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Synthesis, Characterization and Antibacterial Studies of Mono and Binuclear Copper (II) Complexes of 1, 10- Phenantroline using Ethylenediamine as Spacer

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Abstract
Copper is a biologically important element, and several enzymes that rely on it to function have been discovered. However, drug-resistant bacteria are a major problem in the medical world, which causes high mortality rates and increases in health care costs, economic losses. The multidirectional effort has been put to overcome the concern as well as discover new drug molecules. In this aspect, the complexation of organic compounds with metal ions increases the therapeutic potency of the organic compounds. Herein, mono $[Cu(Phen)_2Cl]Cl.H_2O$, and binuclear $[Cu_2(en)(Phen)_4]Cl_4$ complexes were synthesized and characterized with the help of ICP-OES, FT-IR, and UV-Vis spectroscopic techniques. The synthesized complexes are proposed with square pyramidal geometries. Moreover, the complexes are characterized by molar conductance measurement, melting point measurement, solubility test, and halide test. Based on the in vitro antibacterial testing, both complexes are biologically active in all studied microorganisms, including the most drug-resistant Klebsiella pneumonia, Surprisingly, the complexes are water-soluble, and the solubility of the synthesized complexes could be viewed as a potential therapeutic application following in vivo cytotoxicity studies.
Keywords: 1, 10- phenanthroline, ethylenediamine, Cu (II) complexes, and antibacterial activities
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1. INTRODUCTION

Drug resistance bacterial is a major problem in medicine, resulting in high mortality rates, increased healthcare expenses, and economic losses (Abebe & Hailemariam, 2016; Ghatole, Lanjewar, & Gaidhane, 2012; Tigineh, Abiye, Melese, & Abebe, 2021). As a result, a multifaceted effort has been made to address the issue as well as identify novel therapeutic compounds. In this regard, employing a suitable ligand is possible to impose a set of desired attributes on transition metals for a specific application, such as solvophilicity, electrophilicity, and nucleophilicity (Abebe & Tamiru, 2018; Vidhisha, Reddy, Kumar, Srijana, & Satyanarayana, 2014). The selection of appropriate metal ions and ligands for antimicrobial applications is a tuning property (Ghatole et al., 2012). Copper metal ions, 1, 10- phenanthroline, and ethylenediamine ligands are used in this study.

Copper is an important element in biology, and it has been revealed that is essential for the activity of some enzymes (Mahalakshmi & Raman, 2016). When utilized as a ligand, the lone pairs of electrons provided by the two nitrogen atoms make ethylenediamine as a chelating ligand for coordination compounds(Abebe, Atlabachew, Liyew, & Ferede, 2018); in medical investigations, it has been used as an antibacterial agent(Shahabadi & Mahdavi, 2013, Abebe, Atlabachew, Liyew, & Ferede, 2018)

The 1, 10-phenanthroline ligand exhibited the greatest antibacterial action due to its planar shape (M. D. Hossain et al., 2017; Shahabadi & Mahdavi, 2013; Singh, Kumar, Puri, & Singh, 2012; Sunitha, Jogi, Ushaiah, & Kumari, 2012). However, it could not be employed directly for medicinal applications due to its higher cytotoxicity, which is caused by its strong chelating nitrogen atoms interacting with biometals and inhibiting metalloenzymes (Fayad et al., 2013). Hence coordinating with metal ions to reduce toxicity is a way for lowering toxicity (Abebe et al., 2020). Lewis basicity causes 1, 10-phenanthroline to coordinate with the Lewis acid (Cu^{2+} ion) merely works as a drug carrier to transfer the active metal ion in this process (Fayad, Al-Noor, Mahmood, & Malih, 2013; Gomleksiz, Alkan, & Erdem, 2013).

The synthesis and characterization of mixed ligand complexes of copper with 1, 10-phenanthroline, and other ligands have been documented in the literature (M. D. Hossain et al., 2017; Shahabadi & Mahdavi, 2013; Singh, Kumar, Puri, & Singh, 2012; Sunitha, Jogi, Ushaiah, & Kumari, 2012; Fayad et al., 2013; Abebe & Tamiru, 2018; Vidhisha, Reddy, Kumar, Srijana, & Satyanarayana, 2014). The synthesis and characterization of copper (II) complexes of 1, 10-phenanthroline with ethylenediamine as a spacer, however, has yet to be published. As a result, this research aims to make mono- and binuclear copper (II) complexes of 1, 10-phenanthroline using ethylenediamine as a spacer, characterize them, and look into their antibacterial activities.

2. MATERIALS AND METHODS

2.1. Chemicals

1, 10-phenanthrolinemonohydrated (BDH Chemical Ltd., Poole, England, > 99 percent), $CuCl_2.4H_2O$ (Analar BDH, > 98 percent), ethylenediamine, silver nitrate (BLULUX Laboratories Ltd., India, > 99 percent), acetone, acetonitrile, chloroform, sulfuric acid (Sigma Aldrich, > 98 percent), methanol (Hi-Media Laboratories).

2.2. Instruments and Methods

A JANEWAY 4200 conductivity meter was used at room temperature with a 10^{-4} M solution of each component in deionized water to estimate the molar conductance (Tamiru et al., 2019). Electronic spectra in the 200-800 nm region were acquired on a Sanyo SP65 UV-Vis spectrophotometer. In the vibrational range of 400- 4000 cm^{-1}, a Perkin Elmer spectrum BX spectrophotometer was used to record Fourier-transform infrared (FT-IR) KBr pellets. Copper content was determined using a PerkinElmer Optima 8000 V HF Version ICP-OES spectrometer after digestion in a complex of concentrated perchloric acid and nitric acid and diluting with distilled water (Tamiru, Abebe, Abebe, & Liyew, 2019). The melting points were determined using an SMP30 digital melting point device. The AgCl precipitate was utilized to make thermal gravimetric chloride measurements (Abebe et al., 2018).

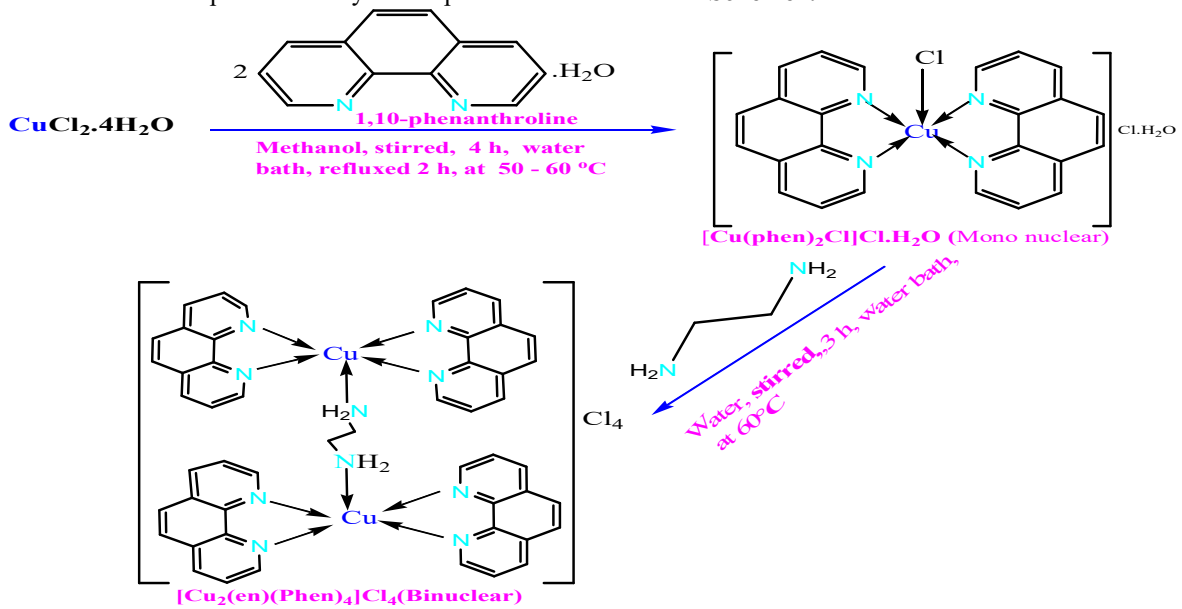
2.3. Synthesis Copper (II) Complexes

2.3.1. Bis(1, 10- Phenanthroline) Copper (II) Chloride Monohydrate, $[Cu(phen)_2Cl]Cl.H_2O$

A dropping funnel was used to introduce a methanol solution of 1, 10-phenanthroline monohydrate (1.74 g, 20 ml) to a methanol solution of $CuCl_2.4H_2O$ (0.75 g, 20 ml) that was magnetically stirred in a water bath (Beyene, B, Mihirteu, Ayana, & Yibeltal, 2020). The mixture was stirred for 4h, yielding a greenish homogenous solution. The mixture was then refluxed for 2 h at 50-60 degrees Celsius. The solvents are removed using a rotary evaporator. The greenish-blue powder was collected and washed three times with acetone to eliminate unreacted 1, 10-phenanthroline (yield: 94 percent, 2.117 g).

2.3.2. Bis(1,10- Phenanthroline) Copper(II)- μ -Ethylenediamine Bis(1,10- Phenanthroline) opper(II) Chloride, $[Cu_2(en)(Phen)_4]Cl_4$

An aqueous solution of ethylenediamine (0.640 g, 0.71 ml) added into an aqueous solution of $[Cu(phen)_2Cl]Cl.H_2O$ (0.994 g, 35 ml) in a 100 ml round bottom flask, and magnetically stirring for 3 h in a water bath at RT (Beyene, B, Mihirteu, Ayana, & Yibeltal, 2020). The blue-black homogenous solution was obtained. The mixture was then refluxed for 1 h at 50-60 degrees Celsius(Abebe et al., 2017). The solvent was then evaporated with a rotary evaporator, and the blue-black powder was collected (Yield: 68 percent, 1.384 g). The overall reaction paths of the synthetic procedures are shown in **Scheme1.**



Scheme1: Synthesis paths of Cu(II) complexes

2.4. Antibacterial Activity Testing

The complexes had good antibacterial activity against the tested bacteria, with inhibition zones ranging from 12.53 ± 3.40 mm to 18.30 ± 1.67 mm and 15.33 ± 1, 36 to 17.60 ± 0.87 mm, respectively (Beyene, B, Mihirteu,

Ayana, & Yibeltal, 2020; Abebe et al., 2018).

The antibacterial activity of the compounds was determined by calculating their MICs. Two Gram-positive bacteria (Staphylococcus aureus and Streptococcus pyogenes) and two Gram-negative bacteria (Escherichia coli and Klebsiella pneumonia) had the lowest MICs (Abebe et al., 2018). Disc diffusion methods were used to investigate them (Abebe & Hailemariam, 2016). The bacteria were grown on Muller Hinton agar (MHA) and nutritive Blood agar (BA), with diagnostic sensitivity tests, carried out on diagnostic sensitivity test agar (Oxoid Ltd BASINGSTOKE England) (Abebe et al., 2017).

The bacteria strains were maintained in the correct blood agar base at 4°C (Abebe et al., 2017). Antibiotic discs gentamicin were used as a control (antibacterial drug gentamycin was evaluated for the antibacterial activities and the result was compared to those of the free ligands and their complexes) (Abebe et al., 2018).

The Minimum Inhibitory Concentration (MIC) of the complex is the lowest medication concentration that inhibits microorganism growth for 24 hours at 37 degrees Celsius. The minimum inhibitory concentration (MIC) against each bacterium was determined by serial dilution of aqueous solutions of complexes (100 mg/L, 150 mg/L, 200 mg/L, 250 mg/L, 300 mg/L, 350 mg/L, 400 mg/L,and 450 mg/L). The antibacterial activities of the examined compounds' were assessed by measuring the growth inhibition zone against the tested microorganisms, and the activity indices (%) of the tested compounds were calculated using the formula(Abebe & Hailemariam, 2016);

$$\% \text{ Activity Index} = \frac{A-B}{B} * 100$$

Where: A - Inhibition zone of tested compounds(average diameter)
B - Inhibition zone for standard compounds (average diameter)

3. RESULTS AND DISCUSSIONS

3.1. Physical Characterization

For the mononuclear complex, a 1:2 mole ratio ($CuCl_2.4H_2O$: 1, 10-phenanthroline), and for the binuclear complex, a 1:1 mole ratio (one mole of the precursor complex: one-mole of ethylenediamine) was used(Abebe & Hailemariam, 2016). The products are stable in the air. Water, methanol, ethanol, acetonitrile, and DMSO are all polar solvents that can dissolve the synthesized complexes. The molar conductance measurements were taken in deionized water for 10^{-4} M of each metal complex solution (Table 1). All complexes are non-electrolytes. However, the lower conductance from the precursor complex to the final complex is a result of increasing molar mass and surface area (Abebe et al., 2017). As a result of the decrease in the kinetic energy given by the electric field from the measurement device, the ion's speed of mobility drops (Abebe et al., 2017; Abebe & Hailemariam, 2016)).

Qualitative chloride estimation; the presence of chloride in the outer sphere of the complexes was indicated by the formation of curdy white precipitate solution after the addition of excess aqueous $AgNO_3$ solution, whereas in quantitative chloride estimation, (Abebe & Hailemariam, 2016); the experimental values of chloride are in good agreement with the theoretical value (Table 1), confirming the achievements of the proposed molecular structure of the complexes. Metal estimation from ICP-OES was found to be in good agreement with a theoretical value, supporting a hypothesized chemical formula for the complexes(Tamiru et al., 2019; Dowarah & Singh, 2020).

Table 1. shows the metal complexs' analytical data

Compounds/color-Appearance	M.wt. (g/mol)	ΛM (Scm^2mol^{-1})	M. Pt. (°C)	Yield (%)	Elemental estimation Calculated (Found) (%)	
					Cl	Cu
$[Cu(Phen)_2Cl]$ Cl .H_2O/ Greenish-powder	512.5	9.4752	216 (Mel)	94	7.08(6.67)	28.83 (28.75)
$[Cu_2(Phen)_4en]Cl_4$ / Blue black-powder	1049	10.6464	136 (Mel)	68	13.53(12.90)	7.837 (7.42)

3.2. FT-IR spectra

The infrared spectra of the ligands and their complexes are summarized (Figure 1, Table 2).

In $[Cu(phen)_2Cl]Cl.H_2O$, the bands at 1586 cm^{-1}(s) and 1623 cm^{-1}(s), which correspond to vC=C and v C=N stretching in free 1,10-phenanthroline, shifted to 1629 cm^{-1}(w) and 1501 cm^{-1}(w), respectively(Tamiru et al., 2019). They were also found in $[Cu_2(phen)_4en]Cl_4$ at 1623 cm^{-1} (w) and 1429 cm^{-1} (w), respectively(Tamiru et al., 2019;Dowarah & Singh, 2020). Similarly, in $[Cu_2(phen)_4en]Cl_4$, the ethylene diamine characteristic bands at 3337 cm^{-1}(s) vN-H (NH_2) and 1314 cm^{-1}(s) vC-N are displaced to 3229 cm^{-1} (w) and 1222 cm^{-1} (w), respectively (Dowarah & Singh, 2020).

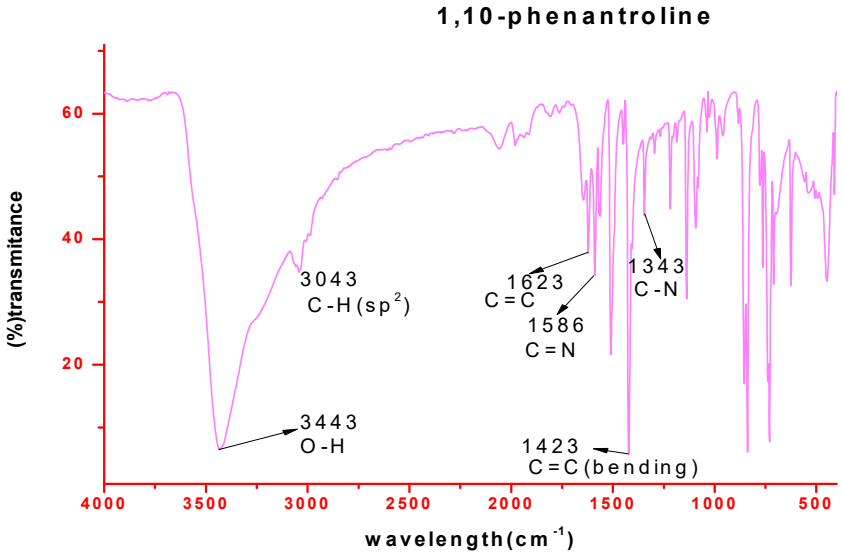
The distinctive band of vO-H(H_2O), displaced to 3344 cm^{-1} (s) in $[Cu(phen)_2Cl]Cl.H_2O$, verifies the existence of water of crystallization at 3443 cm^{-1} (s) in 1, 10-phenanthroline monohydrate (Tamiru et al., 2019).

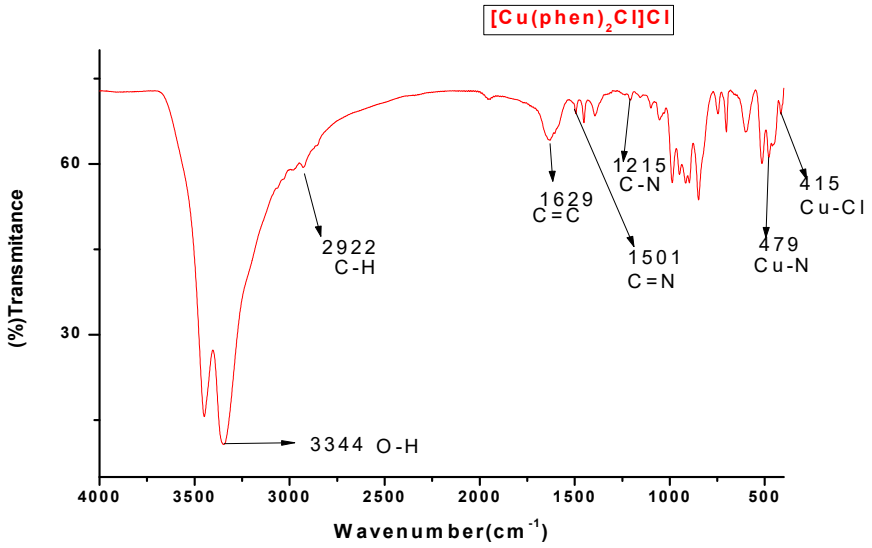
The v C-H cm^{-1} stretch of the aromatic ring vibration has been ascribed to the band at 3043 cm^{-1} in 1, 10-phenanthroline, 2922 cm^{-1} in the precursor, and 3121 cm^{-1} in the binuclear complexes. The vibrational bands shifted, indicating that the coordinated chloride atoms were gradually replaced by the ligands 1, 10-phenanthrolines, and ethylenediamine (Figure 1) (Tamiru et al., 2019; Abebe et al., 2020; Abebe et al., 2017)).

In $[Cu(phen)_2Cl]Cl.H_2O$, the absorption bands at 479 cm^{-1} and 415 cm^{-1} are indicative of vCu-N and Cu-Cl stretching, respectively. Furthermore, the faint band at 515 cm^{-1}, which is indicative of $\upsilon(Cu\text{-}N)(NH_2)$ in $Cu_2(phen)_4en]Cl_4$, demonstrates that chlorine has been completely replaced by ethylenediamine(Abebe et al., 2020; Abebe et al., 2017). Strong broad bands at 3429 cm^{-1} and 3229 cm^{-1} were attributed to ethylenediamine's $\upsilon N\text{-}H(NH_2)$ stretching frequency in $[Cu_2(phen)_4en]Cl_4$, confirming the coordination of ethylenediamine via nitrogen atom in both sites (Tamiru, Abebe, Abebe, & Liyew, 2019).

Table 2. shows the ligands and their complexes' characteristic vibration frequencies

Compounds	Absorption frequencies (cm^{-1})							
	$\upsilon_{(O-H)}$	$\upsilon_{(N-H)}$	$\upsilon_{(C-H)}$	$\upsilon_{(C=N)}$	$\upsilon_{(C=C)}$	$\upsilon_{(C-N)}$	$\upsilon_{(Cu-N)}$	$\upsilon_{(Cu-Cl)}$
1,10-phenanthroline mono hydrated	3443	-	3043	1586	1623	1343	-	-
Ethylenediamine	-	3424, 3337	2925	-	-	1314	-	-
$[Cu(phen)_2Cl]\ Cl.H_2O$	3344	-	2922	1501	1629	1215	479	415
$[Cu_2(phen)_4en]Cl_4$	-	3429-3229	3121	1429	1623	1222	455	-





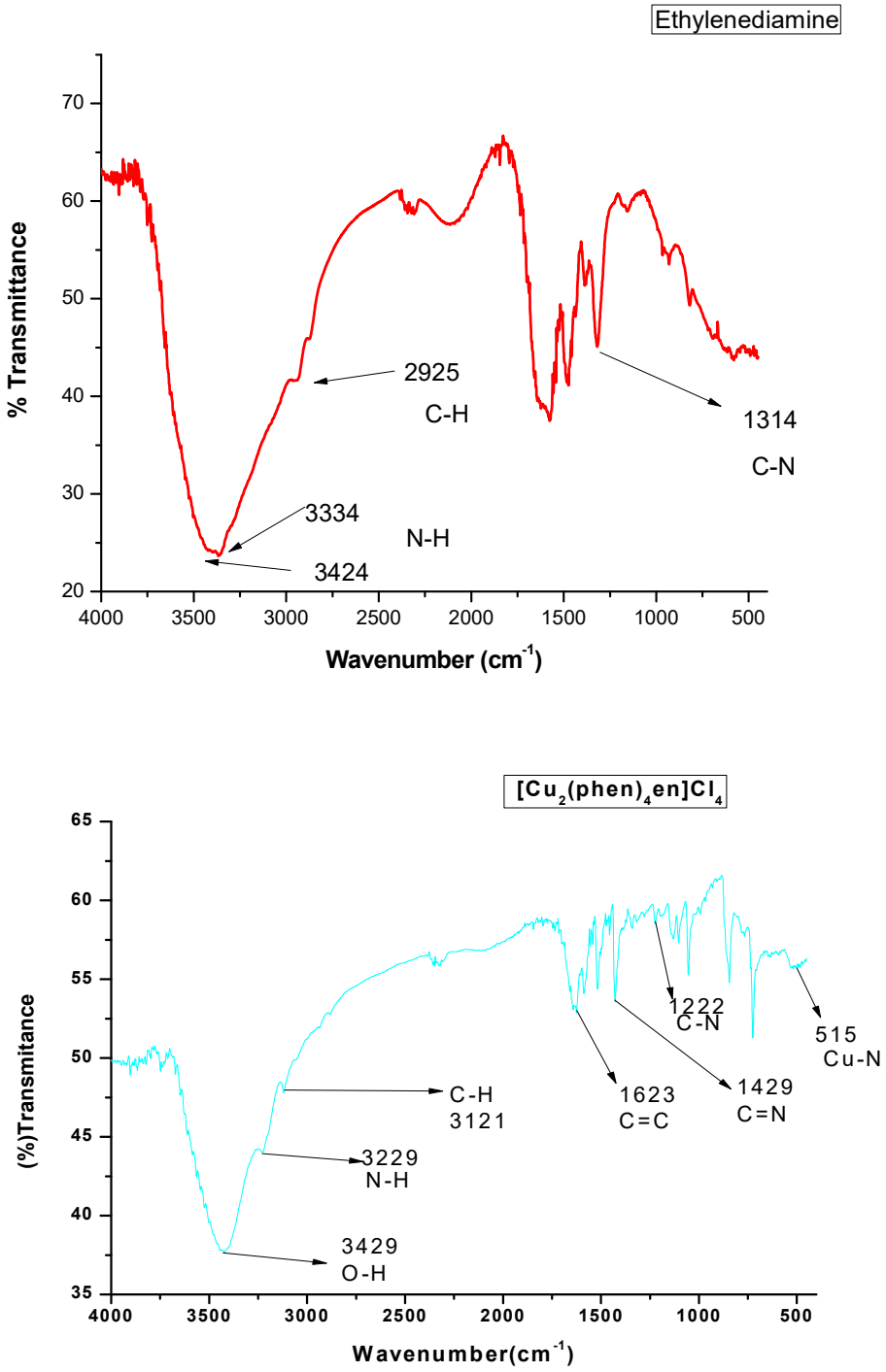


Figure 1. The FT-IR Spectra of the synthesized complexes

3.3. Electronic Spectral

The electronic spectra of the synthesized complexes shown in (Table 3). The ligands' electronic spectra, as well as the $[Cu(phen)_2Cl]$ $Cl.H_2O$ complexes (methanol) and $[Cu_2(phen)_4en]Cl_4$ complexes (distilled water), were recorded(Abebe et al., 2020; Abebe et al., 2017). For 1, 10-phenanthroline, two absorption bands at 228 nm and 262 nm are ascribed to n→π*(C=C) and n→π* (C=C), respectively. The $[Cu(phen)_2$ $Cl]Cl.H_2O$ complex shifts these bands to 230 nm and 283 nm, confirming the coordination of 1, 10-phenanthroline with the copper ion (Abebe et al., 2020; Abebe et al., 2017).

The highest absorption bands in the $[C_{u2}(phen)4(en)]Cl_4$ complex shift to 230 nm, π→π* (C=C), 309 nm, n→π* (C=C) when ethylenediamine is coordinated. Furthermore, the band is formed via a straightforward d-d

transition in the $CuCl_2.4H_2O$ starting material(Abebe et al., 2020; Abebe et al., 2017). Both complexes (1 and 2) transform into distinct doublet absorption bands at 548 nm and 541 nm, which are ascribed to $^2B_{1g}\rightarrow{}^2A_{1g}$ and $^2B_{1g}\rightarrow{}^2B_{2g}$ transitions (Table 3) (Abebe et al., 2020; Dowarah & Singh, 2020).

Table 3. shows the electronic spectrum data of the examined ligands and their complexes.

Compounds	**λ max**(nm)	Assignments
$CuCl_2.4H_2O$	292, 548 , 541	LMCT, $^2B_{1g}\rightarrow{}^2A_{1g}$ and $^2B_{1g}\rightarrow{}^2B_{2g}$
1,10-phenanthroline	228, 262	$\pi\rightarrow\pi^*_{(C=N)}$, $n\rightarrow\pi^*_{(C=C)}$
Ethylenediamine	289	$n\rightarrow\pi^*_{(C=N)}$
$[Cu(phen)_2\ Cl]\ Cl.H_2O$	283, 293	$\pi\rightarrow\pi^*_{(C=N)}$, $n\rightarrow\pi^*_{(C=C)}$,
	644 and 626	$^2B_{1g}\rightarrow{}^2A_{1g}$ and $^2B_{1g}\rightarrow{}^2B_{2g}$
$[Cu_2\ (phen)_4en]\ Cl_4$	230, 309 , 345	$\pi\rightarrow\pi^*_{(C=N)}$, $\pi\rightarrow\pi^*_{(C=N)}$,
	415 and 520	$^2B_{1g}\rightarrow{}^2A_{1g}$ and $^2B_{1g}\rightarrow{}^2B_{2g}$

LMCT = Ligand to metal charge transfer

3.4. Antibacterial Activity Testing

The biological activities of the synthesized Cu(II) complexes differ from those of the starting materials (Table 4), implying that complexes in the media are inert (Tamiru et al., 2019). For instance, $CuCl_2.4H_2O$ had a strong bacterial activity with inhibition zones ranging from 15.70 ± 1.11 to 19.93 ± 0.5 mm. Due to its flat shape and extended conjugation, the free 1,10-phenanthroline ligand exhibits the largest antibacterial activity, with inhibition zones ranging from 18.57 ± 1.29 mm to 30.87±1.75 mm (Table 4) for all four microorganisms (Abebe et al., 2017; Fayad et al., 2013).

On the studied microbes, the free ligand ethylenediamine demonstrated sufficient activity, with inhibition zones ranging from 17.20 ± 1.21 mm to 18.43 ± 2.35 mm. However, they could not be directly employed for medical applications due to the cytotoxicity of the starting ingredients (Abebe et al., 2018). Their toxicity is reduced by coordinating them with metal ions (Abebe & Hailemariam, 2016). As a result, toxicity is reduced when 1, 10-phenanthroline, and ethylenediamine are coordinated with copper (II). Compounds are just used as a drug carrier to transport the active metal ion in this process (Frei et al., 2020, Komar & Barton, 2013).

The eye-catching phenomenon found in this investigation was the synthesized mono- $[Cu(Phen)_2Cl]Cl.H_2O$ and binuclear $[Cu_2(en)(Phen)_4]Cl_4$ complexes, which demonstrated drug concentrations at which a visible inhibition on microorganism growth was seen (Abebe & Hailemariam, 2016). By preparing serial dilutions of different concentrations of the complexes at 100 mg/L, 150 mg/L, 200 mg/L, 250 mg/L, 300 mg/L, 350 mg/L, 400 mg/L, and 450 mg/L, the minimum inhibitory concentration (MIC) against each bacterium was established (Table 5 and 6). As a result of these data, it may be deduced that bacteria development was severely hampered at greater concentrations (Abebe & Hailemariam, 2016, Fayad et al., 2013). The experiments were repeated three times to ensure that the results were consistent. The diameter zone of inhibition the standard deviations ((±) summarized in the MICs values for the substances (Table 4) (Tamiru et al., 2019).

Table 4. Antibacterial activity of chemicals and antibiotics (gentamycin) in 500 mg/L.

IZ(mm)	Compounds					
	1,10-Phenanthroline	$CuCl_2 \cdot 4H_2O$	$[Cu(phen)_2Cl]Cl.H_2O$ (%index)	$[Cu_2\ (phen)_4en]Cl_4$ (%index)	Ethylenediamine	Gentamycin
S. aureus	21±2.0	19.27±0.70	16.93±1.10(-43.43)	17.27±2.41(-42.30)	18.43±2.35	29.93±0.12
E. coli	30.87±1.75	19.93±0.5	12.53±3.40(-35.07)	17.40±1.49(-9.84)	18.03±2.24	19.30±0.58
S.pyogen	18.57±1.29	17.80 ±0.72	18.30±1.67(-41.35)	17.60±0.87(-43.59)	18.23±0.80	31.20 ±0.00
K.pne	20.30±0.82	15.70±1.11	17.77±2.45(-42.92)	15.33±1,36(-50.75)	17.20±1.21	31.13±0.23

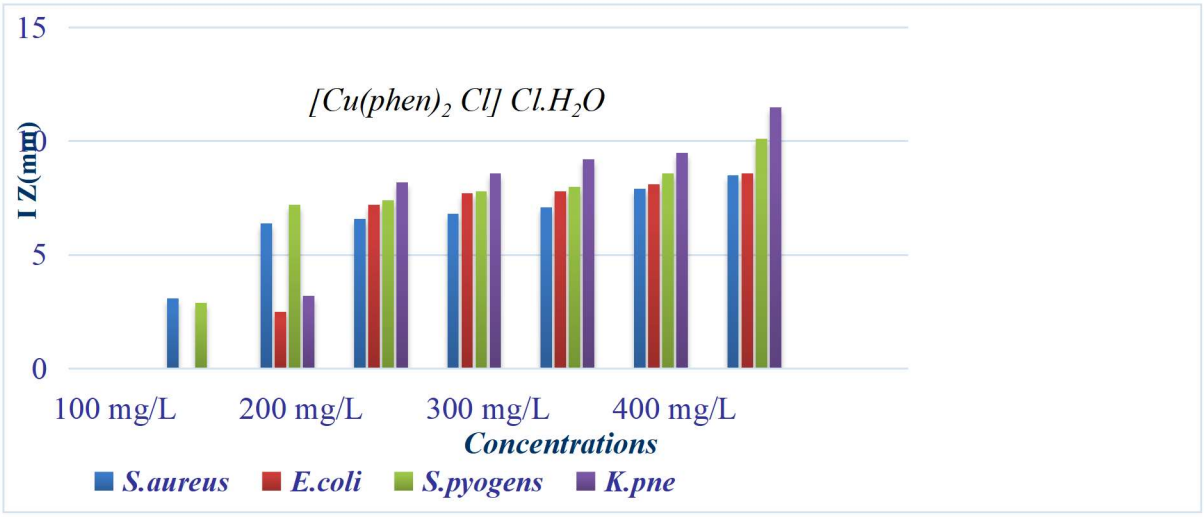


Figure 2.$[Cu(phen)_2Cl]Cl.H_2O$ complex MIC

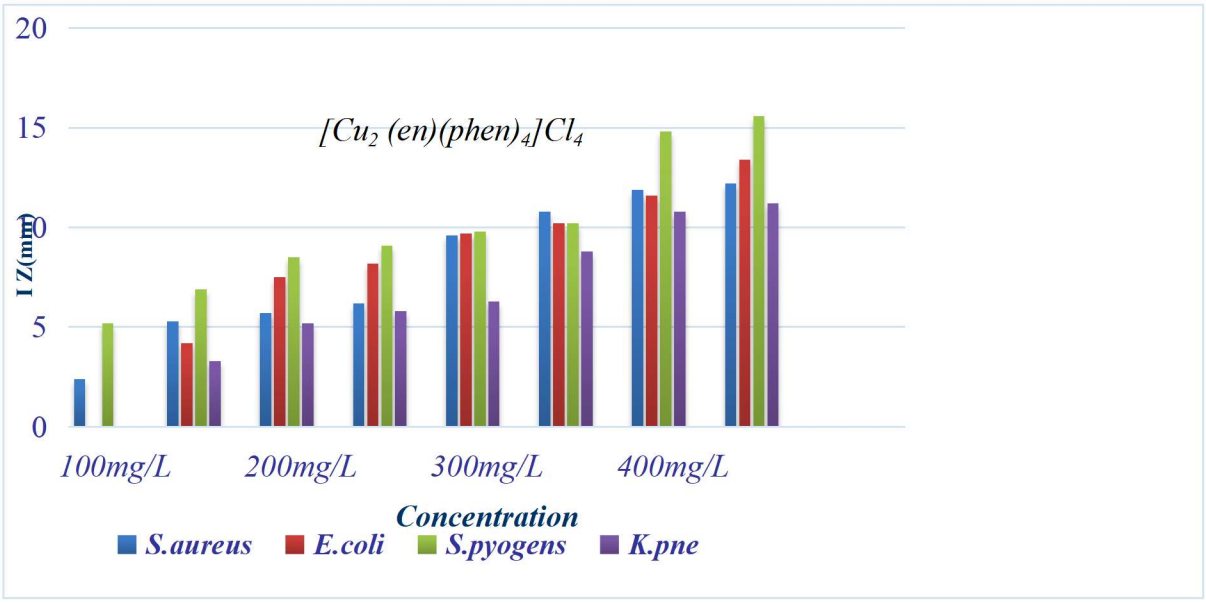


Figure 3. $[Cu_2(phen)_4en]Cl_4$ complex MIC

Table 5. Minimum inhibition concentration of $[Cu(phen)_2 Cl]Cl.H_2O$ complex

Microorganisms	MIC (mg/L)							
	100	150	200	250	300	350	400	450
E. coli	+	+	–	–	–	–	–	–
S. aureus	+	–	–	–	–	–		
K. Pneumonia	+	+	–	–	–	–	–	–
S.Pyrogens	+	–	–	–	–	–	–	–

Table 6. Minimum inhibition concentration of $[Cu_2 (phen)_4en]Cl_4$ complex

Microorganisms	MIC (mg/L)							
	100	150	200	250	300	350	400	450
E. coli	+	–	–	–	–	–	–	–
S. aureus	–	–	–	–	–	–		
K. Pneumonia	+	–	–	–	–	–	–	–
Pyrogens	–	–	–	–	–	–	–	–

Note: + = Bacterial growth,– = Bacterial growth is prevented.

CONCLUSIONS

The complexes were synthesized and characterized effectively. The characterization techniques confirm that both ligands are coupled with copper ions via N-donor atoms in all synthesized complexes. The electronic data demonstrate that the expected molecular structure of the synthesized complexes was achieved. As a result, the square pyramidal geometries are attributed in both Cu(II) complexes. In the in vitro antibacterial study, the synthesized complexes are biologically active in all examined pathogens. Surprisingly, the compounds are water-soluble and this confirms that, after in vivo cytotoxicity testing, the synthesized complexes could be evaluated as a potential medical application.

REFERENCES

Abebe, A., Atlabachew, M., Liyew, M., & Ferede, E. (2018). Synthesis of organic salts from 1, 10-phenanthroline for biological applications. *Cogent Chem, 4*(1), 1476077.

Abebe, A., Bayeh, Y., Belay, M., Gebretsadik, T., Thomas, M., & Linert, W. (2020). Mono and binuclear cobalt (II) mixed ligand complexes containing 1, 10-phenanthroline, and adenine using 1, 3-diamino propane as a spacer: synthesis, characterization, and antibacterial activity investigations. *Future Journal of Pharmaceutical Sciences, 6*, 1-9.

Abebe, A., & Hailemariam, T. (2016). Synthesis and assessment of antibacterial activities of ruthenium (III) mixed ligand complexes containing 1, 10-phenanthroline, and guanide. *Bioinorg Chem Appl, 2016*.

Abebe, A., Sendek, A., Ayalew, S., & Kibret, M. (2017). Copper (II) mixed-ligand complexes containing 1, 10-phenanthroline, adenine, and thymine: Synthesis, characterization, and antibacterial activities. *Chem. Int, 3*(3), 230-239.

Abebe, A., & Tamiru, G. (2018). A hexatonic coordination compound from Co (II) and a cationic ligand derived from 4, 4′-bipyridine: Synthesis, characterization, and investigation for biological application. *Cogent Chem, 4*(1), 1564162.

Ajibade, P. A., & Idemudia, O. G. (2013). Synthesis, characterization, and antibacterial studies of Pd (II) and Pt (II) complexes of some diaminopyrimidine derivatives. *Bioinorg Chem Appl, 2013*.

Beyene, B, B., Mihirteu, A. M., Ayana, M. T., & Yibeltal, A. W. (2020). "Synthesis, characterization and antibacterial activity of metalloporphyrins: Role of the central metal ion.". *Results in Chemistry, 2*, 100073.

Dowarah, J., & Singh, V. P. (2020). Anti-diabetic drugs are recent approaches and advancements. *Bioorg Med Chem, 28*(5), 115263. doi:10.1016/j.bmc.2019.115263

Fayad, N. K., Al-Noor, T. H., Mahmood, A. A., & Malih, I. K. (2013). Synthesis, characterization, and antibacterial studies of Mn (II), Fe (II), Co (II), Ni (II), Cu (II), and Cd (II) mixed-ligand complexes containing amino acid (L-valine) and (1, 10-phenanthroline). *JCMR, 3*(5).

Frei, A., Zuegg, J., Elliott, A. G., Baker, M., Breese, S., Brown, C., . . . Jung, N. (2020). Metal complexes as a promising source for new antibiotics. *Chem. Sci, 11*(10), 2627-2639.

Fuertes, M. A., Alonso, C., & Pérez, J. M. (2003). Biochemical modulation of cisplatin mechanisms of action: enhancement of antitumor activity and circumvention of drug resistance. *Chem. Rev, 103*(3), 645-662.

Gao, Y., van Belkum, M. J., & Stiles, M. E. (1999). The outer membrane of Gram-negative bacteria inhibits the antibacterial activity of brochocin-C. *Appl. Environ. Microbiol, 65*(10), 4329-4333.

Ghatole, A., Lanjewar, K., & Gaidhane, M. (2012). Syntheses, characterization, antimicrobial activity of Copper (II), zinc (II), and Cobalt (II) complexes of the bi-dented substituted 2-((E)-2-((2-chloro-6-ethoxyquinolin-3-yl) methylene amino) thiazol-4-yl) phenol having ON donor sites. *J. Pharm. Res, 5*(5), 2758-2762.

Gomleksiz, M., Alkan, C., & Erdem, B. (2013). Synthesis, characterization, and antibacterial activity of imidazole derivatives of 1, 10-phenanthroline and their Cu (II), Co (II), and Ni (II) complexes. *S. Afr. J, 66*, 107-112.

Hossain, M. D., Rana, U., Chakraborty, C., Li, J., Nagano, R., Minowa, T., & Higuchi, M. (2017). Effect of metal-the metal distance in Ni (ii)-based metallo-supramolecular polymers: DNA binding and cytotoxicity. *RSC Adv, 7*(60), 38008-38013.

Komar, A., & Barton, J. (2013). The path for metal complexes to a DNA target Chem. *Comb, 49*, 3617.

Mahalakshmi, R., & Raman, N. (2016). A therapeutic journey of mixed ligand complexes containing 1, 10-phenanthroline derivatives: a review. *Int. J. Curr. Pharm. Res, 8*(3), 1-6.

Mitkina, T. V., Zakharchuk, N. F., Naumov, D. Y., Gerasko, O. A., Fenske, D., & Fedin, V. P. (2008). Syntheses, structures, and electrochemical properties of inclusion compounds of cucurbit [8] until with cobalt (III) and nickel (II) complexes. *Inorg, 47*(15), 6748-6755.

Podunavac-Kuzmanović, S., Leovac, V., & Cvetković, D. (2008). Antibacterial activity of cobalt (II) complexes with some benzimidazole derivatives. . *Serbian Chem. Soc, 73*(12), 1153-1160.

Shahabadi, N., & Mahdavi, M. (2013). DNA Interaction Studies of a Cobalt (II) Mixed-Ligand Complex Containing Two Intercalating Ligands: 4, 7-Dimethyl-1, 10-Phenanthroline and Dipyrido [3, 2-a:-c] phenazine. *int. sch. res. notices, 2013*.

Singh, K., Kumar, Y., Puri, P., & Singh, G. (2012). Spectroscopic, thermal, and antimicrobial studies of Co (II), Ni (II), Cu (II), and Zn (II) complexes derived from bidentate ligands containing N and S donor atoms. *Bioinorg Chem Appl, 2012*.

Stănilă, A., Braicu, C., & Stănilă, S. (2011). Antibacterial activity of copper and cobalt amino acids complexes. *Not Bot, 39*(2), 124-129.

Sunitha, M., Jogi, P., Ushaiah, B., & Kumari, C. G. (2012). Synthesis, characterization, and antimicrobial activity of transition metal complexes of Schiff base ligand derived from 3-ethoxy salicylaldehyde and 2-(2-Aminophenyl) 1-H-benzimidazole. *J. Chem, 9*(4), 2516-2523.

Tamiru, G., Abebe, A., Abebe, M., & Liyew, M. (2019). Synthesis, structural investigation, and biological application of new mono-and binuclear cobalt (II) mixed-ligand complexes containing 1, 10-phenanthroline, acetamide, and ethylenediamine. *EJST, 12*(1), 69-91.

Tigineh, G. T., Abiye, M., Melese, A., & Abebe, A. (2021). Synthesis, structural investigations, and in vitro biological activity of Co (II) and Fe (III) mixed ligand complexes of 1, 10-phenanthroline and 2, 2′-bipyridine. *Chem Biol Drug Des*.

Turro, J, N., Barton, J. K., & ToMALIA, D. A. (1991). "Molecular recognition and chemistry in restricted reaction spaces. Photophysics and photoinduced electron transfer on the surfaces of micelles, dendrimers, and DNA" *Accounts of chemical research, 24*(11), 332-340.