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Antibacterial and antioxidant activities of curcumin/Zn metal complex with its chemical characterization and spectroscopic studies

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ABSTRACT

Curcumin is an active component of the rhizome turmeric. Curcumin/zinc (Cur/Zn) complex was synthesized and characterized using the elemental analysis, the molar conductance, FT-IR, UV–Vis,^{1}HNMR, scanning (SEM), transmission electron microscopy (TEM) and X-ray diffraction (XRD). The molar conductance value is very low, referring to the absence of Cl^{-} ions inside or outside chelate sphere confirming non electrolytic nature. Based on IR and electronic spectra curcumin C═O group in enol form chelated to Zn (II) ion. The surface morphology of curcumin chelate with Zn showed elevated in particle size and irregular grains shaped with elongated morphology. Transmission electron microscopy revealed that the curcumin chelate with Zn has spherical black spots like shape with particle size range from (33–97 nm). The antioxidant activities of curcumin and Cur/Zn complex were assessed. Results showed that the Cur/Zn complex showed potent antioxidant activities than curcumin. For antibacterial activity, Curcumin/Zn showed inhibitory effect against both (+ve and –ve) gram bacteria (*Bacillus subtilis* and *Escherichia coli*) at very low concentration. Cur/Zn recorded antibacterial and inhibition activity at 0.009 against *E. coli* and at 0.625 against *B. subtilis*. Cur/Zn complex showed higher capacity in scavenging the ABTS radical, FARAP capacity and metal chelating activity than curcumin itself and it showed more scavenging and inhibition activity for DPPH. The synthesized complex of Cur/Zn showed potent antioxidant and antibacterial activities than curcumin itself and it may benefit in treatment of aging and degenerative diseases with elevated and excessive production of free radicals.

1. Introduction

From kitchen to clinic, several health benefits related to curcumin as an agent against AlZheimer disease. Curcumin is an essential active compound of the turmeric, manufactured from *Curcuma longa* rhizome. *Curcuma longa* belongs to *Zingiberaceae* (ginger) family. Curcumin is an essential active compound of curcuminoids that give curcumin its distinguished shinny yellow color and it is used mainly as a food flavoring [1].

Besides curcumin widespread use as a food flavoring, turmeric has been used in traditional Chinese medicine. It has been recognized that curcumin benefits of Alzheimer's patients, especially in rural India, who eat curry dishes [2,3].

Most recent studies have examined the medicinal therapeutic effects of active compound curcumin, including antimicrobial,

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antioxidant, antihyperlipidemic, anti hepatotoxic and anti-inflammatory effects [4,5]. Curcumin either alone or loaded with other compounds or drugs have been previously reported to inhibit the progression growth of cancer cells and afford the apoptotic effects on cancer cells beside reversing the chemoresistance [5].

Thus, curcumin induced great improvement of the cytotoxic effects induced by diverse chemotherapeutic drugs on the immature cancer cells. Curcumin has a lot of health benefits and many therapeutic actions [6].

More recently, curcumin metal-complexes have attracted the attention around the world. Curcumin complexes have a lot of properties as compared to curcumin alone. Curcumin, is a yellow polyphenol. It is one of the essential active compounds of the curcuminoids [7].

Curcumin is used as a spice in a lot of Asian countries as a flavor and color in food and also used as a traditional alternative medicine against a lot of chronic diseases, including autoimmune, metabolic, cardiovascular and other types of diseases [7,8]. The therapeutic effects of curcumin is attributed to its potent pharmacological properties as it has hypoglycemic, antiinflammatory, antioxidant and antimicrobial properties [9].

With all mentioned features, curcumin was used as an active ingredient in many products such as: Antiaging, but there are limitations against its use only due to intense yellow pigmentation and poor solubility in water in addition to its instability and degradation by either heat or light [10].

Thus, there is urgently need for new metal complexes of curcumin with other inorganic metals as the solubility and drug release time of curcumin metal complex can be enhanced after its complexation with transition metal as Zinc [11].

Zinc (Zn) is considered as one of the essential trace metals. Zn plays a high role in the cellular mechanism. Zinc induces antiviral activity against SARS-CoV-2 [12]. Zinc oxide nanoparticles has many antibacterial applications and a lot of anticancer properties [13].

Synthesis of active novel compounds is very important due to their different applications in this era for many and applied applications [14]. Recently, a new class of coordination polymers, such as Metal Organic Frameworks have shown potent promising capabilities for broad range of applications [15].

Gram positive and gram negative families of bacteria are highly epidemic and may be the main cause of respiratory infectious disease [16]. There are a lot of limitations for antibacterial and antifungal drugs as they becomes resistant to these bacterial strains [16]. The emergence of multi-drug resistant is the current issue now a days [17]. The current study have been established to explore the inhibitory activities of Cur/Zn complex.

The slogan of the world become back to nature due to high health benefits of natural compounds and thus this study focused on resolving the gap between natural active compounds and complexation of these active compounds with inorganic metals to elevate its efficacy with minimizing any side effects, this concept will enhance the therapeutic actions of curcumin itself and thus benefits from these complexes in treatment of several diseases resulted from oxidative stress with high antibacterial activities. It is proved that oxidative stress is one of the major causes that contributes more to the physiological alterations [18].

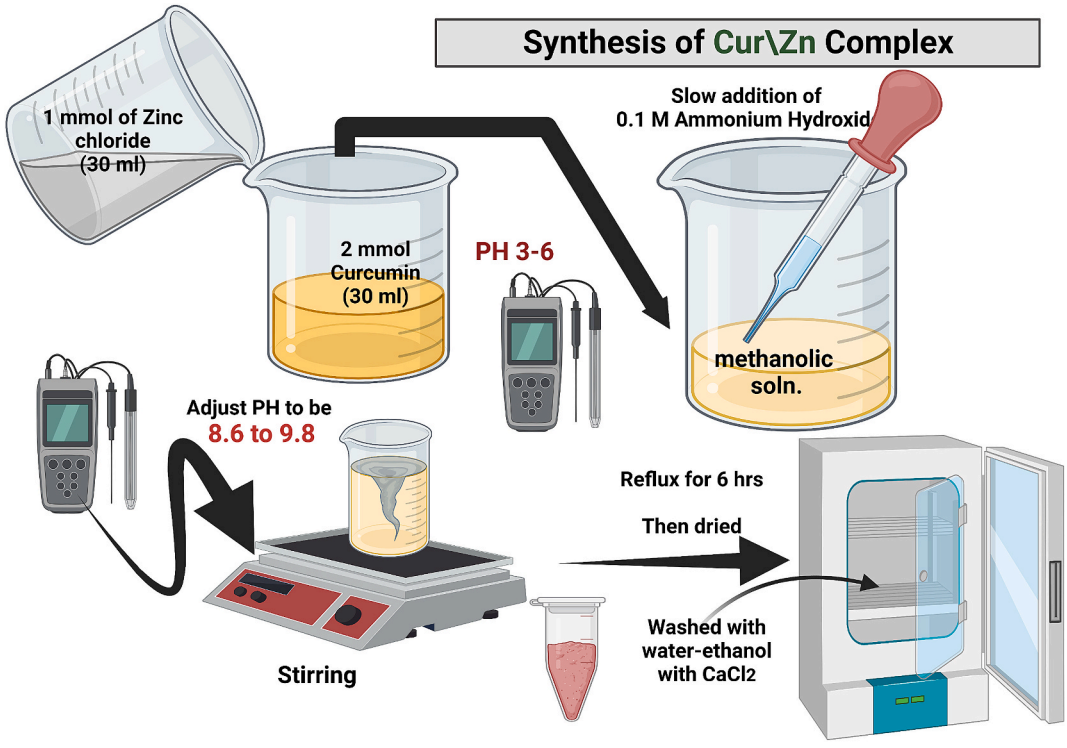


Fig (1). Synthesis of Curcumin/Zn complex.

Thus, the objective of the current study was to complex curcumin with Zn transition metal and make chemical characterization for the prepared complex with assessment of its antibacterial and antioxidant activities.

2. Materials and methods

2.1. Chemicals

Chemicals used were received from Fluka and Aldrich Companies with high degree of purity. Curcumin (Cur) and Zinc(II) chloride, other chemicals used as it is without purification due to high purity rate, such as: Ethanol (HPLC-grade), Ammonium hydroxide, anhydrous calcium chloride, DPPH reagent and agar broth meda).

2.2. Synthesis of curcumin complexity

Curcumin-Zinc (Cur/Zn) complex was synthesized as (Fig. 1) by using aqueous methanol solution at 80C°. The synthesis of Cur/Zn performed by adding $ZnCl_2$ (1 mmol) to ethanolic solution of curcumin (2 mmol, 30 mL) with molar ratio (Zn (II):Curcumin) was 1:2. The pH of the resulted solution was ranged between 3 and 6. By using a solution of (0.1 M ammonium hydroxide), the pH was adjusted to be within 8.6–9.8 to reach the complete chelation. Followed by stirring and refluxing at 80 C° for 10–20 min. The resulted solid complex was isolated, filtered, then washed with a mixture of (water, ethanol) for 3 times and finally, the complex was dried under vacuum over anhydrous $CaCl_2$.

2.3. Measurements

The elemental analyses C, and H were performed by using the microanalysis using a PerkinElmer CHN 2400 (USA). The conductivity measurements for curcumin chelates carried out for solution of 1×10^{-3} mol/cm^3 using dimethylsulfoxide (DMSO) and were measured using Jenway conductivity meter. The electronic absorption spectra of cur complexity were recorded in DMSO solvent within 800–200 nm range using UV/Vis Spectrophotometer. The infrared spectra were recorded on a Bruker FT-IR Spectrophotometer (4000–400 cm^{-1}). The ^{1}H NMR spectra were recorded on Varian Mercury VX300 NMR spectrometer. The morphological surface were estimated by a scanning (SEM) and transmission (TEM) electron microscopes generated at 20 kV, where the shapes and sizes were visualized using JEOL 100s microscopy. The X-ray diffraction patterns for Cu (II) Cur complexity were recorded on analytical X-ray powder diffraction with secondary monochromatic.

2.4. Preparation of Zn^{2+}Curcumin complex for determination of it's stability

A homogenous powder of Cur/Zn was obtained using mortar ($ZnCl_2$ was mechanically mixed with curcumin (Zn^{2+}: Curcumin 1:1 mol). Then (1:1 v/v) solution of $MeOH/H_2O$ was added to the complex, then gentle shaking was made at 25–27 °C until a complete complexation was produced. Drying of the complex at 60 °C until evaporation of water has occurred. Ethanol was removed by washing with distilled water then a Powder of Cur/Zn complex is formed.

2.5. Antibacterial activity against (B. Subtilis and E.coli)

Using a fresh agar-culture plate, a scoop from a broth was gently streaked into agar culture and incubated at 30 °C. 2 mL from either curcumin and cur/Zn were directly inoculated into the first well (without dilution); 1 mL was aspirated and then transferred to the next well filled with 1.0 mL Muller Hinton Broth. All wells were incubated at 30 °C for 24 h. After incubation, the wells were then completely removed from the incubator and placed on a dark for checking the growth.

2.6. Antioxidant assay activities

2.6.1. ORAC assay

The antioxidant activity of either curcumin and/or curcumin/Zn were carried out based on Liang et al. [19]. 10 μL of either cur and cur/Zn were incubated at 37 °C, for only 10 min with 30 μL fluoresceine. Measurement at (485 nm) for only 1 h.

2.6.2. Metal chelation assay

This assay was carried out as mentioned previously by Santos et al. [20], 20 μL of $FeSO_4$ (0.3 mM) was prepared freshly, were mixed with either 50 μL of Cur and 50 μL Cur/Zn complex. 30 ;μL of ferrozine (0.8 mM) were added to the well. The decline in the color intensity measured at 562 nm by using spectrophotometer.

2.6.3. DPPH assay

The antioxidant activity of either Cur or Cur/Zn were measured by using DPPH assay as previously mentioned by Boly et al., [21]. 100 μL of DPPH reagent was added, the reaction was then incubated at 25–27 °C for about 1/2 h in the dark. The measurement was recorded at 540 nm.

2.6.4. ABTS assay

The ABTS antioxidant assay was carried out by Arnao et al. [22]; 192 mg of ABTS were dissolved in dist. Water and then the volume was completed to 100 mL with dist. water. For about 1/2 h in dark. The decline in ABTS color intensity was measured at 734 nm.

2.7. Statistical analysis

Statistical analysis was done by using SPSS software and post hoc power were used. Significant value was recorded at ($P < 0.05$).

3. Results

3.1. Microanalytical with the conductance studies

The complexation of curcumin with and Zn (II) was subjected to elemental analysis. Carbon, hydrogen confirming that the reaction molar ratio is 1:2 (Zn:Curcumin). For zinc (II) complex. The curcumin complexity structure are also elucidated using: data of (infrared, electronic spectra, ^{1} H NMR, SEM and TEM. The conductance measurement for zinc Curcumin solutions of 1×10^{-3} mol/cm^3 in dimethyl sulfoxide solvent Λ_m = is 21 Ω^{-1} mol^{-1} cm^{-1}, which is very low, referring to the absence of Cl^-ions inside or outside chelate sphere confirming non-electrolytic nature [23] and this was confirmed by $AgNO_3$ test.

3.2. Spectral measurements data of curcumin and curcumin metal complexity

3.2.1. Electronic spectra

The UV–Vis spectra for curcumin was shown in Fig. 2A Ethanolic solution of Curcumin showed characteristic UV–visible absorption at 200–800 nm with maximum absorption band at wavelength equal to 425 nm. Band appeared at 260 nm with weak absorption. Owing to dipole electronic allowed excitation type of π-π* due to extended system of conjugation, maximum absorption bands were appeared. Where an electrostatic interaction occurred between (ethanol, polar solvent) and polar chromophores in curcumin, so ethanol make stabilization for bonding electronic ground states and the π* excited states. This interaction causes the n-π* transition to excite to higher energy and π-π* transition to be with lower energy. So absorptions bands, π-π* and n-π* for curcumin move close to each other [24]. While for Zn-Cur complexity as shown in Fig. 2B at 205, 255, 420, 440 nm. The first appeared bands at 205–300 nm referred to transition type of π-π*, while bands existed at region of 300–440 nm can be due to transitions type of n-π* [25]. The ligand cur contain two bands of absorption at 255 and 425 nm, where after complexation the first band shifted to lower while second band shifted to higher value confirming the involvement of the (C═O)carbonyl group of cur/Zn in metal chelation form.

3.2.2. Infrared spectra

For curcumin free ligand, IR spectrum (Fig. 3A and Table 1) showed a shoulder band at 3500 cm^{-1} referring to stretching vibrations of O–H phenolic with a broad band ranged from 3150 to 3500 cm^{-1}, which is attributed to ν(OH) group (in enol form), also a stretching vibration for aromatic (C═C) appeared at 1427 cm^{-1} and for aliphatic chain ν(C═C), was at 1504 cm^{-1}. Other bands were appeared at (720 and 807 cm^{-1}) assigned to the aromatic stretching vibrations of (–C═CH) [26,27]. At 1271 cm^{-1} there is an intense band appeared owing to δ (C–O) bending vibration of OH phenolic group. IR spectra for Zn(II) curcumin chelate as shown in (Fig. 3B) is so close and differ from curcumin ligand. By making a comparison between infrared bands for free ligand curcumin and zinc curcumin

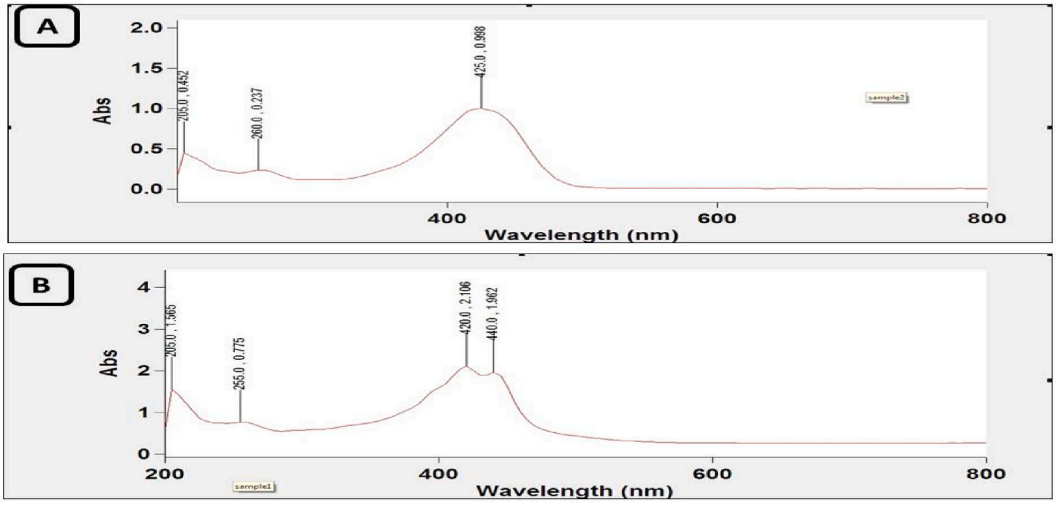


Fig (2). UV spectra of curcumin and curcumin/Zn complex
(A) UV–Vis for Cur (B) UV–Vis for Cur/Zn.

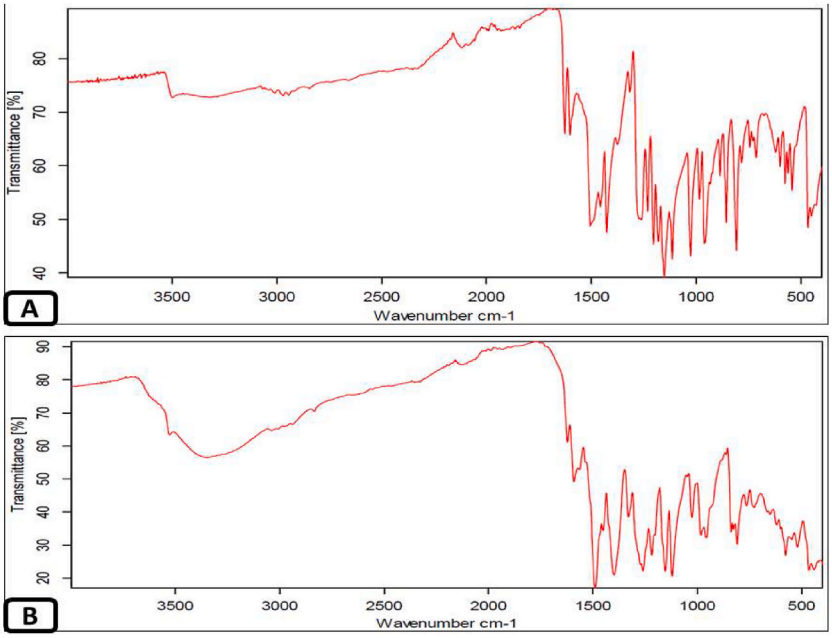


Fig (3). FT-IR of curcumin and Curcumin/Zn metal complex
(A) FT-IR for Cur (B) FT-IR for Cur/Zn.

Table 1
IR bands (cm^{-1}) for cur and Cur/Zn metal chelate.

Compound	ν (O–H)	ν (CO) keto	ν(C═C) aliphatic	δ (CO) enol ν (C═C)aromatic	δ (CO) phenol	δ (C═CH) aliphatic	N (M − O)
Cur	3510	1626 1598	1504	1427	1271	807 770	–
Cur/Zn	3288	1626 1601	1504	1426	1259	806 712	470

complexity it turns out that, the infrared spectrum for free curcumin showed stretching vibration at 1626 and 1598 cm^{-1}which is attributed to ν (C═O), this band is shifted to lower energy in Cur chelates [28], confirming that curcumin C═O group in enol form chelated to Zn(II). Also for curcumin chelate the presence of an intense band in the range 1271–1279 cm^{-1} attributed to bending vibration δ (C–O) of phenolic group, confirming absence of phenolic –OH in the cur complex. The new bands appeared at 454–470 cm^{-1} assigned to stretching frequency of ν (M − O) [29–31]. The broadening band which caused by presence of coordinated or un-coordinated water molecules, the stretching vibration of phenolic hydroxyl group cannot be recorded at range of 3200–3500 cm^{-1}.

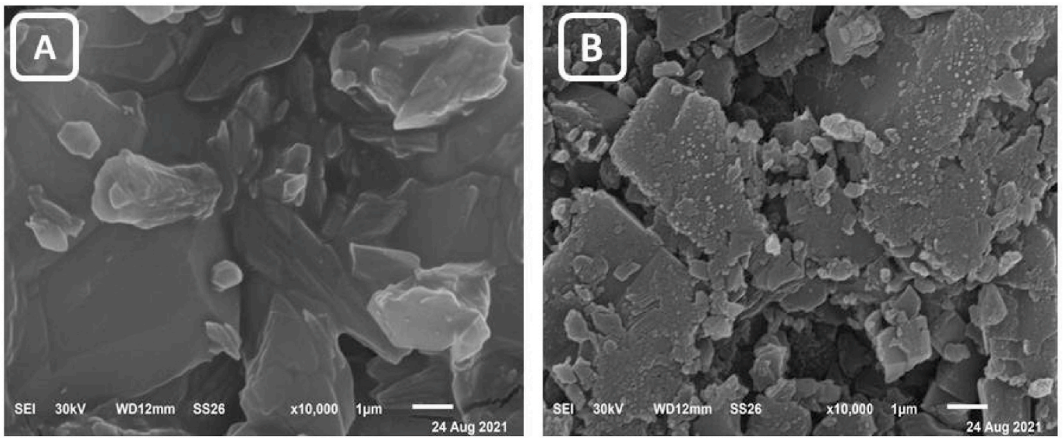


Fig (4). SEM of (A) curcumin and (B) curcumin/Zn metal complex.

For Zn- complexity, the presence of molecules of H_2O is confirmed by appearance of band at ~3400 cm^{-1} and other bands appeared at 500–600 cm^{-1} and 900 cm^{-1} referred to metal-water bond [32].

3.2.3. ^{1}HNMR

The ^{1}HNMR for free curcumin ligand the chemical shifts [33]: 2.51 (DMSO), $\delta = 3.36$ (H_2O; moisture water), $\delta = 3.85$ (3H; $AOCH_3$), d = 6.07 (1H; Carbon1), d = 6.73 (1H; Carbon 3), d = 6.82 (1H; Carbon 9), d = 7.17 (1H; Carbon 10), d = 7.33 (1H; Carbon 6), $\delta = 7.59$ (1H; Carbon 4), $\delta = 9.66$ (1H; AOH) and $\delta = 10.05$ (1H; AOH enol). For Zn(II), δ (ppm): 2.406 (Dimethylsulfoxide), $\delta = 3.634$ (H_2O), $\delta = 3.816$ (3H; $–OCH_3$), $\delta = 5.570$ (1H; Carbon 1), $\delta = 6.665$ (1H; Carbon 3), $\delta = 6.795$ (1H; Carbon 9), $\delta = 7.178$ (1H; Carbon 10), $\delta = 7.245$ (1H; Carbon 6), $\delta = 7.322$ (1H; Carbon 4), $\delta = 9.547$ (1H; -aromatic OH) for (1H; enolic –OH) $\delta =$ disappeared. In the spectrum of Zn (II), protons of aromatic ring CH and diene of –CH system have shifted owing to changes in the produced complex configuration. The signal of –OH enol group disappeared owing to chelation between -Oxygen-calcium. At 2.00 ppm, the peaks appeared may be due to moisture or any impurities in chemicals used, and they dos not change after complexation between metal ions and curcumin [33].

3.3. Scanning electron microscopy (SEM)

The surface morphology for the free ligand curcumin Fig. 4A and its synthesized zinc chelate Fig. 4B was clarified by SEM analysis. The crystals of Zn(II) curcumin complexity, have particles differ in shapes and size. The free curcumin ligand has Solid pieces with protrusions shape while for the curcumin chelate shows the agglomeration of particles with a morphological controlled structure and the presence of small grains in non-uniform size.

After agglomeration, images of curcumin chelate showed increased in particle size and irregular grains shaped with elongated morphology. The particles of the Zn(II) was in the range of 0.15 μm microns. These particles of zinc complexity is with the range of nano size structure.

3.4. Transmission electron microscopy (TEM)

Describing for TEM images for curcumin (Fig. 5A) and synthesized Zn(II) curcumin complexity (Fig. 5B). The orderly matrix of zinc chelate of curcumin in the pictograph was clarified. This confirm that Cur/Zn complex has a homogeneous material. Spherical black spots were noticed in the Zinc(II) curcumin chelate with particle size of 33–97 nm.

3.5. XRD of cur/Zn complex

For Cur/Zn complexity, the XRD patterns are in Fig. 6 and Table 2. The analysis of XRD was used mainly to elucidate the involvement of copper elements in the complex. According to these patterns, we can confirm that Cur/Zn complexity and crystalline structure formed. By using the Deby-Scherrer equations (Eq. (1) and Eq. (2)) and by applying (FWHM) of prominent intensity peak (100% relative intensity peak) for main characteristic peaks, the size of the complex crystallinity can be calculated [34]. Where symbol D is the size of a particle of crystal gain, K is the value of Cu grid 0.94 which is constant, and λ wavelength which is 1.5406 Å, θ is the position of the peak and β is the width of the integral peak. Based on the highest intensity value and by making a comparison with other peaks, the size particle can be calculated. According to obtained data, the particle size is within the range of 33–97 nm.

$$D = \frac{K\lambda}{\beta \cos\theta} \tag{1}$$

$$\beta = \frac{\lambda}{D \cos\theta} - \varepsilon \tan\theta \tag{2}$$

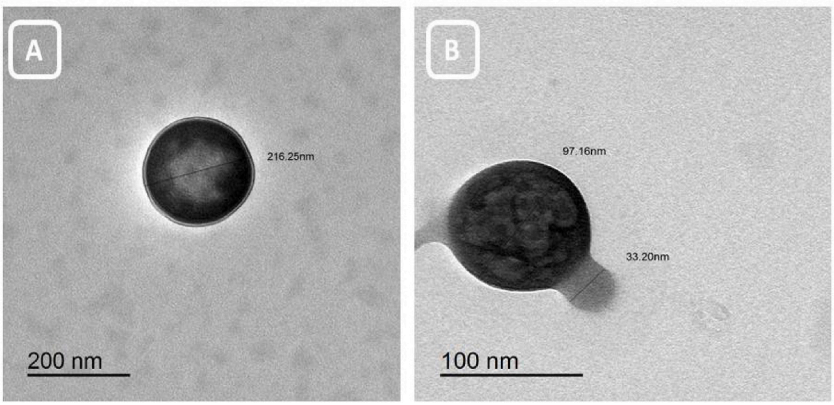


Fig (5). TEM of (A) curcumin and (B) curcumin/Zn metal complex.

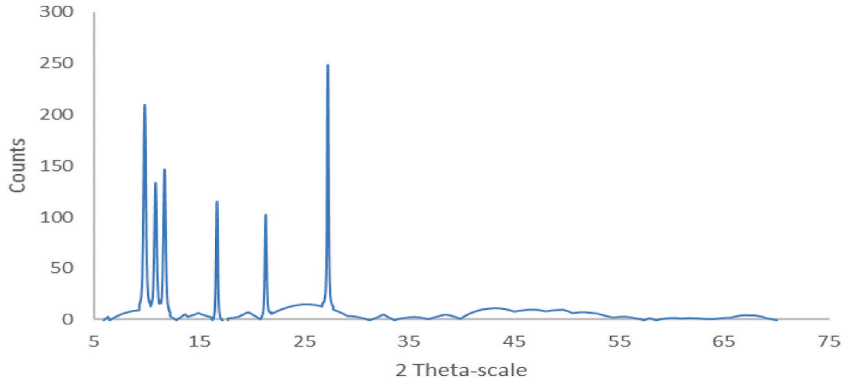
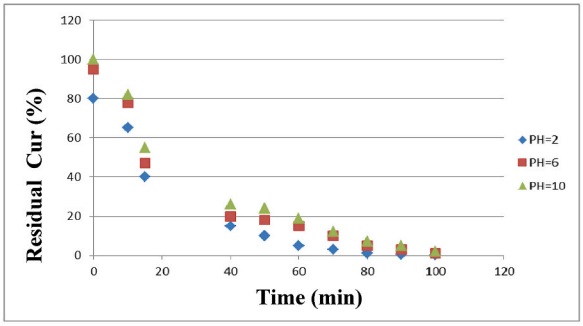


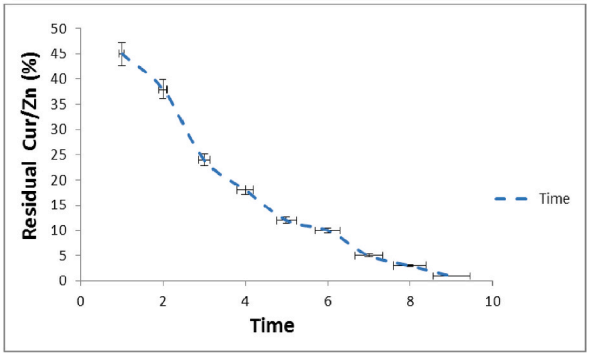
Fig (6). XRD of Cur/Zn complex.

Table (2)
XRD data of Cur/Zn complex.

Pos. [°2 Th.]	Height [cts]	FWHM [°2 Th.]	d-spacing [Å]	Rel. Int. [%]
9.9011	198.44	0.2496	8.92624	84.39
10.9299	123.83	0.2496	8.08828	52.66
11.8001	139.29	0.2496	7.49368	59.24
16.7704	116.37	0.1872	5.28225	49.49
21.4127	98.86	0.1872	4.14640	42.04
27.3158	235.14	0.1560	3.26226	100.00



A: Kinetic degradation of curcumin (Cur) at different PH values of 0.1 M buffer solution at 35C°.



B: Kinetic degradation of Cur/Zn complex at different PH values of 0.1 M buffer solution at 35C°.

Fig (7). Kinetic degrdation of (A) Curcumin and (B) Curcumin/Zn.

Since the dislocation density and strains are the appearance of the dislocation network in the complexes. The dislocation density (δ) was evaluated as Eq. (3).

$$\delta = \frac{1}{D^2} \tag{3}$$

3.6. Stability determination

3.6.1. Curcumin

The stability of Cur is poor [35]. When Cur is exposed to sunlight it may decompose [36]. By adding 0.1 M PBS, pH = 7 to Cur, most of the Cur was decomposed after only 1 h. At different pH values ranges from (2–10) buffer solutions were assayed for this degradation (Fig. 7A). explains the kinetics of degraded curcumin at different pH values, at 35C°, by using UV/visible spectrophotometer. The percent of concentration for the residual curcumin versus time was linear at all tested pH values, confirming presence of degradation at 35C° [37]. For acidic pH conditions, high stability of curcumin due to conjugated diene structure. However a proton will be removed from OH phenolic group at conditions of neutral-basic pH.

3.6.2. Cur/Zn complex

The kinetics of cur/Zn complex was performed in different pH buffers. In acidic media, Zinc complex is decomposed as $Zn(Cur)_2$ (total) + $2H^+ = Zn^{2+} + H_2Cur$ (degraded). It was found that zinc Cur complex is very stable in pure water up to 25 h at 35 °C. The complex is decomposed at acidic pH 2 (Fig. 7B) and its dissociation was decreased at pH 10, confirming that the stability of the complex depends on the amount of H+. In acidic buffer, dissociation was found to be 90%). And reaches to equilibrium constant after 14 h. By comparing stability zinc complex with curcumin at time interval, is much higher. Due to at PH = 2 curcumin was degraded completely after only 2 h.

3.7. Antioxidant activities of curcumin and curcumin/Zn metal complex

The chelating activity carried out by using different analysis methods, are shown in Table 3. ABTS, FRAB, DPPH and Metal chelation methods were obtained. The capacity of Cur/Zn complex to scavenge the ABTS radical (Fig. 8 A), FARAP (Fig. 8B) capacity and metal chelating activity was higher than curcumin itself, the same as the chelating activity of Cur/Zn was higher than Curcumin itself (Table .3).

On the other hand, the highest scavenging ability was for Cur/Zn by recording lower absorbance than curcumin itself and thus more scavenging and inhibition for DPPH. Thus, this metal complex with greatest chelating capacity than curcumin itself (Table .3) and (Fig. 8C).

3.8. Antibacterial activity evaluation

Biological assessment was performed of Cur/Zn metal complex against Gram- + ve (*Bacillus subtilis*) and Gram-ve (*Escherichia coli*) bacteria. Results for the antimicrobial activities of curcumin and its metal complex with Zn are shown in Table .4 and Fig. 9. The minimum inhibition concentration of curcumin/Zn metal complex against both Gram-positive and negative bacteria respectively, were found to have inhibitory and antibacterial activity at low concentrations at a very low concentration at 0.009 against *E. coli* and inhibitory effect at 0.625 against *B. subtilis* for curcumin/Zn.

4. Discussion

Previously, it was suggested that the OH group of Cur is essentially responsible for the scavenging property against excessive production of free radicals and Curcumin/Zn (II) complex can be considered as a mimic for antioxidant enzyme (SOD) superoxide dismutase activity and thus, it can scavenge the free radicals [38–40].

IR-studies of Curcmin/Zn metal complex has afforded that the phenolic –OH group of Curcumin is not involved in the complexation with Zn. Hence, the Curcumin-Zn complex not only responsible for the antioxidant property of Curcumin but also may enhance scavenging of the free radical properties than curcumin itself.

The metal complex of Curcumin/Zn possessed better action to decline oxidative stress series [41] that could be the cause for a lot of degenerative diseases. The Curcumin/Zn complex was shown to inhibit bacterial activity at minimum concentration [42].

The stoichiometry of metal: ligand and the geometry of curcumin/Zn metal complex is also important for its antioxidant property.

Table (3)
Antioxidant activity of curcumin and its metal complex with Zn (Curcumin/Zn).

Sample test	FRAB (μM eq/mg)	Metal Chelation (μM EDTA eq/mg)	ABTS (μM trolox eq/mg)	DPPH (μM trolox eq/mg)
Curcumin	7.85 ± 1.34	9.05 ± 1.74	102.78 ± 8.13	304.18 ± 14.62
Cur/Zn	1240.16 ± 100.24	739.27 ± 90.14	2217.85 ± 105.23	228.89 ± 14.11

Trolox eq: Trolox equivalents; SD: Standard deviation.

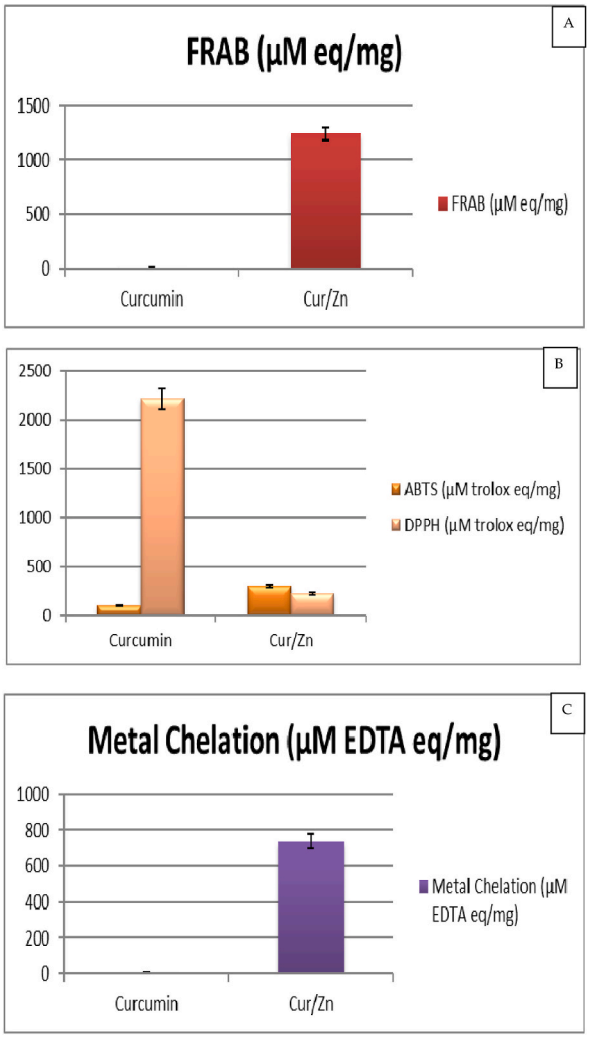


Fig (8). Antioxidant activity of Curcumin and curcumin/Zn metal complex (DPPH, ABTS, FARAB and Metal chelation).

Table (4)
Minimum inhibitory concentration (mg/ml sample) of Curcumin and its metal complex with Zn.

Sample	Minimum inhibitory concentration (mg/ml)	
	Bacillus subtilis (ATCC6633)	*Escherichia coli* (ATCC8739)
Control (DMSO)	0.0 ± 0.00^{c}	0.0 ± 0.00^{c}
Curcumin	1.25 ± 0.14^{a}	2.5 ± 0.31^{a}
Curcumin/Zn	0.625 ± 0.014^{b}	0.009 ± 0.002^{b}

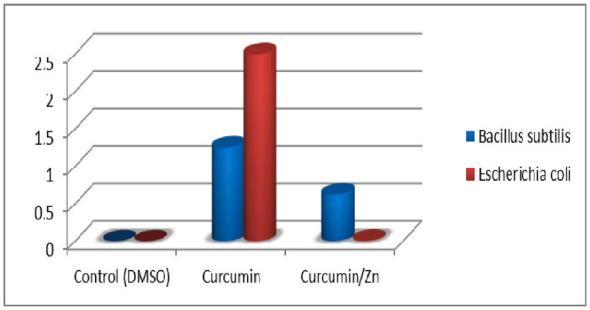
Means were expressed as (mean ± SE) and significant where ($p \leq 0.05$) using Duncan's range test, as the highest value has (a) symbol and declining in values were assigned alphabetically.

Barik et al. [39] have suggested that the Curcumin with transition metal complex is more effective as antioxidant agent and mimic the essential antioxidant enzyme (super oxide dismutase) which play an essential role as a potent antioxidant agent.

The results of the current study were in agreement with previous study of Thakam and Saewan [10] who proved that curcumin with transition metal complexes have more antioxidant activities than curcumin itself and scavenge DPPH than ligand itself as proved in the current study.

In accordance with the previous studies, previously Curcumin–barium (Ba^{2+}) complex has been shown to elevate and enhance the stability of curcumin more than 50% and similar results were obtained in the current study for curcumin/Zn complex. The stability of curcumin was found to be elevated to about 70% in curcumin complex as a pluronic micelles [43].

Another complex of curcumin/pd metal complex was synthesized to increase the solubility and stability of curcumin. Cur/Zn



Fig(9). Antibacterial activity of curcumin and curcumin/Zn metal complexes.

complex also enhanced it's cellular uptake as compared to curcumin alone [44].

Curcumin with Ag nanoparticle elevates the stability of curcumin in complexes. Curcumin decline the size of silver nanoparticles and thus elevates curcumin solubility [43]. Curcumin/oxidovanadium(IV) complex has shown high solubility of curcumin after 48 h when Cl-metals were used in the synthesis and formation of curcumin complexes [44]. Banerjee et al. [45] demonstrated that the complexation of curcumin with oxovanadium moiety resulted in more stability against any degradation of curcumin. A Mn^{2+}/curcumin complex was also bio-synthesized and proved the same results. Mn^{2+}/curcumin complex was reported to be more stable in the physiological normal saline [46].

The curcumin/gallium elevates the stability and bioavailability of curcumin in both in vitro and in vivo cancer models [47]. All these studies proved the success of the stability and potent antioxidant activities of curcumin/Zn and it may enhance immune activities due to potent action of Zinc metal as it help in elimination of viruses from the cells and thus enhance the antioxidant activities and antibacterial activities.

Curcumin can inhibit the bacterial virulence, inhibit the bacterial biofilm formation and prevent the bacterial adhesion to the host cellular receptors via the bacterial quorum regulation system. Curcumin has many properties, including faster metabolism, low cellular toxicity, low intestinal absorption [48] which confirm its potent applications as an antibacterial agents. Curcumin exhibits bactericidal activity and can be used combined with other substances to elevate its antibacterial properties [49]. Previous studies have shown that curcumin has strong antibacterial activity against both (Gram + ve and Gram –ve) bacteria [50]. Curcumin can inhibit the bacterial growth by targeting the bacterial growth, bacterial cell wall, bacterial cell membrane, DNA, protein and other cellular structures [50]. Curcumin is a photosensitizer and exerts high anti-bactericidal effects on different bacteria under blue light excitation. Additionally, curcumin may exhibit synergistic effects with other bacteriostatic substances in combined therapies to elevate antibacterial properties such as Zinc metal (Zn).

Zinc exhibits marked antimicrobial activities as Zn can interact with bacterial core and its surface where Zn can enter inside the bacterial cells, and exhibits distinct bactericidal mechanisms [51] this findings confirm the current finding by the great ability of Cur/Zn complex in inhibition of bacterial growth.

For different antibacterial mechanisms, at the gene level, curcumin can downregulate the bacterial gene expression and enhance the DNA damage to achieve the potent bacteriostatic effects [52].

Additionally, Mun et al. [53] found that curcumin has a potent significant and potent antibacterial effects on the levels of bacterial protein. Furthermore, curcumin affect the permeability of the cytoplasmic membranes located in the cytoplasm of gram (-ve) and gram (+ve) bacterial cells [53] these results come parallel with the current finding that prove that antibacterial activity of Cur/Zn against *Bacillus subtilis* and *Escherichia coli* at low concentration.

Curcumin disrupts the associated membrane proteins and the permeability of bacterial cell membranes. Damage to the cell membrane and increased the cellular permeability can elevate the sensitivity of bacteria to other antibiotics [54]. Curcumin combined with the bacterial peptidoglycan to disrupt the bacterial complete membrane, leading to the cellular lysis [55].

5. Conclusions

(Cur/Zn) metal complex was bio-synthesized and characterized by using elemental analysis, molar conductance, IR, UV-spectra, ^{1}HNMR, scanning, transmission electron microscopy and XRD. The current results confirmed that Cur/Zn metal complex was efficient with potent antioxidant capacities for alleviation of excessive production of free radicals and consequence oxidative stress series via confirmation by different antioxidant analysis as (ABTS, DPPH, metal chelation and FRAB). Cur/Zn complex showed potent inhibition and antibacterial activity against two strains of bacteria (*Bacillus subtilis and Escherichia coli*). These results open new gate for treatment of diseases result from severe oxidative stress as Alzheimer and other related oxidative stress diseases due to high antioxidant and antibacterial activities of Cur/Zn metal complex.

Author contribution statement

Eman Al-Thubaiti: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data included in article/supplementary material/referenced in article.

Additional information

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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