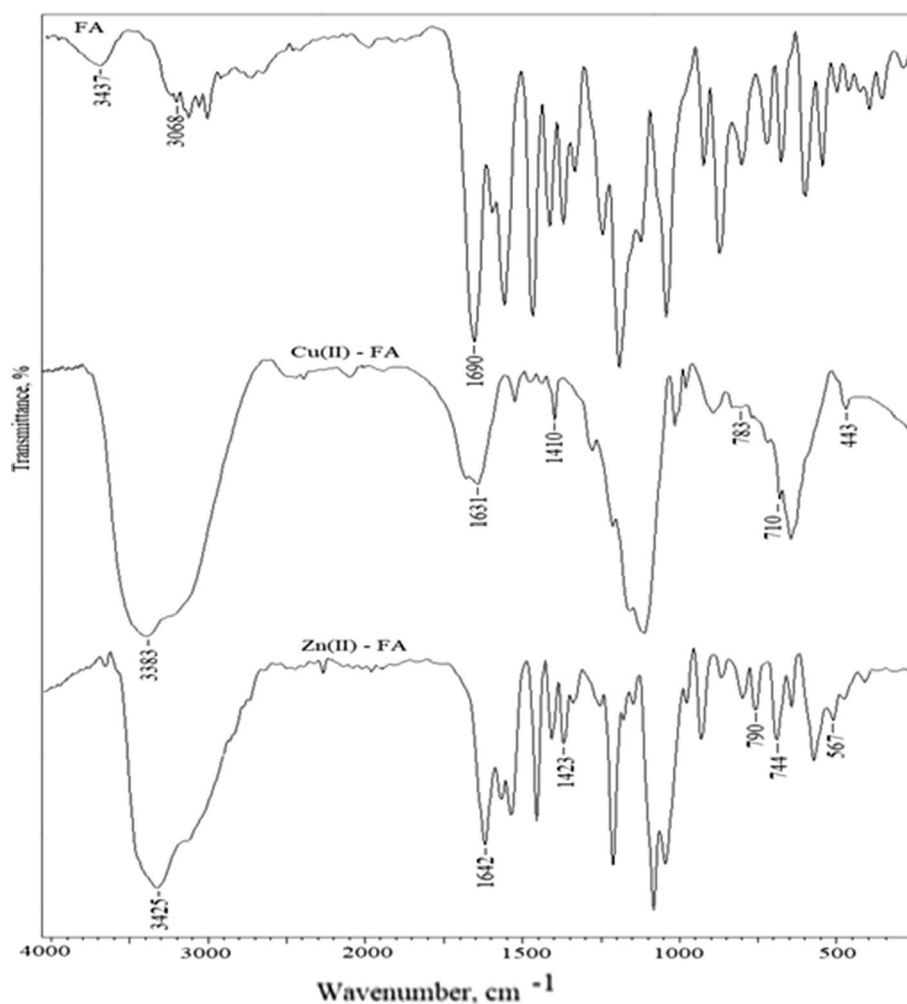
Table 3 Some selected Infrared frequencies (cm^{-1}) and tentative assignments for (A) FA; (B) $[\text{Cu}(\text{FA})_2]\text{SO}_4 \cdot 3\text{H}_2\text{O}$ and (C) $[\text{Zn}(\text{FA})_2]\text{SO}_4 \cdot \text{H}_2\text{O}$

A	B	C	Assignments
3437 m, br	3383 m, br	3425 m, br	$\nu(\text{O}-\text{H})$; aromatic
3068 m	–	–	$\nu(\text{O}-\text{H})$; COOH
1690vs	–	–	$\nu(\text{C}=\text{O})$; COOH
–	1631 s	1642vs	$\nu_{\text{as}}(\text{COO}^-)$
–	1410 ms	1423 ms	$\nu_{\text{s}}(\text{COO}^-)$
–	783 m	790 s	$\delta_{\text{b}}(\text{COO}^-)$
–	710w	744 s	
–	443 m	567w	$\nu(\text{M}-\text{O})$

Keys: s=Strong, w=Weak, v=Very, m=Medium, br=Broad, ν =Stretching, δ_{b} =Bending

group $\nu(\text{O}-\text{H})_{\text{COOH}}$ stretching vibrations at 1690 and 3068 cm^{-1} , respectively (Table 3). The infrared spectra of the two complexes were compared with those of the free ligand in order to determine the site of coordination that might be involved in chelation. On coordination to a metal, the ligand bands were shifted to lower or higher frequencies with concomitant variation in intensity (Fig. 3) (Kalinowska et al. 2014). In the spectra of Cu(II) and Zn(II) chelates, the positions and intensities of various aromatic peaks were modified, and the peaks ascribed to carboxylic group vibrations vanished. Two extremely strong peaks were found at 1631, 1642 and 1410, 1423 cm^{-1} attributed to $\nu(\text{COO}^-)$ asymmetric and symmetric stretches, respectively, with an average $\Delta\nu$ value of $\sim 200 \text{ cm}^{-1}$ suggesting unidentate coordination mode of the carboxylate group (Zordok et al. 2012). A peak at 3437 cm^{-1} in the spectra of FA ligand was ascribed to the stretching $\nu(\text{OH})_{\text{ar}}$ vibrations of the substituent in the ring. This peak was pushed toward lower wavenumber in the spectra of metal chelates ($3383\text{--}3425 \text{ cm}^{-1}$), suggesting that hydroxyl substituents could participate in metal binding. Coordination via oxygen of carboxylate and

Fig. 3 Infrared spectra for FA ligand and its complexes

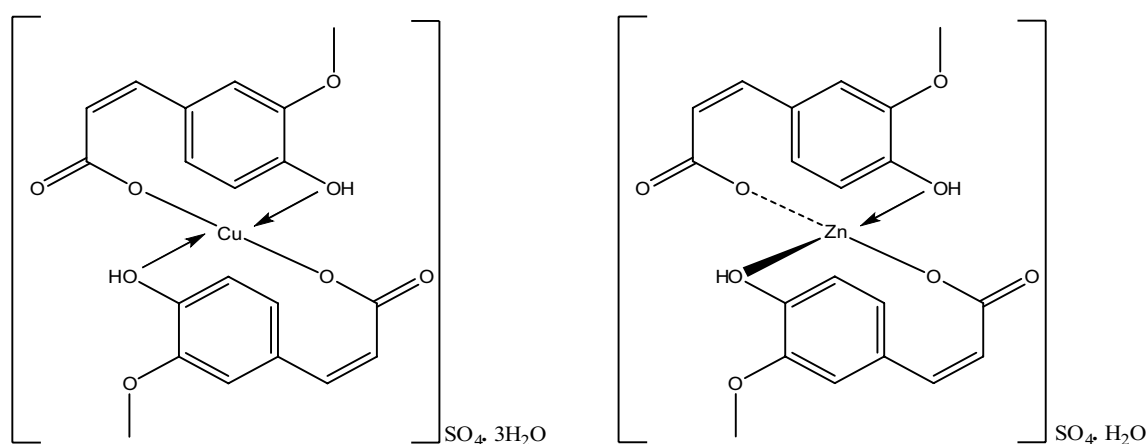


hydroxyl substituent was confirmed by $\nu(\text{M}-\text{O})$ peaks at 443 cm^{-1} for Cu(II) and 567 cm^{-1} for Zn(II) (Zordok et al. 2012). FA was therefore a bidentate ligand that is coordinated with metal via oxygen atoms in carboxylates and hydroxyl substituents (Scheme 1).

Thermal analysis

The stoichiometry of the resultant volatile decaying components as well as the properties of the complexes was studied employing thermal analyses. The TG decay stages with the temperature maximum and weight loss for the complexes were indexed in (Table 4) and presented graphically in (Fig. S2) TG data for FA manifested two stages of decaying with temperature maxima $303\text{ }^{\circ}\text{C}$ and $493\text{ }^{\circ}\text{C}$ with total weight loss amounted to 99.90% (cal. 99.99%). The thermal decomposition of Cu(II) complex showed first stage at $113\text{ }^{\circ}\text{C}$ with a mass loss of 8.37% (cal. 9.00%) due

to removal of three hydrated H_2O molecules. The second step occurred at $145\text{ }^{\circ}\text{C}$ with loss of 16.01% (cal. 15.98%) assignable to elimination of sulfate anion. The third step occurred at $256\text{ }^{\circ}\text{C}$ assignable to elimination of partial decomposition of the organic ligand. The last step at 411 and $450\text{ }^{\circ}\text{C}$ with removal of 19.00% (cal. 19.51%) corresponded to further decomposition of the organic ligand with production of $\text{CuO} + \text{C}$ as final product. For Zn(II) complex, the first step appeared at $90\text{ }^{\circ}\text{C}$ with mass loss 2.98% (cal. 3.18%) was due to removal of hydrated H_2O molecule. The second step started at $259\text{ }^{\circ}\text{C}$ and corresponds to removal of sulfate anion with mass loss of 16.55% (cal. 16.98%). The third one step appeared at $537\text{ }^{\circ}\text{C}$ with partial degradation of the organic ligand with mass loss of 37.69% (cal. 37.49%). The last step at $796\text{ }^{\circ}\text{C}$ with weight loss of 4.49% (cal. 4.59%) assigned to further degradation of the organic moiety leaving $\text{ZnO} + 12\text{C}$ as final residue.



Scheme 1 Coordination mode of FA with Cu(II) and Zn(II)

Table 4 The maximum temperature $T_{\text{max}}(^{\circ}\text{C})$ and weight loss values of the decomposition stages for FA and its metal complexes

Compounds	$T_{\text{max}} (^{\circ}\text{C})$	Weight loss (%)		Lost species
		Calc	Found	
FA	86.61	303	86.82	Decomposition of the organic ligand ($\text{C}_8\text{H}_8\text{O}_4$)
	13.38	493	13.08	Further dissociation of the organic ligand (C_2H_2)
$[\text{Cu}(\text{FA})_2]\text{SO}_4 \cdot 3\text{H}_2\text{O}$	9.00	113	8.37	Loss of hydrated $3\text{H}_2\text{O}$ molecule
	16.01	145	15.98	Loss of sulfate anion
	40.19	256	40.00	Decomposition of the organic ligand ($\text{C}_{10}\text{H}_9\text{O}_7$)
	19.51	411, 450	19.00	Further dissociation of the organic ligand (C_9H_9) with formation of $\text{CuO} + \text{C}$ as final product
$[\text{Zn}(\text{FA})_2]\text{SO}_4 \cdot \text{H}_2\text{O}$	3.18	90	2.98	Loss of hydrated H_2O molecule
	16.98	259	16.55	Loss of sulfate anion
	37.49	537	37.69	Decomposition of the organic ligand ($\text{C}_7\text{H}_{16}\text{O}_7$)
	4.59	796	4.49	Further dissociation of the organic moiety with formation of $\text{ZnO} + 12\text{C}$ as final product

NMR spectroscopy

The ^{13}C and ^1H chemical shifts were important indicators in the study of the structure of complexes, including FA. In the ^{13}C NMR spectra of the complexes signals corresponding to the carbonyl groups (C9) were not recorded, which shows the COO^- group involvement in the formation of the bonds with metal atoms. The signal of the C4 phenolic groups (147.86 ppm) in the spectrum of Cu(II) and Zn(II) complexes was shifted relative to (146.9, 146.1 ppm), respectively. This showed that the oxygen of the phenolic group was bound with metal atoms in the complexes. The ^1H NMR characteristic signals spectra of FA and Zn(II) complex are given in Table 5. ^1H NMR spectrum of FA showed singlet signals at 12.13 and 9.56 ppm due to carboxylic (COOH) and phenolic (OH) protons, respectively. For complex Zn(II), ^1H NMR spectrum exhibited singlet signal at 8.84 ppm due to phenolic proton (Fig. S4). This shift indicated the participation of the phenolic group in complex formation. On the other hand, the carboxylic proton was absent in the spectrum of complex supporting the participation of the deprotonated COOH group in coordination to the metal center (Reddy et al. 2016).

Table 5 The ^{13}C NMR and ^1H NMR chemical shifts (ppm) for ferulic acid and metal complexes (atom numbering in Fig. 1)

Atom position	Ferulic acid	Cu(II)	Zn(II)
C1	125.73	125.14	126.22
C2	111.06	112.13	111.9
C3	149.02	148.10	147.90
C4	147.86	146.9	146.11
C5	115.57	115.99	116.8
C6	122.79	122.9	123.01
C7	144.49	144.01	147.9
C8	115.47	111.55	112.33
C9	167.98	–	–
C10	55.61	56.1	55.99
Ha	12.13	–	–
Hb	6.36	–	6.33
Hc	7.28	–	7.40
Hd	7.08	–	7.23
He	3.81	–	3.88
Hf	9.56	–	8.84
Hg	7.48	–	7.44
Hh	6.78	–	7.01

Spectrophotometric analysis of ferulic acid and its metal complexes in the solution

Electronic absorption spectral study

The assignments of electronic absorption bands of ferulic acid reagent and its metal complexes were measured in alkaline medium within the range of 200–800 nm against the blank solution, (Fig. 4). It was observed that Zn(II) and Cu(II) with ferulic acid reagent formed colored complexes in alkaline medium using borate buffer (pH = 10.0) for Zn(II) complex and using phosphate buffer (pH = 8.0) for Cu(II) complex with maximum absorbance values at 395 and 415 nm, respectively.

Optimization of analytical conditions

Various factors have been taken to select the optimal required conditions for the quick formation and stability of the studied complexes.

Effect of pH and buffer solutions

The pH effect on the formation of the complexes was investigated by using 0.1 M NaOH and 0.1 M HCl solutions, and the appropriate pH value was modified using a pH meter within the pH range of 1.0–12.0. It was observed that the suitable pH range for complete formation of the complexes was from pH = 7.0 to 11.0, (Fig. 5). Also, the absorbances were steadily decreased in more acidic or more alkaline solutions which can be attributed to incomplete formation and partial dissociation of the complexes. In order to fix the pH of the media, the effect of different buffer solutions (borate, phosphate and universal) was investigated. It was

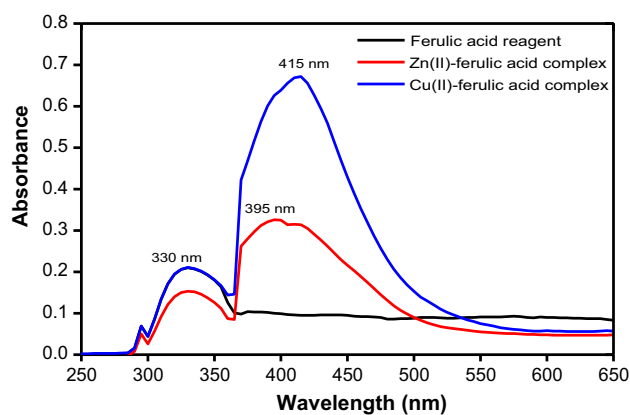


Fig. 4 Absorption spectra of ferulic acid (2.0×10^{-4} M) against buffer blank; Zn(II)-ferulic acid and Cu(II)-ferulic acid complexes against the reagent blank; Where, Zn(II) or Cu(II) = (1.0×10^{-4} M) and ferulic acid (2.0×10^{-4} M). The used excess of ferulic acid decreased the absorbance intensity of the complexes

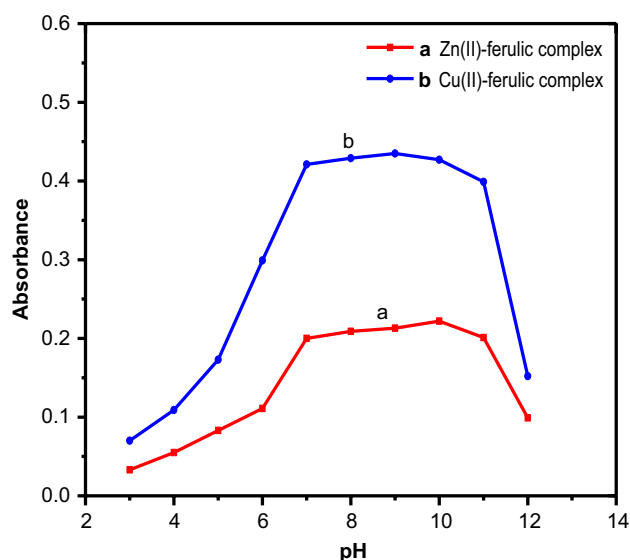


Fig. 5 Effect of pH on the formed complexes, Zn(II) or Cu(II) (1.0×10^{-4} M), ferulic acid (2.0×10^{-4} M)

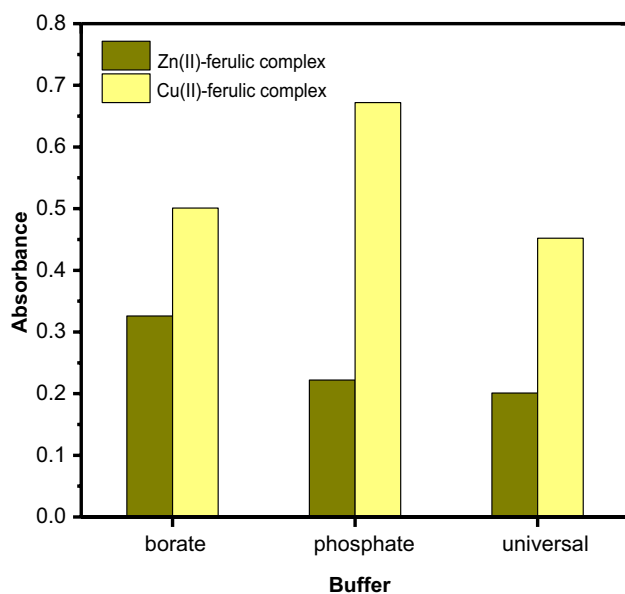


Fig. 6 Effect of different buffers on formed complexes, Zn(II) or Cu(II) (1.0×10^{-4} M), ferulic acid (2.0×10^{-4} M)

observed that the maximum absorbance and color intensity of the complexes were achieved using 5.0 mL borate buffer (pH = 10.0) and 4.5 mL phosphate buffer (pH = 8.0) for Zn(II) and Cu(II) complexes, respectively, (Fig. 6).

Effect of reagent concentration

The reagent concentration effect was tested by measuring the absorbance of the solutions containing fixed concentration 1.0 mL of (1.0×10^{-3} M) of metal ion [Zn(II) or Cu(II)]

and varying concentrations (0.5–4.0 mL of 1.0×10^{-3} M) of ferulic acid reagent. Additionally, the highest absorbance was observed using 2.0 mL of (1.0×10^{-3} M) of ferulic acid reagent. The excess of ferulic acid up to 2.0 mL of (1.0×10^{-3} M) reduced the absorbance intensity.

Effect of surfactants

In order to increase the sensitivity of the complexes, the influence of various concentrations varying between 0.2 and 2.0 mL (1.0×10^{-2} M) of the abovementioned surfactants was tested. The absorbance values were increased by many surfactants but the maximum values were observed using 1.2 mL (1.0×10^{-2} M) of CPB for Zn(II) complex and by 1.0 mL (1.0×10^{-2} M) of SLS for Cu(II) complex, (Fig. 7).

Other conditions (order of the addition, time and temperature)

The effect of the order of addition on the performance of the spectrophotometric measurements was investigated to choose the most appropriate one for the maximum absorbance values of the formed complexes. It was evident that the order (metal ion-ferulic acid reagent-buffer-surfactant) results in maximum absorbance values. In addition, the influence of temperature on the absorbance measurements was studied from 5.0 to 85.0 °C. It was found that the absorbance values of the complexes were increased between 20.0 and 45.0 °C; then, the decrease in the absorbance was noticed between 45.0 and 85.0 °C, (Fig. 8). Thus, the absorbance measurement at room temperature was fine. Finally, the influence of time on the stability of the formed complexes was tested within the range of 0.0–120.0 min and after 24, 48 h. The results indicated that the complexes were formed spontaneously, but they reached their maximum absorbance values after 15.0 min for Zn(II) and Cu(II) complexes. Also, the complexes remained stable for a long time about 48 h, (Fig. 9).

Stoichiometric ratio of the reaction

Job's method of continuous variation (Job 1928) was applied to determine the molar ratio between metal ion and ferulic acid reagent. In this method, an equimolar solutions of metal ion [Zn(II) or Cu(II)] and reagent were mixed in different proportions from 0.1 to 0.9 mL (1.0×10^{-3} M) of the same concentration, whereas the total molar concentration was held constant. The absorbance was measured at the recommend wavelengths and plotted against mole fraction, (Fig. 10). The results showed that the ratio was found to be 1:2 for both complexes.

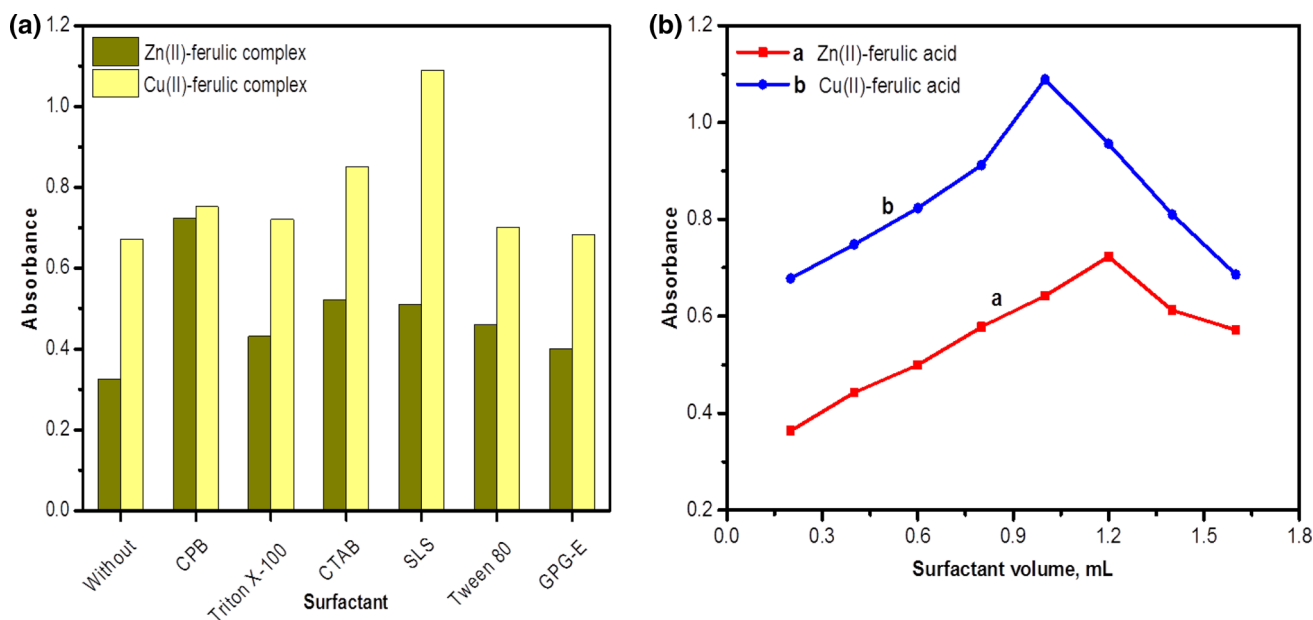


Fig. 7 a Effect of surfactants type and b surfactant volumes on the formed complexes [Zn(II) or Cu(II)= 1.0×10^{-4} M, ferulic acid= 2.0×10^{-4} M]

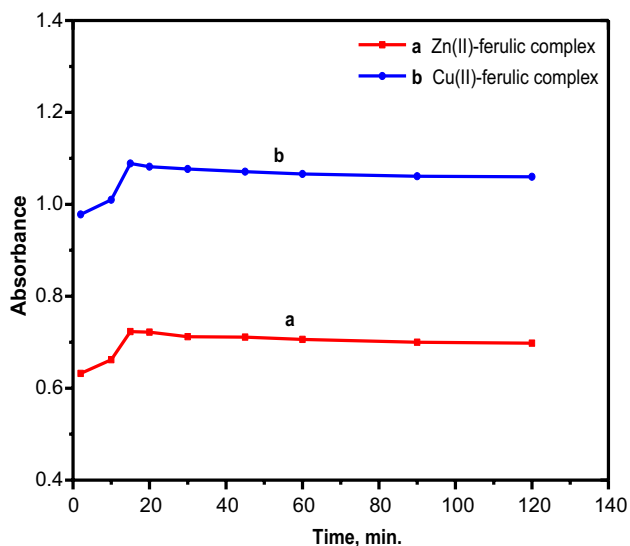


Fig. 8 Effect of time on the formed complexes Zn(II) or Cu(II) (1.0×10^{-4} M), ferulic acid (2.0×10^{-4} M)

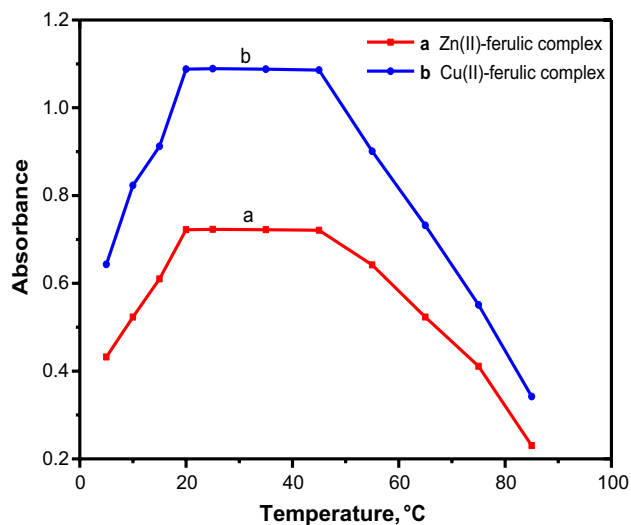


Fig. 9 Effect of temperature on the formed complexes Zn(II) or Cu(II) (1.0×10^{-4} M), ferulic acid (2.0×10^{-4} M)

Stability constant of the complexes

The stability constant of the complexes was calculated from Job’s method by the following equation (Tirmizi et al. 2012).

$$K_f = \frac{[A_2/A_1]}{[1 - A_2/A_1] \times [C_L - C_M \times A_2/A_1]}$$

where A_1 = absorbance at break point, A_2 = actual absorbance, C_M = concentration of metal and C_L = concentration of ligand. The stability constants of the complexes were found to be 2.771×10^5 and 2.826×10^5 for Zn(II) and Cu(II) complexes, respectively.

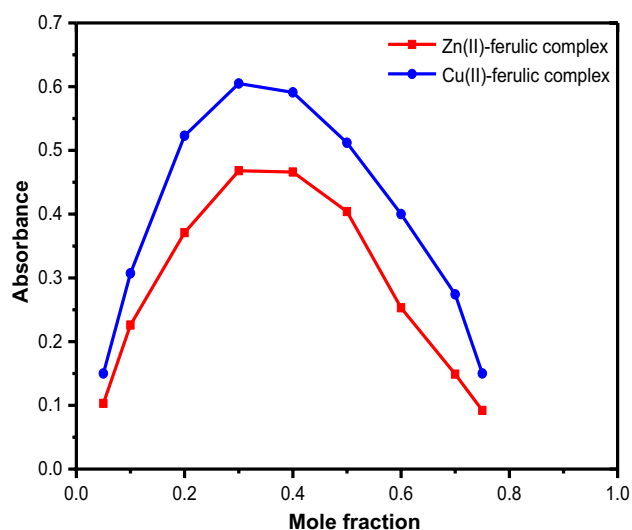


Fig. 10 Stoichiometry of the complexes by Job's method, [metal ion] = [ferulic acid] = 1.0×10^{-3} M

Calibration curve and analytical characteristics of the proposed spectrophotometric methods

The calibration graph of the investigated complexes was made from the absorbance measurements which performed using the abovementioned optimized conditions. Good linear relationship was obtained in the concentration range of 2.0–70.0 and 4.0–140.0 $\mu\text{g mL}^{-1}$ for Zn(II) and Cu(II) complexes, respectively, (Fig. 11). A Ringbom plot was also conducted to select the optimum concentration range for the system that obeyed Beer's law. It was achieved at intermediate concentration values of (8.0–60.0 $\mu\text{g mL}^{-1}$) and (10.0–120.0

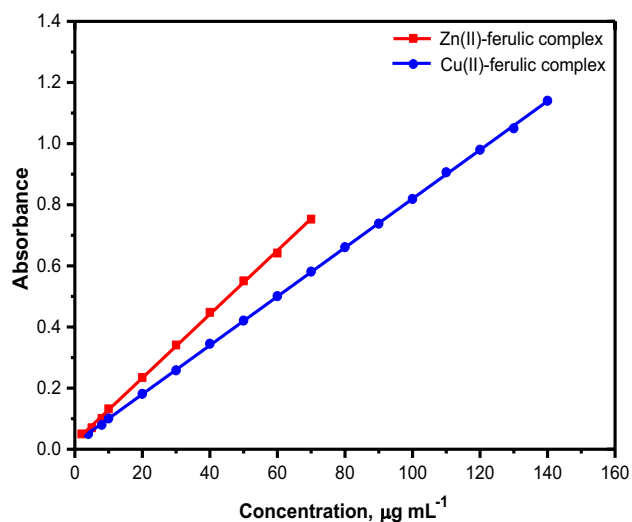


Fig. 11 Calibration curves of the complexes

$\mu\text{g mL}^{-1}$) for Zn(II) and Cu(II) complexes, respectively. The spectrophotometric methods have good reproducibility for a set of seven measurements of (40.0 $\mu\text{g mL}^{-1}$) of Zn(II) and (60.0 $\mu\text{g mL}^{-1}$) of Cu(II) under optimum conditions. Some statistical parameters were calculated to show the high sensitivity, excellent linearity and good accuracy and precision of the proposed spectrophotometric methods as indicated in Table 6.

Effect of foreign ions (Interferences)

The effect of some foreign ions which were added relative to (40.0 $\mu\text{g mL}^{-1}$) of Zn(II) and (60.0 $\mu\text{g mL}^{-1}$) of Cu(II) was investigated (Fig. S3). Then, the absorbance was measured according to the abovementioned procedures. The tolerance limit was defined as the amount of foreign species causing $< \pm 5\%$ error in the absorbance values. The tolerance limits of different foreign ions that were likely to interfere during the spectrophotometric methods are indicated in Table 7. It was found that Al^{3+} , Ba^{2+} , Cd^{2+} , Ca^{2+} , Mn^{2+} , Hg^{2+} , Sn^{4+} , Ce^{3+} , Co^{2+} , Cr^{3+} , La^{3+} , Mg^{2+} , Ni^{2+} , K^+ , Li^+ , Na^+ , Sm^{3+} , As^{3+} , Pb^{2+} , Mo^{6+} , U^{6+} , Nd^{3+} , Pr^{3+} , Gd^{3+} , Y^{3+} , Th^{4+} , Ga^{3+} , Bi^{3+} , Se^{4+} , V^{5+} , Cl^- , CO_3^{2-} , NH_4^+ , SO_4^{2-} , NO_3^- , PO_4^{3-} , $\text{S}_2\text{O}_3^{2-}$ and CH_3COO^- did not interfere, while Pd^{2+} , Cu^{2+} , Sr^{3+} , Fe^{3+} interfered with Zn(II)-ferulic complex. Also, Pd^{2+} , Zn^{2+} , Fe^{3+} , Sn^{4+} , Sr^{3+} interfered with Cu(II)-ferulic complex. Fe(III) was masked by using urea (Park et al. 2001). The methods were selective and free from most interfering ions. The results indicated the possible use of the proposed methods for the determination of Cu(II) and Zn(II) in diverse samples.

Table 6 Analytical data of the proposed spectrophotometric methods

Parameter	Zn(II)	Cu(II)
Linearity, $\mu\text{g mL}^{-1}$	2.0–70.0	4.0–140.0
Ringbom plot, $\mu\text{g mL}^{-1}$	8.0–60.0	10.0–120.0
Standard deviation (SD)	0.00721	0.002708
Relative standard deviation (RSD %)	0.0180	0.004513
Standard error of the mean (SEM)	0.00272	0.001023
Molar absorptivity (ϵ), $\text{L mol}^{-1} \text{cm}^{-1}$	1.3161×10^4	8.826×10^3
Sandell's sensitivity, $\mu\text{g cm}^{-2}$	0.00496	0.00719
Limit of detection (LOD), $\mu\text{g mL}^{-1}$	2.2833	1.1184
Limit of quantification (LOQ), $\mu\text{g mL}^{-1}$	6.9193	3.3892
Student <i>t</i> test	4.0365	1.9540
Correlation coefficient	0.9997	0.9999
Intercept (<i>a</i>)	0.02485	0.02031
Slope (<i>b</i>)	0.01042	0.00799
S.D. of slope (S_b)	8.0056×10^{-5}	2.104×10^{-5}
S.D. of intercept (S_a)	0.00301	0.00168

Table 7 Effect of foreign ions on the proposed spectrophotometric methods

Foreign ions	Zn(II)-ferulic complex	Cu(II)-ferulic complex
	Tolerance limit ($\mu\text{g mL}^{-1}$)	
K^+ , Li^+ , PO_4^{3-} , Ag^+	5000	5000
Al^{3+} , Ba^{2+} , Cd^{2+} , Mo^{6+} , Ga^{3+}	4000	4500
Sn^{4+} , Ce^{3+} , Co^{2+} , SO_4^{2-}	3500	3000
Ca^{2+} , Mg^{2+} , Ni^{2+} , Mn^{2+} , Se^{4+}	3000	2500
La^{3+} , Sm^{3+} , U^{6+} , As^{3+} , Gd^{3+} , Y^{3+}	2500	2300
V^{5+} , Pb^{2+} , Cl^- , CH_3COO^-	1900	2000
Na^+ , Fe^{2+} , Zn^{2+} , NO_2^- , Bi^{3+}	1800	1900
Cr^{3+} , CO_3^{2-} , NH_4^+ , Pr^{3+} , Th^{4+}	1600	1000
Hg^{2+} , $\text{S}_2\text{O}_3^{2-}$, NO_3^- , Nd^{3+}	1000	900
Sn^{4+}	900	70
Pd^{2+} , Sr^{3+}	40	50
Fe^{3+}	35	45
Zn^{2+}	–	30
Cu^{2+}	25	–

Analytical applications

The proposed spectrophotometric methods were applied for the determination of zinc and copper in industrial sample (brass alloy), vegetables samples (spinach, broccoli), biological sample (human blood) and water samples (waste water, sea water, tap water) under all optimum conditions. The analytical results of these samples are given in Table 8. Good recoveries in the range from 99.70 to 100.50% were obtained for zinc and copper in these samples, demonstrating the accuracy of the proposed methods. The results showed

Table 8 Determination of Zn and Cu in some industrial, biological, vegetables and water samples

Metal	Samples	suggested method ^a for metal ions		Recommended method ^b ($\mu\text{g mL}^{-1}$)	Recovery %	RSD % ($n=5$)
		Taken ($\mu\text{g mL}^{-1}$)	Found ($\mu\text{g mL}^{-1}$)			
Zn	Brass alloy	34	33.93	33.85	99.79	0.211
	Spinach	16	15.96	15.89	99.75	0.249
	Broccoli	15	15.04	14.97	100.26	0.112
	Blood	18	17.95	17.88	99.72	0.278
	Waste water	45	44.88	44.90	99.73	0.270
	Sea water	25	24.94	24.89	99.76	0.240
	Tap water	15	15.02	15.05	100.13	0.103
C	Brass alloy	66	65.91	65.85	99.86	0.140
	Spinach	14	14.03	14.08	100.21	0.106
	Broccoli	10	10.05	10.13	100.50	0.156
	Blood	16	15.97	14.89	99.81	0.192
	Waste water	50	49.86	49.79	99.72	0.281
	Sea water	30	29.90	29.86	99.70	0.295
	Tap water	10	10.04	9.99	100.40	0.103

^aSuggested method for determination of Zn and Cu with ferulic acid reagent

^bRecommended method (Fabre and Reynes 2010)

good agreement with that obtained from the recommended method and prove the applicability of the proposed methods. As a result, we can infer that the methods can be widely used for the determination of zinc and copper in a variety of models with excellent precision, selectivity and sensitivity.

Comparative study of the suggested methods with other reported detectability spectrophotometric methods

The performances of the suggested methods were compared with that of the other existing UV–visible spectrophotometric methods (Table 9). It was clear from the table that the suggested methods were simple, selective, not complicated and required less time to complete the analysis more than many other spectrophotometric methods. The other advantages of the proposed methods were their sensitivity and their wider linear ranges. Moreover, the methods were free from many interfering ions.

Microbial applications

To estimate the biological potential of the FA and their metal complexes were tested against different bacterial strains. The ferulic acid ligand (FA) has no effect against *Escherichia coli*, *Citrobacter*, *Salmonella Typhi*, *Staphylococcus aureus*, *Bacillus cereus* and *Listeria monocytogenes* bacteria. The results in Table 10 and Fig. 12 revealed that the newly synthesized complexes have noticeable bactericidal activity and their activities increased when complexed with the metal ions. This indicated that chelating agents inhibit bacterial growth when complexes with many metals. The assessments of biological activity of the newly

Table 9 Comparison of the suggested methods with other reported detectability spectrophotometric methods for the determination of Cu(II) and Zn(II)

Reagent	λ_{\max} (nm)	pH	Beer's law ($\mu\text{g mL}^{-1}$)	Molar absorptivity ($\text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$)	References
1-((4-(1-(2-hydroxyphenylimino)ethyl)phenyl)diazanyl)naphthalene-2-ol (HPEDN) for Cu(II)	500.0	9.0	1.7–5.4	0.5038×10^4	Raafid et al. (2020)
4-amino-3-mercaptop-6-[2-(2-thienyl)vinyl]-1,2,4-triazin-5(4H)-one (AMT) for Cu(II)	434.0	4.5	0.7–25.0	1.90×10^4	Alharthi and Al-Saidi 2020
Cefixime for Cu(II)	336.0	4.68	1.015–8.122	8.29×10^3	Lutfullah et al. 2010
4-(2-thiazolylazo)resorcinol (TAR) for Cu(II) and Zn(II)	200.0–500.0	5.0–10.0	2.0–20.0	–	Rahmani et al. 2015
2-hydroxy-5-(2-hydroxynaphthalen-1-yl)diazanyl benzoic acid for Zn(II)	500.0	7.0	1.0–18.0	1.516×10^4	Alabidi et al. 2021
2-hydroxy-N'-(1-(pyridin-2-yl)ethylidene) benzohydrazide (HPEBH) for Zn(II)	351.0	5.0	0.653–6.53	6.27×10^4	Reddy et al. 2016
pyridoxal thiosemicarbazone (PDT) and 2-acetyl pyridine thiosemicarbazone (2-APT) for Zn(II)	430.0 and 360.0	5.0–7.0 and 8.0–10.0	0.26–2.62 and 0.25–2.56	1.8×10^4 and 2.9×10^4	Admasu et al. 2016
Ferulic acid (FA) for Zn(II) and Cu(II)	430.0 and 465.0	10.0 and 8.0	2.0–70.0 and 4.0–140.0	1.3161×10^5 and 8.826×10^4	Present work

Table 10 Antibacterial activity values of the synthesized compounds

Compounds	Microbial species					
	<i>S. aureus</i>	<i>Listeria</i>	<i>E. coil</i>	<i>Citrobacter</i>	<i>Salm. typhi</i>	<i>B-cereus</i>
FA	0	0	0	0	0	0
Cu(II)-FA	$11.3^{3+} \pm 1.5$	$1.5^{+1} \pm 0.11$	$3^{+1} \pm 0.6$	$1.9^{+1} \pm 0.22$	$1.5^{+1} \pm 0.7$	$4.0^{+2} \pm 0.4$
Zn(II)-FA	$2.5^{+1} \pm 0.1$	$0.5^{\text{NS}} \pm 0.2$	$1.0^{\text{NS}} \pm 0.1$	$3^{+2} \pm 0.02$	$1.0^{+1} \pm 0.3$	$3.5^{+2} \pm 0.7$
Control (DMF)	0	0	0	0	0	0
Amoxycillin/Clavulanic	1.9 ± 0.3	1 ± 0.02	1.7 ± 0.11	1.4 ± 0.05	0	0

Statistical significance P^{NS}; P not significant, $P < 0.05$; P⁺; P significant, $P > 0.05$; P⁺; P highly significant, $P > 0.01$; P⁺; P very highly significant, $P > 0.001$; student's *t* test (Paired)

synthesized complexes were performed compared with FA ligand. Cu(II) complex was found to have the highest activity against all the tested organisms relative to all compounds. The sequence of inhibitory capacities growth was: Cu(II) > Zn(II) > Amoxycillin/Clavulanic > FA (for *S. aureus*), Cu(II) > Amoxycillin/Clavulanic > Zn(II) > FA (for *Listeria*), Cu(II) > Amoxycillin/Clavulanic > Zn(II) > FA (for *E. coil*), Cu(II) > Zn(II) > Amoxycillin/Clavulanic > FA (for *Citrobacter*), Cu(II) > Zn(II) > Amoxycillin/Clavulanic > FA (for *Salm. typhi*), Cu(II) > Zn(II) > Amoxycillin/

Clavulanic > FA (for *B-cereus*). We concluded from these results that metal complexes have a remarkable activity against pathogenic bacteria and that explained on the basis of chelation theory the chelation could facilitate the ability of a complex to cross a cell membrane of the pathogens and also ease their diffusion through the lipid layer of spore membrane to the site of action and ultimately killing them (El-Shwiniy et al. 2020; Okulik and Jubert 2005; Zaky and Yousef 2011; Mohamed and Sharaby 2007).

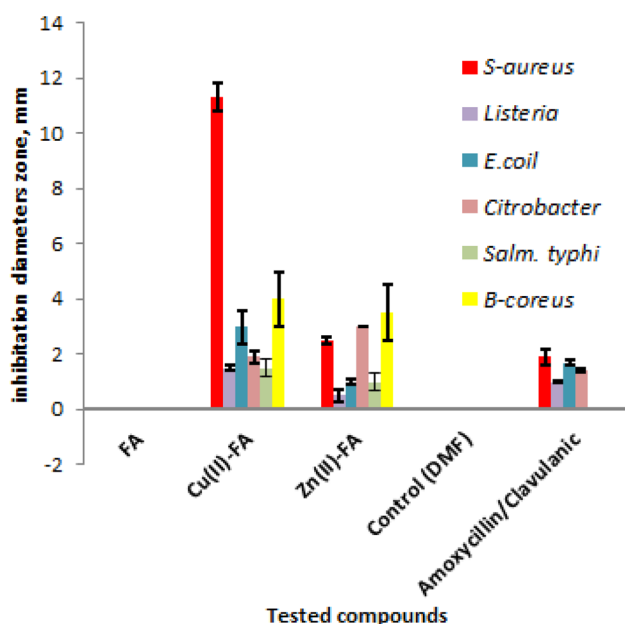


Fig. 12 Biological activity statistical representation for FA and its complexes

Conclusion

This work studied new spectrophotometric methods for the determination of Zn(II) and Cu(II) by forming colored complexes with ferulic acid. The suggested methods revealed high sensitivity, accuracy, precision and good reproducibility. These methods were successfully applied for the determination of zinc and copper in brass alloy, blood, spinach, broccoli, sea water, waste water and tap water. We introduced the synthesis and characterization of novel Zn(II) and Cu(II) complexes containing FA as ligand. Based on the results of the physicochemical and spectral techniques, the data showed that FA acted as a bidentate with metal ions. The results revealed that Cu(II) complex was the more active. The potential antimicrobial effects of the new metal complexes indicated that they could be used effectively.

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Data availability The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Informed consent All authors consent to publication.

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