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Synthesis, Spectral, Electrochemical and Biological Studies on Co(II), Ni(II), Cu(II) and Zn(II) Complexes Derived from 4-(2-Aminoethyl)benzene-1,2-diol and Terephthalaldehyde

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A novel Schiff base ligand (L) has been synthesized using 4-(2-aminoethyl)benzene-1,2-diol (dopamine) and terephthalaldehyde. This hexadentate ligand has been used to synthesize cobalt(II), nickel(II), copper(II) and zinc(II) complexes with stoichiometry (1:2). Several techniques were used to characterize the compounds, including elemental analysis, molar conductivity, magnetic moment, mass spectra, cyclic voltammetry, SEM and powder XRD. Co(II), Ni(II), Cu(II) and Zn(II) have octahedral geometry based on physico-chemical characterization studies. Using cyclic voltammetry (CV), the redox properties of the metal complexes were extensively studied. These metal complexes were studied by SEM analysis to determine their surface morphology Solvatochromic behaviours of synthesized compounds have been assessed using UV-vis absorption spectroscopy. By disc diffusion method, the ligand and its metal(II) complexes were tested for antibacterial activity against two Gram-positive bacteria, two Gram-negative bacteria and one fungus. Using the HRBC membrane stabilization method, the Schiff base ligand and its copper(II) complex were evaluated for their anti-inflammatory properties. *In vitro* anticancer activity of the copper(II) complex was investigated by MTT assay on the human breast cancer cell line (MCF-7). According to the results, the copper(II) complex inhibits breast cell growth better than the Schiff base. Using an α-amylase inhibitory assay method, the ligand and its copper(II) complex were also tested for their antidiabetic effects *in vitro*. In comparison with the Schiff base ligand, the copper(II) complex showed the best activity.

Keywords: Schiff base ligand, Metal(II) complexes, Cyclic voltammetry, Anticancer.

INTRODUCTION

Schiff base ligands and its metal complexes has broadened massively and now encompasses a vast range of organometallic complexes and biological aspects [1]. Schiff base ligands are often referred to as "privileged ligands" since they may easily be produced by condensation between carbonyl compounds (aldehydes or ketones) and primary amine [2]. Schiff base ligands are capable of coordinating many metals and stabilizing them in different oxidation states. Imines and azomethines, also known as Schiff bases, have grown extremely popular for the most part due to their simplicity of synthesis, air stability and relatively low beginning materials [3-5]. Considering that nitrogen and oxygen atoms serve as donor atoms, these compounds have high efficiency and stereo specificity as catalysts in bond forming, oxidation, reduction, hydrolysis and other transformations [6-10]. Large quantities of Schiff bases have also been found to exhibit a wide variety of biological properties. They have been shown to exhibit anti-tumor, antibacterial, anti-fungicidal and anticarcinogenic properties [11-13].

A dopamine molecule comprises a catechol structure with one amine group appended through an ethyl chain. Usually, it is prescribed as an energizer sedate for severe hypotension, slow heart rate and cardiac arrest. Additionally, plants and animals contain dopamine. In the brain, dopamine works as a neurotransmitter: a chemical that neurons (nerve cells) release to communicate with each other. Numerous drugs and herbicides have also been synthesized using dopamine. They have significant properties including neurotransmission, neuromodulation, vasoconstriction and vasodilation as well as antimicrobial, antibacterial, antioxidant, anti-inflammatory, antifungal and antidepressant properties [14,15].

In recent years, coordination complexes have been the subject of intense interest in medicinal chemistry because of the interaction of metal complexes with membranes of bacteria and other microorganisms. Diabetes mellitus is an endocrine disorder, which is responsible for 9% of worldwide deaths. Numerous medications are used to reduce this death rate, but they are not successful in alleviating the complications. Metal complexes are a new therapeutic strategy for treating diabetes. Accordingly, the transition metal complexes have an insulin-mimetic effect as well as an inhibitory effect on amylase and glycosidase [16].

Humans protect themselves from infections, allergens, burns, toxic chemicals, or other noxious stimuli using a primary defense mechanism known as inflammation. Many chronic infections are caused by uncontrolled and persistent inflammation. Despite the fact that inflammation is an important part of the body's defense against infections, the complicated processes involved in inflammation can lead to more severe infections and diseases. Most anti-inflammatory drugs have some side effects. Schiff base ligands and its metal complexes have anti-inflammatory properties and are used to control the inflammation. So, it is necessary to create anti-inflammatory drugs that are effective with fewer side effects [17].

The present work is to prepare a Schiff base ligand derived from the condensation of 4-(2-aminoethyl)benzene-1,2-diol (dopamine) with terephthalaldehyde. The study has been extended to Co(II), Ni(II), Cu(II) and Zn(II) complexes with the prepared ligand. All the synthesized metal(II) complexes have been characterized by IR, ^{1}H & ^{13}C NMR, mass spectra, ESR, UV-visible, cyclic voltammetry in addition to elemental analysis, molar conductivity and magnetic susceptibility. Morphologies of ligand and its metal(II) complexes were analyzed by utilizing SEM. Schiff base ligand and its copper(II) complex were also evaluted for their antibacterial, antihemolytic, anticancer, anti-inflammatory and antidiabetic activities.

EXPERIMENTAL

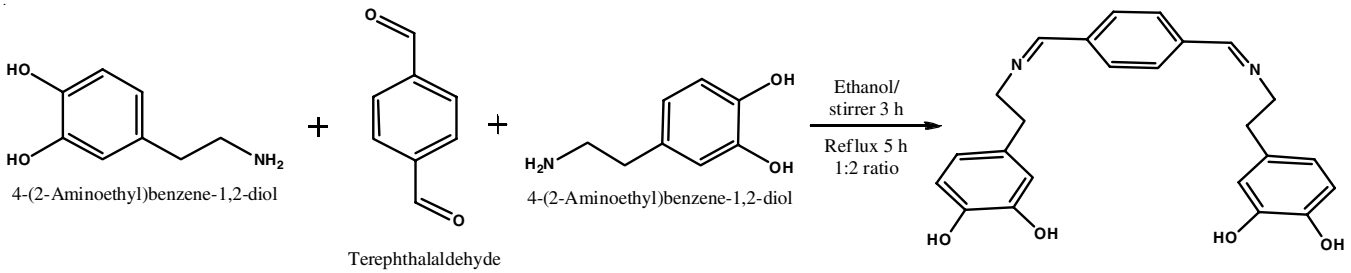
Metal(II) acetate salts were purchased from Sigma-Aldrich Ltd. and used without further purification. Dopamine and terephthalaldehyde of AR grade were purchased from TCI chemicals and the solvents used for synthesis and characterization were of high-performance liquid chromatography grade. Elemental analyses were carried out on EURO EA-3000 RS-32. IR spectra was recorded on 8400 FTIR Shimadzu spectrometer as KBr discs. UV-visible spectra (using DMSO as the solvent) were measured on Shimadzu UV-2100 spectrometer. Melting points were determined on a Buchi 530 apparatus in open capillary tubes. Molar conductance of 10^{-3} M solution of the complexes in DMSO was recorded on Hanna EC 215 conductivity meter by using 0.01 M KCl solution as calibrant. ^{1}H & ^{13}C NMR spectra of Schiff ligand and its metal(II) complexes in DMSO-d_6 were recorded on a Bruker Advance II 400 spectrometer at room temperature using TMS as an internal standard. The ESI mass spectra the compounds were recorded on Q-Tof Mass spectrometer. Magnetic susceptibility measurements were done in a Sherwood Scientific magnetic susceptibility balance at room temperature. The CH Instruments, U.S.A. (Model 1110A-Electrochemical analyzer, Version 4.01) measured electrochemical performance of the metal(II) complexes in HPLC grade DMF containing n-Bu_4NClO_4 as electrolyte. Glassy carbon electrodes (3 mm dia.), Ag/AgCl (3 M KCl) reference electrodes and platinum wire as an auxiliary electrode were used to create the three-electrode system. Scanning electron surface morphological studies were obtained using the JSM-5610 scanning electron microscope (SEM).

Synthesis of Schiff base ligand: In a round bottom flask at room temperature, terephthaldehyde (1 mmol) was added dropwise to methanolic solution of 4-(2-aminoethyl)benzene-1,2-diol (dopamine) (2 mmol) to form a Schiff ligand. A magnetic stirrer was used to thoroughly mix the mixture, which was followed by 6 h of refluxing to produce the dark brown solid product (**Scheme-I**). After being filtered, the product was washed a number of times with methanol and finally dried in vacuum over anhydrous calcium chloride.

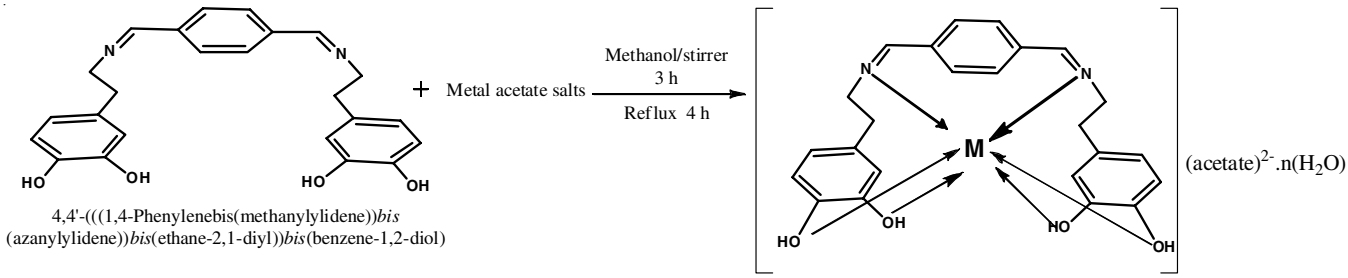
Synthesis of Schiff base metal(II) complexes: The DMSO solution of Schiff base ligand (L, 1 mmol) was slowly mixed with a solution of metal(II) acetate salts of methanol poured into a round bottom flask. After thoroughly mixing the solution, the product was separated by stirring under reflux for 7 h. Obtained products were filtered, washed multiple times with methanol and dried under vacuum over anhydrous calcium chloride (**Scheme-II**). The above general method was used to synthesize Co(II), Ni(II), Cu(II) and Zn(II) metal complexes of Schiff base.

RESULTS AND DISCUSSION

Table-1 listed the physical properties and elemental analysis data of the Schiff base ligand (L) and its metal(II) complexes. Metal(II) complexes have higher melting points than ligands because of their larger molecular size and strong ionic and covalent bonds [18]. Experimental and theoretical results indicate that the proposed compounds are being formed as evidenced by



Scheme-I: Synthesis of Schiff base ligand (L)



Scheme-II: Synthesis of Schiff base Metal(II) complexes [M(II): Co(II), Ni(II), Cu(II) and Zn(II)]

TABLE-1
ANALYTICAL DATA OF THE SCHIFF BASE LIGAND AND ITS MONONUCLEAR METAL(II) COMPLEXES

Compounds	m.w.	Colour	m.p. (°C)	Molar conductance (Ω^{-1} cm^2 mol^{-1})	Elemental analysis (%): Calcd. (found)			
					C	H	N	M
Ligand $C_{24}H_{24}N_2O_4$	405.11	Dark Brown	170	–	71.27 (70.10)	5.98 (5.67)	6.93 (6.89)	–
Cobalt(II) complex $C_{29}H_{38}N_2O_{12}Co$	665.56	Dark red	215	50.60	52.33 (51.89)	5.76 (5.67)	4.21 (4.25)	8.85 (8.90)
Nickel(II) complex $C_{29}H_{38}N_2O_{12}Ni$	665.32	Brown	210	70.87	52.35 (51.76)	5.76 (5.56)	4.40 (4.28)	8.82 (8.56)
Copper(II) complex $C_{29}H_{32}N_2O_9Cu$	616.13	Black	195	54.86	56.53 (55.98)	5.24 (5.18)	4.55 (4.51)	10.31 (10.26)
Zinc(II) complex $C_{29}H_{34}N_2O_{10}Zn$	635.98	Light brown	201	75.20	54.77 (52.17)	5.39 (5.12)	4.40 (4.30)	10.28 (10.11)

the percentages of C, H and N. It is insoluble in ethanol, methanol, acetone, chloroform, but is soluble completely in DMF and DMSO. At room temperature, the molar conductivity of the metal complexes was measured in DMSO solution (10^{-3} M). The complexes showed low molar conductance values (50.60-75.20 ohm^{-1} cm^2 mol^{-1}) which indicates that they are 1:2 electrolytic in nature and the anions are outside the coordination sphere and not bonded to the metal ions. Hence, these metal(II) complexes may be formulated as [ML](Z), where, Z = acetate ion and M = Co(II), Ni(II), Cu(II) and Zn(II) [19-21].

FT-IR spectral studies: The noteworthy infrared spectral aspects of Schiff base ligand and its complexes are tabulated in Table-2. The IR spectra of ligand (Fig. 1) shows a strong band at 1646 cm^{-1} assigned to the formation of the azomethine (>C=N-) group and shifted to a lower frequency in the region 1526-1602 cm^{-1} in all the metal(II) complexes indicating the coordination of the azomethine nitrogen [22]. In addition, the hydroxyl group in the ligand is located at 3428 cm^{-1}, but in the complexes, this frequency is downshifted to 3321-3306 cm^{-1} indicating a weakening of -OH bond due to coordination

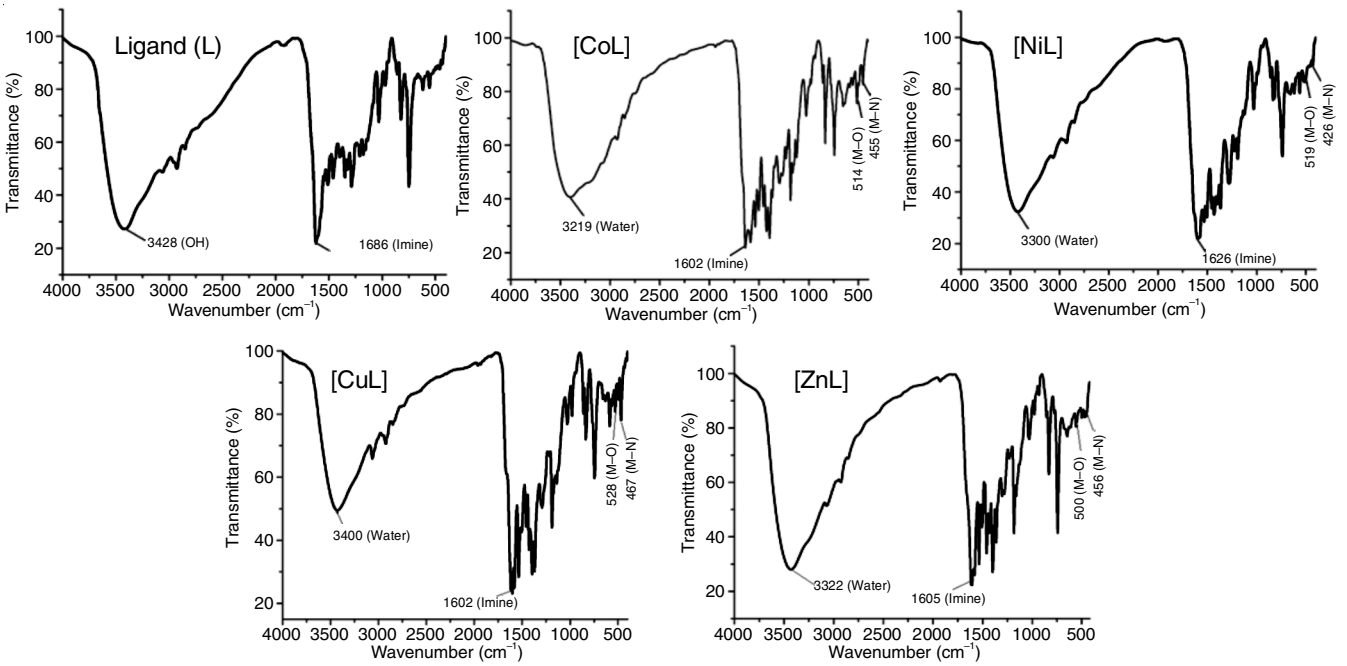


Fig. 1. FT-IR spectra of Schiff base ligand and its mononuclear metal(II) complexes

TABLE-2
IR SPECTRAL DATA ANALYSIS OF THE SCHIFF BASE LIGAND AND ITS MONONUCLEAR METAL(II) COMPLEXES

Compound	ν(-OH) (cm^{-1})	Imine (cm^{-1})	ν(C-O) (cm^{-1})	ν($OCOCH_3$) (cm^{-1})		ν(M-O) (cm^{-1})	ν(M- N) (cm^{-1})
				Asymm.	Symm.		
Ligand (L)	3328	1646	1285	–	–	–	–
[CoL]	3320	1640	1292	1781	1462	490	452
[NiL]	3310	1596	1290	1778	1424	565	422
[CuL]	3321	1615	1289	1780	1432	559	447
[ZnL]	3306	1618	1295	1780	1456	528	456

through enolic -OH. The enolic oxygen is coordinated to the metal ion without deprotonation [23,24]. Furthermore, the shift in C-O band from 1280 cm^{-1} (in ligand) to 1275-1270 cm^{-1} (in complexes) provides further support. In all the complexes, the band in the ranges from 1778-1782 cm^{-1} and 1462-1400 cm^{-1} are due to symmetric and asymmetric stretching frequency of acetate ion which clearly confirmed that the acetate ions are outside the coordination sphere [25]. The new bands observed in IR spectra of complexes in the regions 565-490 cm^{-1} and 422-456 cm^{-1} may be attributed to vibrations in the ν(M-O) and ν(M-N) modes, respectively [26].

NMR studies (^{1}H and ^{13}C NMR): ^{1}H NMR data and assignments of Schiff base ligand was obtained in DMSO-d_6 at room temperature with tetramethylsilane (TMS) as an internal standard. Schiff base ligand shows multiplet in the region δ 6.53-7.70 ppm is due to phenyl proton. A signal for phenyl –OH for the ligand is observed at δ 9.89 ppm [27] as shown in Fig. 2.

^{13}C NMR spectrum of the free ligand L shows a sharp signal at 169.15 ppm, which may be assigned to azomethine carbon. The carbon atom of the -OH phenyl group exhibited a peak at 157.89 ppm as shown in Fig. 3.

Electronic spectral and magnetic moment studies: The electronic spectra and magnetic moments of Schiff base ligand and its metal(II) complexes are shown in Table-3 and Fig. 4. Electronic spectra of the Schiff ligand (HL) show two strong bands at 251 nm and 287 nm, attributed to π-π* and n-π*,

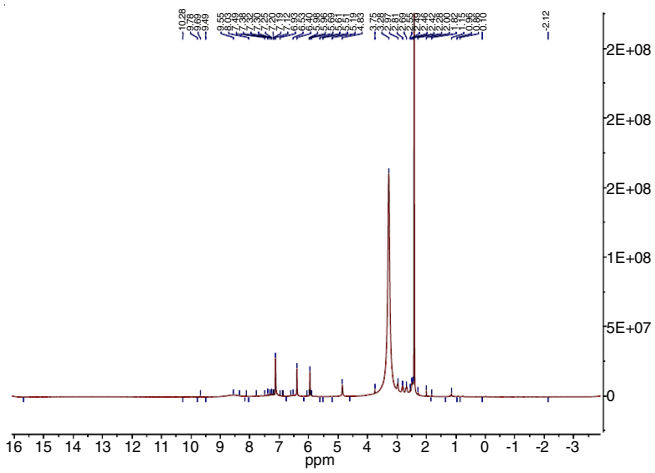


Fig. 2. ^{1}H NMR of Schiff base ligand (L)

respectively. Spectra of the metal(II) complexes show these bands shifted higher, denoting the presence of coordination of the nitrogen atom to the metal ion.

The electronic spectra of Co(II) complex shows band at 546 nm is due to charge transfer (L-M) and two bands at 584 nm and 662 nm due to $^4T_{1g}$ (F)→$^4A_{2g}$ (F) and $^4T_{1g}$ (F)→$^4T_{2g}$ (P) transitions respectively, corresponding to an octahedral geometry is further confirmed by its magnetic moment value of 4.21 B.M. [28]. Nickel(II) complex shows two bands in the region 564 nm and 664 nm, which corresponds to $^3A_{2g}$→$^3T_{1g}$(F)

TABLE-3
UV-VISIBLE SPECTRAL DATA ANALYSIS OF THE SCHIFF BASE LIGAND AND ITS MONONUCLEAR METAL(II) COMPLEXES

Compounds	Absorption (nm)	Band assignment	Geometry	Magnetic moment (BM)
Ligand	251	INCT	–	–
	287	INCT		
[CoL]	254	INCT	Octahedral	4.21
	301	INCT		
	444	LMCT		
	540	$^4T_{1g}$ (F) → $^4T_{1g}$ (P)		
	741	$^4T_{1g}$ (F) → $^4A_{2g}$ (F)		
[NiL]	261	INCT	Octahedral	3.11
	310	INCT		
	450	LMCT		
	484	$^3A_{2g}$ (F) → $^3T_{1g}$(P)		
	574	$^3A_{2g}$(F) → $^3T_{1g}$(F)		
[CuL]	257	INCT	Distorted octahedral	1.80
	299	INCT		
	477	LMCT		
	591	$^2B_{1g}$ → $^2A_{1g}$		
[ZnL]	258	INCT	Octahedral	Diamagnetic
	289	INCT		
	447	LMCT		

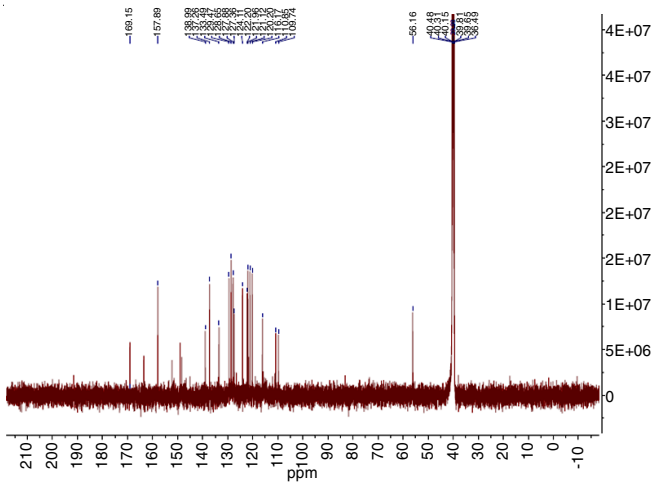


Fig. 3. ^{13}C NMR for Schiff base ligand (L)

and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$, respectively and also charge transfer band exhibits at 418 nm. The observed magnetic moment value is 3.11 B.M. [29]. These results suggested the presence of octahedral geometry for Ni(II) complex. The electronic spectrum of Cu(II) complex exhibits charge transfer band at 410 nm and a *d-d* transition band at 546 nm is assigned to $^2E_g \rightarrow {}^2T_{2g}$ and the magnetic moment value is 1.80 B.M. [30], which indicates a distorted octahedral geometry for Cu(II) complex. The spectrum of Zn(II) complex showed a band at 418 nm, which is due to charge transfer. The absence of absorption peaks at the visible region indicates an octahedral geometry around Zn(II) ion in the complex [31].

Solvatochromic effect: At room temperature, the effect of the solvent on UV-vis absorption behaviours of the Schiff base ligand (A) and its metal(II) complexes (B-E) was studied. The absorption spectra are often measured in solvents of different polarity and it is found that the position, as well as the intensity and shape of the absorption band, change with the nature of the solvents. The polarity of a solvent is determined by its solvation behaviour, which depends on the interaction between the solvent and the solute. These compounds (A-E) were analyzed in nine different solvents such as acetone, acetonitrile, chloroform, methanol, ethanol, DMSO, DMF, dichloromethane and ethyl acetate as shown in Fig. 5. In this study, it was found that their absorption maxima caused a evident bathochromatic shift (positive solvatochromism) in polar solvents, which could be due to changes in dipole moment and hydrogen bonding strength [32].

ESR studies: The X-band ESR spectrum of the Schiff base Cu(II) complex using DPPH as a reference is shown in Fig. 6. The g value observed for mononuclear Cu(II) complex is $g_{\parallel} = 2.21$, $g_{\perp} = 2.04$. According to the $g_{\parallel} > g_{\perp} > 2.0023$ trend observed for this complex, the unpaired electron was localized in Cu(II) ion's $d_{x^2-y^2}$ orbital, which corresponds to an octahedral geometry [33]. This compound shows a considerable covalent nature for the M-L bond represented by $g_{\parallel} < 2.30$. Exchange between copper centers is calculated using the formula $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$. The calculated G value is foud to be 4.7, which is greater than 4 indicating that the exchange coupling effects are not employable in the copper(II)complex [34].

Mass studies: Mass spectra of the ligand and its mononuclear metal(II) complexes are shown in Fig. 7. Schiff base ligand $C_{24}H_{24}N_2O_4$ shows a molecular ion peak at *m/z* 405 for its monomeric formulation. The *m/z* value observed at 665.56, 665.32, 616.13 and 636.98 [M+1] are the molecular ion peak of $C_{29}H_{38}N_2O_{12}Co$, $C_{29}H_{38}N_2O_{12}Ni$, $C_{29}H_{32}N_2O_9Cu$ and $C_{29}H_{34}N_2O_{10}Zn$ complexes, respectively, which indicate the stoichiometry composition of complexes.

Electrochemical studies: The ligand (L) and its Cu(II) complex were subjected to cyclic voltammetric studies with a view to exmine its electrochemical behaviour. A glassy carbon

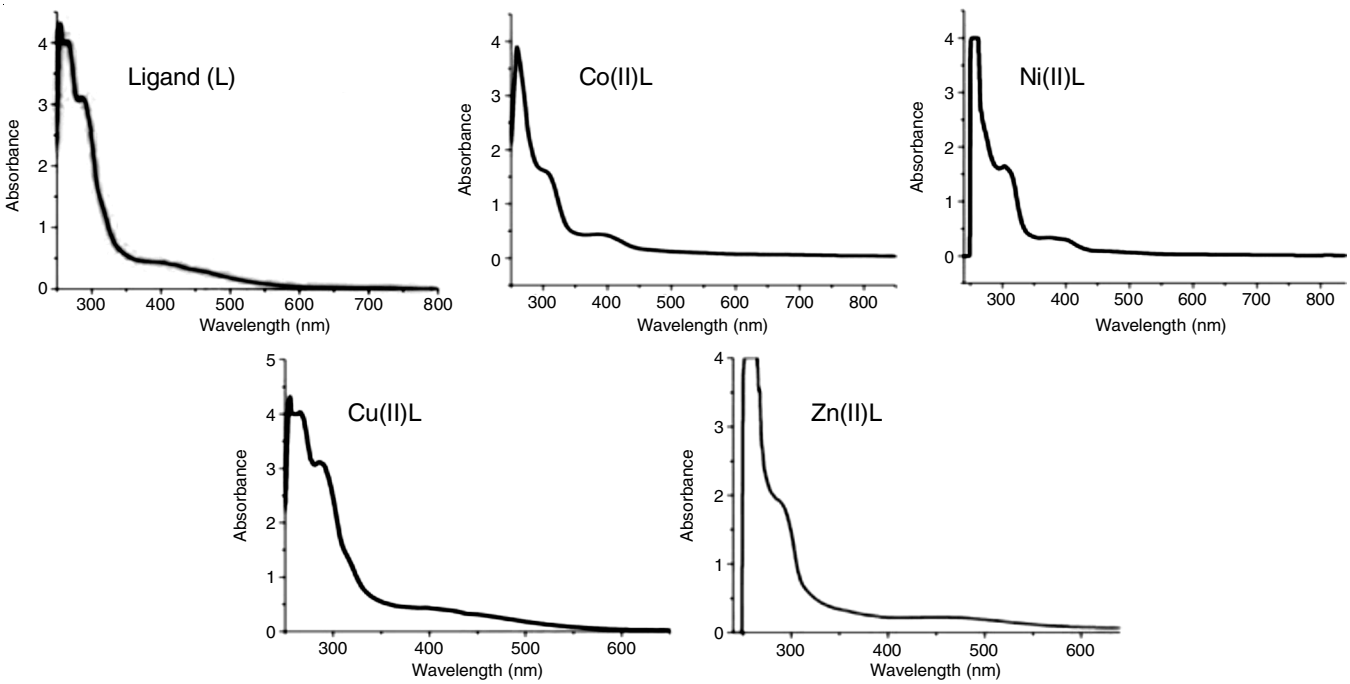


Fig. 4. UV spectra of ligand and its mononuclear metal(II) complexes

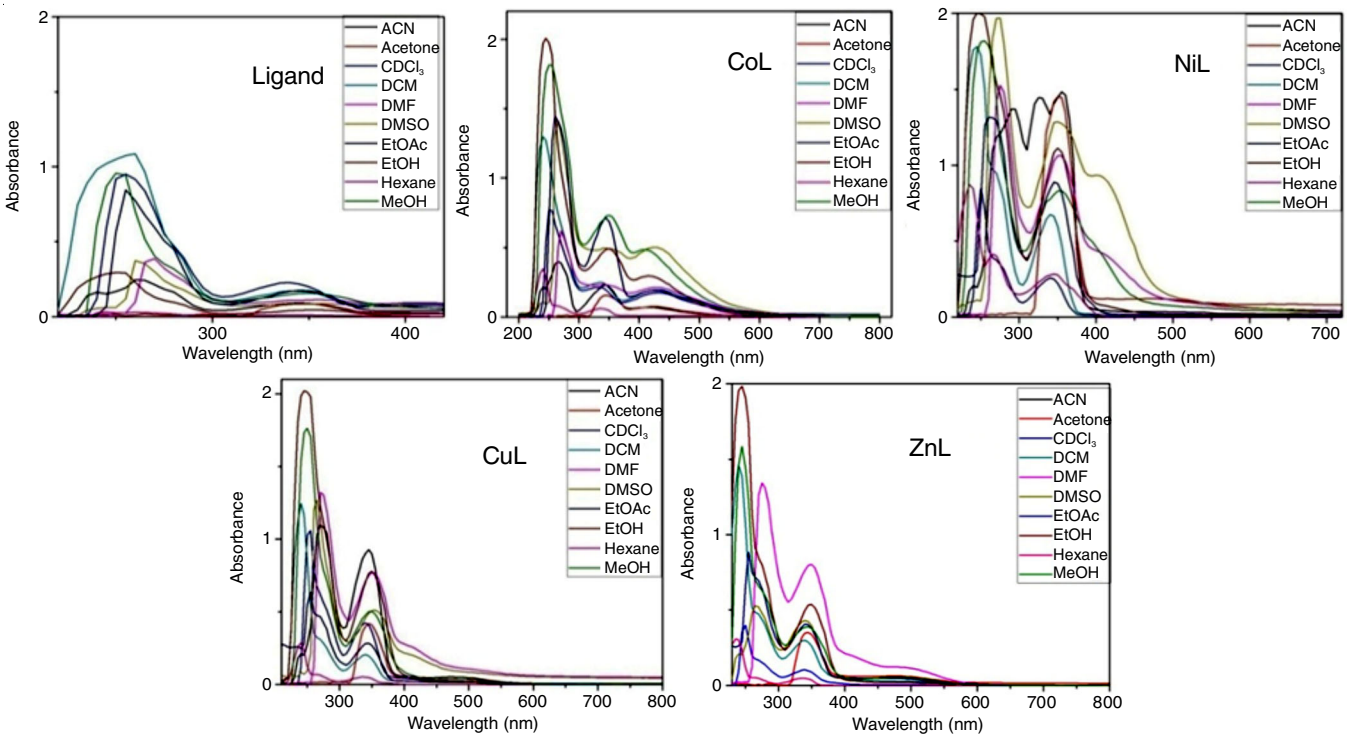


Fig. 5. Solvatochromic effect of Schiff base ligand and its mononuclear metal(II) complexes

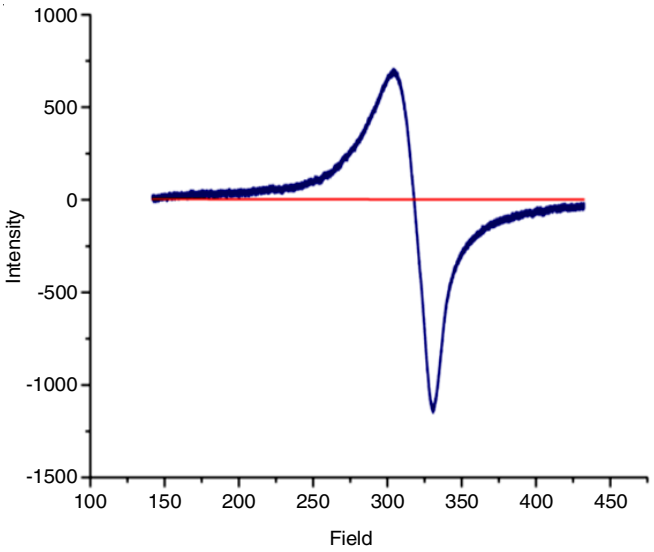


Fig. 6. ESR spectra for Cu(II) complex

electrode was used as working electrode, Ag/AgCl as reference electrode and platinum wire as auxillary electrode. The electro chemical studies were conducted with DMSO solution of the ligand and its copper(II) complex (1×10^{-4} M) and tetrabutylammonium hexaflorophosphate (0.01 M) as supporting electrolyte. Measurements were made over a potential range between -1.2 V to +2.0 V for Schiff base ligand and -1.5 V to +1.2 V for the corresponding comple with a scan rate of 0.1 V/s.

The ligand exhibits a quasi-reversible oxidation peak at E_{pa} = +0.81 V and a reduction peak at E_{pc} = -0.62 V. The cyclic votammogram of Cu(II) complex in DMSO exhibits a ligand-centered quasi-reversible oxidation beak at E_{pa} = +0.74 V and a reduction peak at E_{pc} = -0.52 V. The irreversible reduction peak at E_{pc} = +0.58 V for the free ligand disappeared by the complexation becoming more stable *via* coordination of nitrogen to metal (Fig. 8). The one-electron irreversible reduction peak at E_{pc} = +0.15 V is due to Cu(II)-Cu(I) couple. The irreversibility of the reduction process indicates that the reduced form Cu(I) is more stable than the Cu(II).

SEM analysis: SEM micrographs of the Schiff base ligand and its Co(II), Ni(II), Cu(II) and Zn(II) complexes are shown in Fig. 9. The SEM micrograph of ligand exhibits small irregular size particle morphology. The micrograph of Co(II) and Ni(II) complexes exhibits broken ice-cubed shaped grains. The Cu(II) complex exhibits broken rock and Zn(II) complex showed polycrystalline like morphology.

Antimicrobial activity: *In vitro* biological effects of the ligand and its mononuclear complexes were tested against two Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis),* two Gram-negative (*Klebsiella pneumonia*, *Escherichia coli)* bacteria and one fungus (*Candida albicans)* by the disc diffusion method. The obtained results (Table-4) show the moderate activity as compared with tetracyclin and fluconazole as the reference standards, DMSO solvent was also used as a positive control. The data revealed that the metal(II) complexes have higher activities than the free ligand. This enhancement of the activity of ligand on complexation can be clarified by Overtone's concept and Tweedy's chelation hypothesis [21]. The copper(II) complex shows higher antibacterial and antifungal activities than Co(II), Ni(II) and Zn(II) complexes.

***In vitro* anti-inflammatory activity:** The anti-inflammatory activities of the Schiff base ligand and its copper(II) complex were examined by the HRBCs membrane stabilization method. The percentages of inhibition of synthesized compounds are graphically presented in Table-5. Schiff base ligand and its

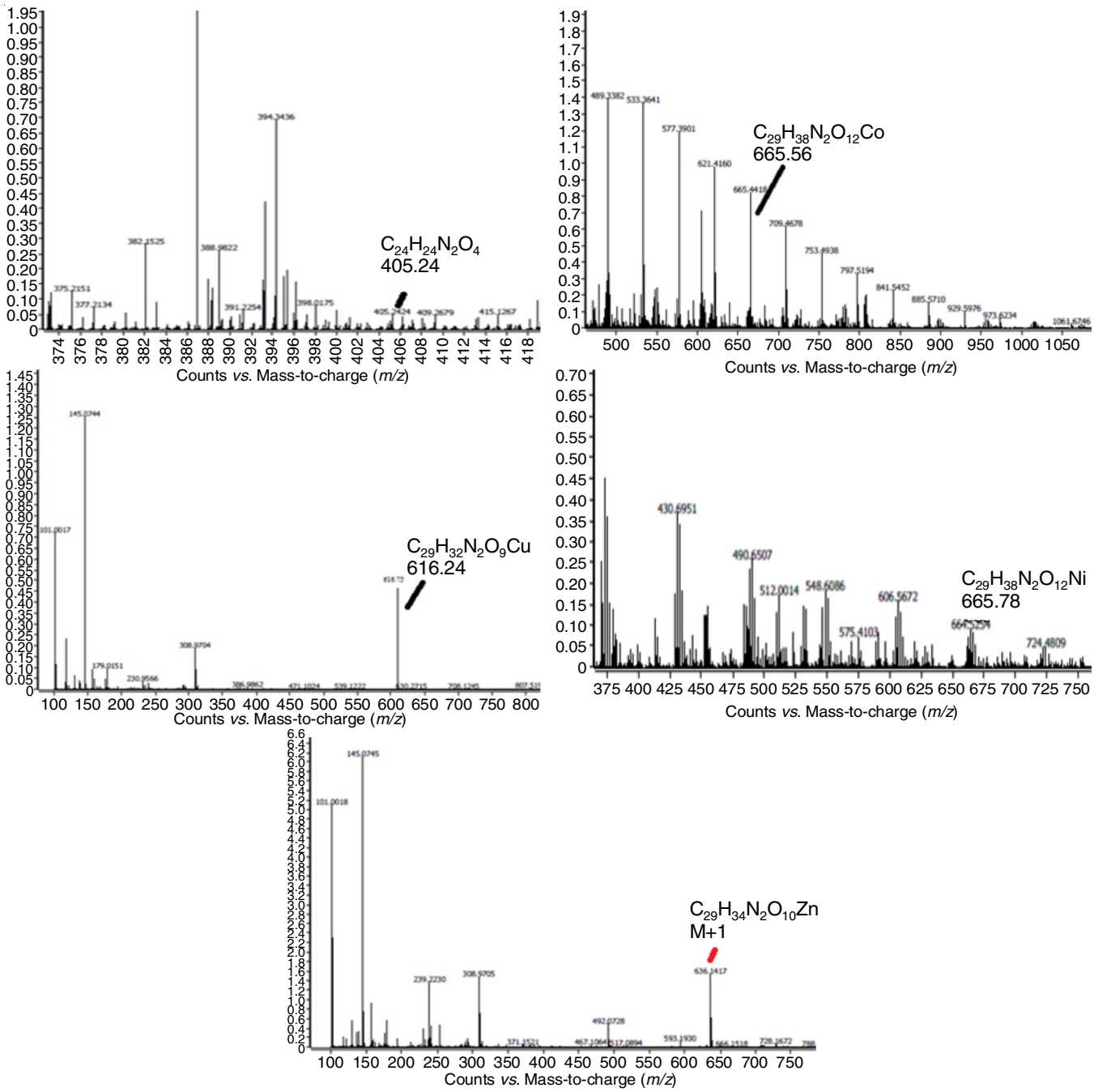


Fig. 7. Mass spectra of Schiff base ligand and its mononuclear metal(II) complexes

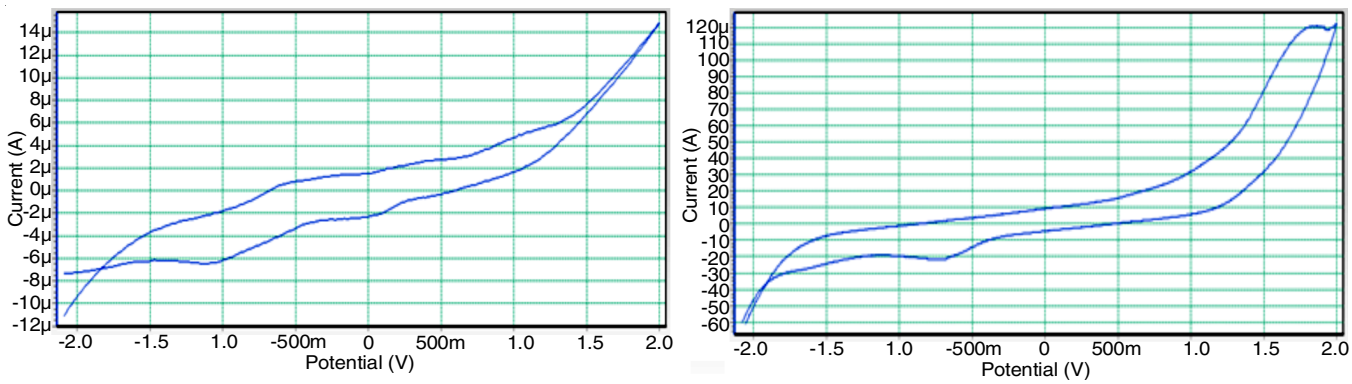


Fig. 8. Cyclic voltammogram of Schiff base ligand and its copper(II) complexes

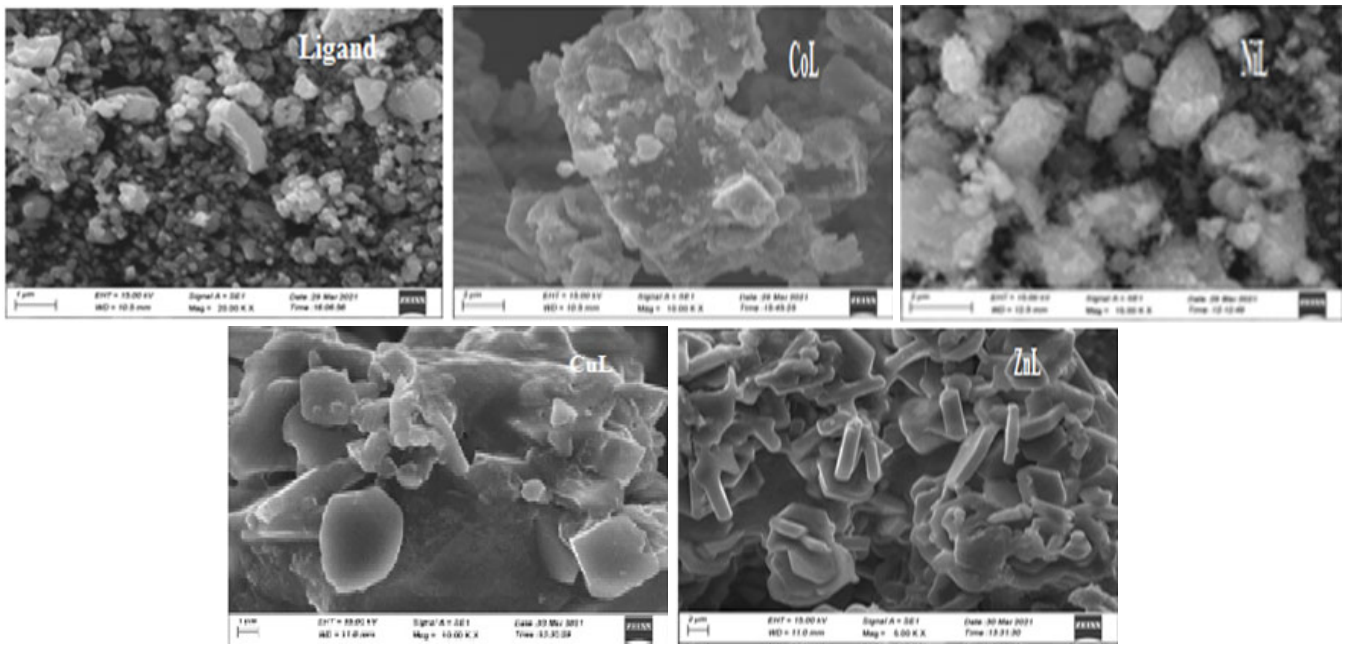


Fig. 9. SEM analysis of Schiff base ligand and its mononuclear metal(II) complexes

TABLE-4
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF THE SCHIFF BASE LIGAND AND ITS METAL COMPLEXES

Sample	Sample concentration (µg/mL)	Zone of inhibition (mm)				
		Gram-positive		Gram-negative		Fungi
		S. aureus	*B. subtilis*	*K. pneumonia*	*E. coli*	*Candida albicans*
Ligand	100	4	7	7	5	6
[CoL]	100	7	8	8	9	9
[NiL]	100	7	8	7	8	8
[CuL]	100	10	16	17	10	10
[ZnL]	100	5	14	16	5	9
Tetracylin		12	18	18	12	–
Fluconazole		–	–	–	–	14

TABLE-5
ANTI-INFLAMMATORY ACTIVITY OF SCHIFF BASE LIGAND AND ITS CuL COMPLEX

Compounds	Concentration (µg/mL)				
	20	40	60	80	100
	% of inhibition at 560 nm				
Standard	56.28	60.14	67.49	72.78	78.69
Ligand	34.15	46.04	52.16	61.98	65.02
CuL	40.12	53.16	55.86	63.25	70.56

copper(II) complex exhibits minimum efficiency compared to standard diclofenac sodium. The percentage inhibition of hemolysis increases with increase in concentration. Copper(II) complex showed maximum inhibition of 70% and the complex stabilized human blood cell membrane in a dose-dependent manner [35].

***In vitro* antidiabetic activity:** The antidiabetic therapeutic approach may reduce the postprandial glucose level in blood by inhibition of α-amylase enzymes, which can be an important strategy in the management of blood glucose [36]. The anti-diabetic activity was examined by the α-amylase inhibition assay. Inhibition activity of Schiff base ligand and its copper(II) complex against α-amylase is shown in Table-6. Copper(II) complex shows more inhibition efficiency than the synthesized Schiff base ligand.

TABLE-6
ANTIDIABETIC ACTIVITY DATA OF SCHIFF BASE LIGAND AND ITS CuL COMPLEX

Compounds	Concentration (µg/mL)					IC_{50} (µg/mL)
	10	20	30	40	50	
	% of inhibition at 540 nm					
Ligand	46.23	51.23	58.24	64.24	76.25	34.73
CuL	41.73	54.10	63.73	69.91	72.65	25.19

***In vitro* anticancer activity:** The anticancer activities of Schiff base ligand and its copper(II) complex were determined by MTT assay on human breast cancer cell line MCF7. The absorbance of the samples at 570 nm at various concentrations (3.125-50 µg/mL), the percentage of cell inhibition and IC_{50} values are reported in Table-7. The percentage of cell viability and IC_{50} values indicated that the copper(II) complex have higher sensitivity towards the breast cancer lines than the Schiff base ligand (Fig. 10). The copper(II) IC_{50} value is encouraging for further clinical testing of potential drugs [33,37].

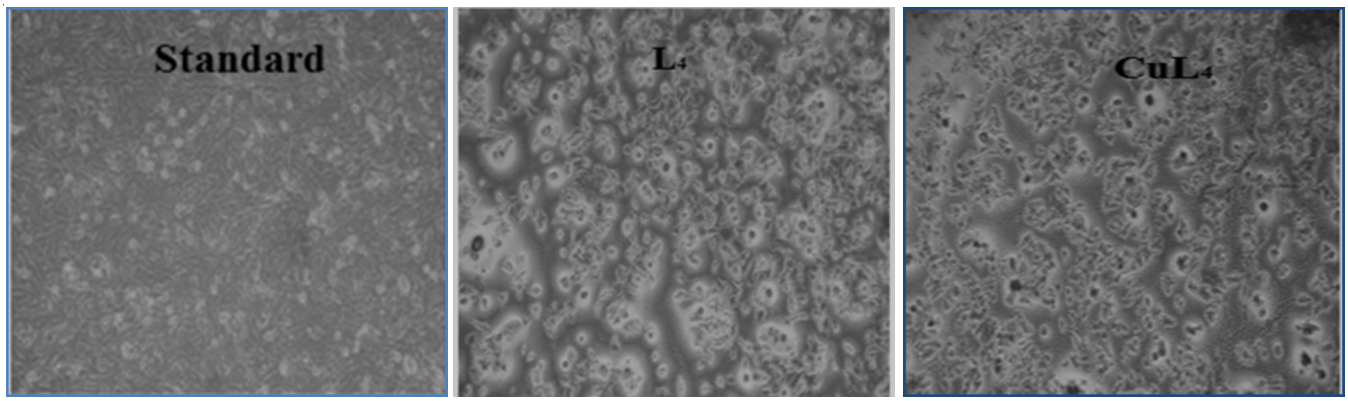


Fig. 10. Anticancer activities of Schiff base ligand and its copper(II) complex

TABLE-7
ANTICANCER EFFECTS OF SCHIFF BASE AND ITS COPPER(II) COMPLEX IN TERM OF % CELL INHIBITION AT VARIOUS CONCENTRATIONS

Conc. (µg/mL)	Ligand		CuL	
	Cell viability (%)	IC_{50} (µM)	Cell viability (%)	IC_{50} (µM)
3.125	98.86		94.72	
6.25	90.86		84.82	
12.5	77.25	41.48	62.91	28.26
25	56.34		43.86	
50	46.77		26.04	

Conclusion

A new Schiff base ligand derived from 4-(2-aminoethyl)-benzene-1,2-diol and terephthalaldehyde and its Co(II), Ni(II), Cu(II) and Zn(II) metal complexes were synthesized and characterized by using elemental and spectroscopic analysis. According to the molar conductance results for all the synthesized metal(II) complexes, are 1:2 electrolytic in nature. Based on electronic, ESR, magnetic, mass data, it was determined that the Co(II), Ni(II), Cu(II) and Zn(II) complexes have an octahedral geometry. Using cyclic voltammetric techniques, the Schiff ligand and its Cu(II) complexes were investigated for their electrochemical behaviour. *In vitro* biological effects of the ligand and its mononuclear complexes were tested against two Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*), two Gram-negative (*Klebsiella pneumonia*, *Escherichia coli*) bacteria and one fungus (*Candida albicans*) by the disc diffusion method. Antimicrobial data indicate that copper(II) exhibits more inhibitory activity than cobalt(II), nickel(II) and zinc(II) complexes. By stabilizing HRBCs, Schiff base ligand and its copper(II) complex were shown to exert anti-inflammatory properties. The activity increases with the concentration of the synthesized compounds. Inhibition activity of Cu(II) complex is superior to that of Schiff base ligand. By using the α-amylase inhibition assay method, the Schiff base ligand and its Cu(II) complex were investigated for antidiabetic activity. Copper(II) complex showed good antidiabetic properties. Schiff base ligand and its copper(II) complex were examined against the growth of the human breast cancer cell line (MCF-7) using the MTT assay process. The copper(II) complex showed higher IC_{50} value than the ligand against the cancer cell line. Overall, the antimicrobial, anti-inflammatory, antidiabetic and anticancer studies revealed that Cu(II) complex exhibit greater activity as compared to Schiff base ligands, which suggests their potential as a new molecular platform for developing and exploring pharmaceutical and physiological implications.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. M. Habibi, S.A. Beyramabadi, S. Allameh, M. Khashi, A. Morsali, M. Pordel and M. Khorsandi-Chenarboo, *J. Mol. Struct.*, **1143**, 424 (2017); https://doi.org/10.1016/j.molstruc.2017.04.114
2. M. Seethalakshmi and T.P. Amaladhas, *Orient. J. Chem.*, **34**, 1411 (2018); https://doi.org/10.13005/ojc/340330
3. A.M. Abu-Dief and I.M.A. Mohamed, *Beni-Suef Univ. J. Basic Appl. Sci.*, **4**, 119 (2015); https://doi.org/10.1016/j.bjbas.2015.05.004
4. R.M. Patil, *Acta Pol. Pharma. Drug Res.*, **64**, 345 (2007).
5. B. Dede and G. Gorgulu, *Acta Phys. Pol. A*, **133**, 256 (2018); https://doi.org/10.12693/APhysPolA.133.256
6. X. Zhou, X. Pang, L. Nie, C. Zhu, K. Zhuo, Q. Zhuo, Z. Chen, G. Liu, H. Zhang, Z. Lin and H. Xia, *Nat. Commun.*, **10**, 1488 (2019); https://doi.org/10.1038/s41467-019-09367-8
7. S. Gautam, S. Chandra, H. Rajor, S. Agrawal and P.K. Tomar, *Appl. Organomet. Chem.*, **2017**, e3915 (2017); https://doi.org/10.1002/aoc.3915
8. R.K. Mohapatra, A.K. Sarangi, M. Azam, M.M. El-ajaily, M. Kudrat-E-Zahan, S.B. Patjoshi and D.C. Dash, *J. Mol. Struct.*, **18**, 1 (2018); https://doi.org/10.1016/j.molstruc.2018.10.070
9. J. Grajewski, *Molecules*, **27**, 1004 (2022); https://doi.org/10.3390/molecules27031004
10. N.L. Mohammed, J.S. Al-shawi and M.J. Kadhim, *Int. J. Sci. Eng. Res.*, **7**, 31 (2019).
11. V.H. Rajurkar and V.N. Kamble, *Orient. J. Chem.*, **30**, 1847 (2014); https://doi.org/10.13005/ojc/300445
12. P.K. Das and S.K. Tripathy, *Int. Res. Innov. Appl. Sci.*, **1**, 7 (2016).
13. A.N. Srivastva, N.P. Singh and C.K. Shriwastaw, *Arab. J. Chem.*, **9**, 48 (2016); https://doi.org/10.1016/j.arabjc.2014.10.004
14. M.J. Kareem, A.A.S. Al-Hamdani, V.Y. Jirjees, M.E. Khan, A.W. Allaf and W. Al-Zoubi, *J. Phys. Org. Chem.*, **2020**, e4156 (2020); https://doi.org/10.1002/poc.4156
15. T. Gomathi, S. Karthik, S. Vedanayaki, *Indian J. Chem.*, **60A**, 26 (2021).
16. K. Balan, P. Ratha, G. Prakash, P. Viswanathamurthi, S. Adisakwattana and T. Palvannan, *Arab. J. Chem.*, **10**, 732 (2017); https://doi.org/10.1016/j.arabjc.2014.07.002

17. T. Gomathi, S. Karthik and S. Vedanayaki, *Int. J. Pharm. Technol.*, **12**, 32235 (2019);
18. N. Raman and S. Ravichandran, *Synth. React. Inorg. Met. Nano-Metal Chem*, **35**, 439 (2005); https://doi.org/10.1081/SIM-200066974
19. S. Malik, A. Singh and N. Ahmed, *Int. J. Sci. Eng. Technol. Res.*, **6**, 1 (2015).
20. A.M. Hammam, M.A. El-Gahami, Z.A. Khafagi, M.S. Al-Salimi and S.A. Ibrahim, *J. Mater. Environ. Sci.*, **6**, 1596 (2015).
21. N.K. Chaudhary and P. Mishra, *Bioinorg. Chem. Appl.*, **2017**, 1 (2017); https://doi.org/10.1155/2017/6927675
22. L. Gavali, *Int. J. Eng. Tech. Manag. Appl. Sci.*, **4**, 72 (2016).
23. A.S. Al-shihri, *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, **60**, 1189 (2004); https://doi.org/10.1016/j.saa.2003.07.005
24. M.S. Nair, D. Arish and R.S. Joseyphus, *J. Saudi Chem. Soc.*, **16**, 83 (2012); https://doi.org/10.1016/j.jscs.2010.11.002
25. K.V. Pai and B.H.M. Jayakumarswamy, *Int. J. Pharm. Technol. Res.*, **3**, 1864 (2011).
26. S.G. Jagdhani, S.K. Narwade, S.B. Kale and B.K. Karale, *Indian J. Heterocycl. Chem.*, **18**, 291 (2009); https://doi.org/10.15406/mojboc.2019.03.00092
27. S. Bal and S.S. Bal, *Adv. Chem*, **2014**, 1 (2014); https://doi.org/10.1155/2014/506851
28. S. Mani, V. Subramanian, N. Ramaswamy and B. Kartha, *Chem. Sci. Rev. Lett.*, **13**, 121 (2015).
29. M.S. Mohamad, *Acta Chim. Pharm. Ind.*, **3**, 140 (2013).
30. S.K. Bhat and J. Singh, *IOSR J. Appl. Chem.*, **10**, 46 (2017); https://doi.org/10.9790/5736-1004014649
31. A.T. Bader, B.I. Al-abdaly and I. Jassim, *J. Pharm. Sci. Res.*, **11**, 2062 (2019).
32. C. Anitha, C.D. Sheela, P. Tharmaraj and R. Shanmugakala, *Int. J. Inorg. Chem.*, **2013**, 1 (2013); https://doi.org/10.1155/2013/436275
33. H.F. Abd El-Halim, G.G. Mohamed and M.N. Anwar, *Appl. Organomet. Chem.*, **2017**, e3899 (2017); https://doi.org/10.1002/aoc.3899
34. R. Jayalakshmi, *J. Adv. Appl. Sci. Res.*, **7**, 1 (2017).
35. D. Gangrade and S. Lad, *J. Chem. Pharm. Res.*, **8**, 1132 (2016).
36. M. Azam, S.I. Al-Resayes, S. Wabaidur, M. Altaf, B. Chaurasia, M. Alam, S. Shukla, P. Gaur, N. Albaqami, M. Islam and S. Park, *Molecules*, **23**, 813 (2018); https://doi.org/10.3390/molecules23040813
37. B. Parasuraman, J. Rajendran and R. Rangappan, *Orient. J. Chem.*, **33**, 1223 (2017); https://doi.org/10.13005/ojc/330321