Synthesis, Characterization, 3D Modeling, Biological 
Activities of Some Metal Complexes of Novel Sulpha 
Drug Schiff Base Ligand and Its Nano Cu Complex

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Abstract: Novel solid Co(II), Ni(II), Cu(II) and Zn(II) complexes of sulpha drug Schiff base ligand (HL) derived from condensation of sulphaquinoxaline and naphthaldehyde namely, 2-{4-[(2-hydroxynaphthalen-1-yl)methyleneamino]benzenesulfonamido} quinoxalin (HNMABSQ), in addition new mixed ligand complexes with 8-hydroxyquinoline (8-HQ) or 1,10 Phenanthroline (1,10 Phen) with HL and these metal (II) ions were synthesized. The structure of complexes were proposed in light of analytical, IR, "H-NMR, Mass, UV-Vis, ESR spectral data, magnetic and thermal studies. The molar conductance data reveal that all the metal chelates were non-electrolytes. The kinetic and thermodynamic parameters for decomposition steps in Co(II), Ni(II) and Cu(II) complexes thermo grams were calculated. On the basis of these studies, most complexes have octahedral geometry but few can attain the square planar arrangement. 3D modeling of the ligand and its metal complexes were studied by PM3 method, also the heat of formations, HOMO, LUMO and dipole moments were calculated to confirm the geometry of the ligand and its complexes. Schiff base ligand and its metal complexes were tested for antimicrobial activities. Nano-Cu- Schiff base complex was synthesized and characterized by scanning electron microscopy (SEM) and its biological activities were studied. The Cu nano complex had higher antibacterial and antifungal activity than the ligand and its metal complexes. Also, all tested compounds inhibited the growth of the liver cancer cell.

Keywords: Sulphaquinoxaline, Schiff Base, Metal Complexes, Spectral Studies, Antimicrobial, Anticancer Activity, Nano Complexes

1. Introduction

Extensive research of Schiff bases have been carried out due to their interesting and important properties, such as their ability to form complexes with most transition metal ions and for their biological activity such as antibacterial, antifungal and antitumor activities [1-4]. Metal complexes of Schiff bases have been investigated because they play an important role not only in the development in coordination chemistry, but also in catalysis, enzymatic reaction, magnetism, molecular architectures [5-7] and exhibit biological applications and pharmaceutical activities [8-10]. Sulphaquinoxaline compounds are largely used as antibacterial [8] antifungal [9] and antitumor [10, 11]. The metal complexes of Schiff base derived from sulfa drugs have gained considerable importance due to their having good complexion ability [12-15]. They exhibit also a range of bioactivities, including antitumor, anti-inflammatory, antibiotic, anti-glaucoma, anti-microbial and anti malarial agent [16-22].

Recently, nano materials have been receiving increased attention due to their tremendous applications in the field of catalysis, sensor technology and fabrication of ultramodern electronic devices [23, 24]. Preparing pure transition-metal nano materials is an important topic [25, 26]. Schiff base ligand and nano Schiff-base-Cu complexes inhibited the growth of the liver cancer cell [27, 28].

So, the present work aimed to synthesize and characterize Co (II), Ni (II), Cu (II) and Zn (II) metal complexes with newly synthesized sulpha drug Schiff base ligand derived from sulphaquinoxaline and naphthaldehyde. The Schiff base ligand, its metal complexes and its Cu-nano complex were tested for antibacterial and antifungal activities. The Cu nano Schiff base complex had higher antimicrobial activity than
the ligand and its metal complexes. Also, all tested compounds inhibited the growth of the liver cancer cell.

2. Experimental

2.1. Materials

The chemicals used were obtained from Aldrich, BDH or Merck products. The solvents used were ethanol, isopropanol, DMF and diethylether. These solvents were either spectroscopically pure or purified by the recommended methods [29] and were tested for their spectral purity.

2.2. The Apparatus and Physical Measurement

Melting points were determined on a digital Stuart SMP³ apparatus. Elemental microanalyses were performed at Microanalysis Center in National Research Center, Giza, Egypt. The electronic absorption spectra of the ligand and their complexes in DMF were recorded at room temperature within the wavelength range 200-800 nm by the aid of UV-Vis spectrophotometer (Shimadzu UV-1601PC). The FT-IR spectra (4000-400 cm⁻¹) of the compounds were recorded as KBr discs using FT-IR (Nicolet is10) spectrophotometer.¹H-NMR spectra were recorded using a Varian spectrometer, FT-290, 90 MHz at Microanalytical Center, Cairo University, Giza, Egypt. Deuterated DMSO-d₆ was used as a solvent and tetramethylsilane (TMS) as an internal reference. Mass spectra of the compounds were recorded on a Shimadzu QP-290, 90 MHz at Microanalytical Center, Cairo University, Giza, Egypt. The electronic absorption spectra of the ligand and its metal complexes. Also, all tested compounds inhibited the growth of the liver cancer cell.

2.3. Synthesis of Schiff Base Ligand (HL)

Ethanoic solutions of sulphaquinoxaline (2.5 gm, 0.008 mol) and naphthaldehyde (1.4 gm, 0.008 mol) in 1:1 molar ratio were mixed and refluxed for 8 hours. The orange precipitate was formed, filtered off, recrystallized from ethanol then dried under vacuum to give orange crystal, yield 90 %, m.p.280 °C.

The purity of the prepared Schiff base ligand was examined by elemental analysis, IR, ¹H NMR, UV-Vis and mass spectra as the following:

- Anal; Calcd: C, 70.59; H, 7.35; N, 10.29 ,Found: C, 70.19; H, 7.13; N, 9.92
- IR (cm⁻¹); υOHphenolic 3355,υC=N 1624,NH 3066,SO₂ass 1135 and SO₂sym 1089.
- ¹H NMR; δ (ppm) 3.33 (s, H, CH₃aliphatic), 6.97-8.28 (m, 15H, CH₃aromatic) and 6.95-8.19 (m, 13H, CH₂aromatic), respectively, δ (8.41) (s, 1H) was assigned to the azomethine proton (-N=CH-) of the Schiff base (HL). Signals at 8.94-9.64 (s, H, NH) and 12.11-12.47 (s, H, OHphenolic). The ¹H NMR spectrum of the ligand HL showed signal at 15.32 which may be due to H-bond formation between the phenolic OH and azomethinegroup. The signals due to the protons of the phenolic OH groups and H-bond completely disappeared on adding D₂O while the other signals still persist at the same positions.
- UV-Vis spectra; λmax (nm), the band located at (282) is due to the low energy π- π* transition of the aromatic system, the band within the (331) can be assigned to π- π* transition within the C=O groups and the band located at (469) is due to an intermolecular charge transfer within the whole molecule (CT).
- Mass fragmentation spectrum of Schiff base ligand under investigation is shown in Fig. 1. Schiff base ligand fragmentation exhibits the molecular ion peak (m/e) = 454, which is the same as that of the molecular weight of the ligand. Generally, the fragmentation of mass spectra of the ligand showed three main pathways, Scheme 1.
Schiff base ligand (HL)

2-[4-[(2-hydroxynaphthalen-1-yl)methyleneamino]benzenesulfonamido]quinoline, (HNMABSQ)
2.4. Preparation of the Solid Complexes

Ethanolic solutions of Schiff base ligand and the metal nitrate salts of Co(II), Ni(II), Cu(II) or Zn(II) ions were mixed in a 1:1 or 1:2 (L:M) molar ratio in the preparation of all complexes, the resulting solutions were stirred for about 1 hour, then refluxed on a hot plate from 6 to 8 hours. The solid complexes which separated out on hot were filtered off after cooling to room temperature, washed with small amounts of bidistilled water, diethylether and finally dried in vacuum desiccator over anhydrous CaCl$_2$. All of the complexes prepared were stable at room temperature, non-hygroscopic, insoluble in common organic solvents except DMF.

2.5. Preparation of Mixed Ligand Complexes

An ethanolic solution of the metal salt was added gradually to an ethanolic solution of the ligand in the molar ratio 1:1 (L: M). The resulting solutions were stirred for one hour, then an ethanolic solution of 8-hydroxyquinoline (8-HQ) or 1,10 phenanthroline (1,10-phen.) was added to the previous solution in the molar ratio 1:1 (8-HQ or 1,10-phen: M), the solutions were continuously stirred for 10 hours. The solid complexes which separated out on stirring were filtered off, washed with hot ethanol then diethylether and finally dried in vacuum desiccator over anhydrous CaCl$_2$. All of the complexes prepared were stable at room temperature, non-hygroscopic, insoluble in common organic solvents except DMF.

2.6. Preparation of Nano Cu-Schiff Base Complex

The copper nanoparticles were prepared using several methods such as thermal reduction, metal vapor synthesis, radiation methods, microemulsion techniques, laser ablation, mechanical attrition, thermal decomposition and chemical reduction [30-31]. Among these methods, the reduction method was the most popular one because of the simplicity of its device and technical process. In the chemical reduction technique, a copper salt was reduced by a reducing agent such as sodium borohydride, hydrazine (N$_2$H$_4$), ascorbate or isopropyl alcohol with cetyltrimethylammonium bromide (CTAB) [32-33]. In this work, the nano compounds were prepared by chemical reduction method using isopropyl alcohol with cetyltrimethylammonium bromide (CTAB) as reducing agent.

Nano Cu-Schiff base complex was synthesized according to Athwale et al [34]. by adding 4 ml of 0.01M ethanolic solution of Schiff base ligand (HL) drop wise to dry clean beaker contains a mixture of 40 ml CTAB (1x10$^{-3}$M) with 4 ml copper nitrate (0.01 M) in ethanolic solution. The reaction mixture was stirred on a magnetic stir plate about 4 hours. Leave the reaction mixture few days. The solution will precipitate forming nano Cu-Schiff base complex giving characteristic golden colour as shown in the following image Fig.2.

The nano-structure was characterized by the electronic and ESR spectra, in addition to scanning electron microscopy (SEM), Fig. 3. The SEM picture of the nano-Cu-Schiff base complex showed a small particle size with a nano feature products. The particles size of nano complex was calculated by smile view program, which gave (39 – 96) nm range.

3. Results and discussion

3.1. Elemental Analysis and Molar Conductance of Solid Complexes

On the basis of elemental analysis, the metal complexes of HL ligand under investigation were assigned to posses the compositions and molecular formulae listed in Table 1. The analytical data of the isolated solid complexes were in good agreement with the proposed structures. The result of elemental analysis of the solid complexes indicated that the metal ions reacted with the ligand in molar ratios 1:2 (M: L) for complexes 1, 4, 7, 10. The results reveal that the ligand act as bidentate towards the metal ions via the azomethine –N atom and phenolic –O atom. The chemical composition of the mixed ligand complexes under investigation (HL) and 8-hydroxyquinoline (8-HQ) or 1,10 Phenanthroline (1,10 phen) with Co(II), Ni(II), Cu(II) and Zn(II) ions were determined from the elemental analysis results which collected in Table 1. The results of the elemental analysis indicated that the metal ions reacted with the ligands (HL) and 8-hydroxyquinoline (8-HQ) or 1,10 Phenanthroline in the molar ratios 1:1 (M: L: 8-HQ or 1,10 phen) for the complexes 2, 3, 5, 6, 8, 9, 11 and 12. The results reveal that the
Schiff base ligand act as bidentate towards the metal ions via the azomethine –N atom and phenolic –O atom. 8-HQ acts as bidentate towards the metal ions via quinoline –N and hydroxyl – O atoms in none and deprotanated form.1, 10 phen acts as bidentate towards the metal ions via two phenanthroline –N atom. The result of elemental analysis also showed that most of the prepared complexes have one or more H₂O or EtOH molecule associated with the complex which are not removed by static vacuum for six hours at room temperature. The molar conductance values (Ω cm² mol⁻¹) of the metal complexes were collected in Table (1). All solid complexes have Ω values in the range 6.64– 19.01 ohm⁻¹ cm² mol⁻¹ which fall within the range of non electrolytes. This indicates that all these complexes are neutral [35].

### Table 1. Analytical and physical data of the metal complexes of the ligand HL

| Compound                        | color       | M.P. °C | M.Wt gm | Analysis (calc. %) Found % | % C    | % H    | % N    | % S    | % M    | Ω Ohm⁻¹ Cm² mol⁻¹ |
|--------------------------------|-------------|---------|---------|---------------------------|--------|--------|--------|--------|--------|-----------------|
| [Co(L)₂(H₂O)₂]H₂O              | orange      | > 300   | 1073    |                           | 55.62  | 4.47   | 9.50   | 5.26   | 5.90   | 17.51           |
| [Co(L)(Phen)(H₂O)NO₃]          | Reddish brown | > 300  | 772     |                           | 58.08  | 3.62   | 11.70  | 3.2    | 8.26   | 11.49           |
| [Co(L)(H₂O)₂]H₂O               | Pale brown  | > 300   | 710     |                           | 57.68  | 3.91   | 10.7   | 3.6    | 7.7    | 17              |
| [Ni(L)₂(H₂O)₂]H₂O              | brown       | > 300   | 1018.7  |                           | 58.18  | 3.75   | 10.64  | 6.10   | 5.88   | 18.52           |
| [Ni(L)(Phen)(H₂O)NO₃]          | brown       | > 300   | 754     |                           | 59.19  | 3.88   | 13.0   | 5.13   | 7.26   | 17.26           |
| [Ni(L)(H₂O)₂]EtOH              | brown       | > 300   | 737.86  |                           | 57.96  | 4.15   | 9.24   | 4.24   | 9.7    | 19.0            |
| [Cu(L)₂]₂EtOH                  | brown       | > 300   | 1061.5  |                           | 61.73  | 3.7    | 9.48   | 5.6    | 6.5    | 13.5            |
| [Cu(L)(Phen)(H₂O)NO₃]EtOH       | green       | 251     | 804.5   |                           | 58.82  | 3.98   | 11.18  | 4.26   | 8.70   | 18.83           |
| [Cu(L)(H₂O)]₃EtOH              | brown       | > 300   | 706.66  |                           | 61.72  | 3.94   | 9.33   | 4.71   | 9.00   | 9.51            |
| [Zn(L)₆H₂O]                    | orange      | > 300   | 1079    |                           | 55.39  | 3.65   | 10.22  | 5.50   | 6.70   | 17.8            |
| [Zn(L)(Phen)(H₂O)NO₃]          | orange      | > 300   | 776     |                           | 58.09  | 3.34   | 11.64  | 4.94   | 9.30   | 7.78            |
| [Zn(L)(H₂O)]₂H₂O               | orange      | 238     | 680     |                           | 59.85  | 3.63   | 10.36  | 4.39   | 9.80   | 6.64            |

### 3.2. IR Spectral Studies

The mode of bonding of the Schiff base complexes was elucidated by investigating the IR spectra of the metal complexes as compared with that of the free Schiff base. The IR spectra of most solid complexes exhibit a broad band within the range 3361- 3442 cm⁻¹, which is attributed to the νOH of water and/or EtOH molecules associated with the complex. Also, the existence of the new bands at 617- 695 cm⁻¹ for complexes 1,2,3,4,5,6,8 and 11 is attributed to pH₂O of coordinated water molecules, indicating the presence of coordinated water molecules in the metal ion complexes. The disappearance of νOH phenolic in the IR spectra of all solid complexes under investigation which are observed at 3355 cm⁻¹ in the IR of the free ligand, denotes that proton displacement from the phenolic νOH group takes through the metal ion. This is confirmed by the existence of new bands at 500- 568 cm⁻¹ in the IR spectra of all metal chelates which are absent in the IR spectra of the free ligand which could be assigned to νM-O bonds. The νC=N band observed at 1624 cm⁻¹ in the IR of the free ligand is shifted to lower wave numbers by 8-12 cm⁻¹ in the IR spectra of all metal complexes under investigation, indicating the coordination of the azomethine nitrogen atoms to the metal ions, which is supported by the existence of new bands in the IR spectra of all metal complexes at 419- 498 cm⁻¹, these bands would be assigned to ν M-N bonds [36]. The complexes 2, 5, 8 and 11show new bands at 1312- 1344 cm⁻¹ due to NO₃⁻ ion which support the coordinated nature of the NO₃⁻ ion [36]. The IR spectra of free ligand HL shows band at 3066 cm⁻¹ indicating that the presence of νOH group, this band lies as it is in all solid complexes under investigation, indicating that the N atom of NH group dos not participate in complex formation. Also, the SO₃⁻ group modes of the ligand appears two bands at 1135and 1089 cm⁻¹ assigned to νasymmetric NO and νsymmetric SO₃⁻ respectively .These bands appear also at its same position in case of all solid complexes under investigation which indicate that the SO₃⁻ group does not coordinated to metal ion.

### 3.3. ¹H-NMR Spectral Studies

¹H-NMR spectra of Schiff base ligand and its Zn (II) complex were recorded in DMSO-d₆. The signal at δ (8.41) (s, 1H) was assigned to the azomethine proton (N=CH-) of the Schiff base (HL) shifted downfield in the region of δ (8.65) (s, 1H), supporting the coordination of the ‘N’ of the –N=CH- group with the metal ion. The peak due to hydroxyl proton originally present at δ ~12.11- 12.47 ppm in free Schiff base ligand is completely absent from the spectra of Zn(II) complex suggesting the bonding through hydroxyl
oxygen atom. The appearance of a peak at signals at 8.9-9.6 (s, H, NH) ppm as a broad singlet could be assigned to N-H group for both the ligand and its Zn(II) complex respectively, suggesting the non-involvement of N-H group in bond formation.

3.4. Mass Spectral Studies

The FAB mass spectrum of the Cu(II) complex showed a molecular ion peak at m/z 21061, which is the same as that of the molecular weight of the complex. This supports the suggested structure for the complex.

3.5. Thermo Gravimetric Analyses

The aim of the present thermal gravimetric analysis (TGA) study is to obtain information concerning to the thermal stability of the investigated chelates and to determine the point at which thermogravimetry, DTG) are useful in attempting to resolve overlapping processes and to determine the point at which the mass loss is most significant, also it useful for some methods of calculation the thermodynamic parameters [35].

The TGA-DTG curves of some metal complexes, namely Co(II), Ni(II) and Cu(II) complexes were recorded from ambient temperature up to 800 °C under N2 gas flow at heating rate of 10°C/min as shown in Fig.4.

For the Co(II) complex, a mass loss occurred within the temperature range 42-126°C corresponding to the loss of 3.2% (Calcd 3.3%) for two molecules of lattice water and at the temperature range 127-297 °C another loss of 6.1% (Calcd. 6.7%) for another two lattice and two coordinate water molecules. In the temperature range 298-356 °C a mass loss of 4.6% (Calcd. 5.0%) corresponding to two HCN molecules. At the temperature range 356.9-473 °C a loss of 36.5% (Calcd. 37.1%) for C23H19N3S as apart of ligand decomposition. At higher temperature range 473.9 - 789 °C a loss of 36.3% (Calcd. 37.1) corresponding to C23H19N3S as another part of CoO. For the Cu(II) complex, a mass loss occurred within the temperature range 41.5 – 231.7 °C, corresponding to the loss of 3.02% (calc.3.3%) for two water molecules (Lattice and coordinated) and at the temperature range 232.2 – 369 °C, another loss of 23.8% (calc.23.6) % for another one coordinate water with 2HCN and C8H16N2O4S as apart from the ligand. At higher temperature range 397 - 778 °C a loss of 59% (Calcd. 58%) corresponding to C23H19N3S4O4 decomposition of the compound then it gives CoO.

For the Ni (II) complex, a mass loss occurred within the temperature range 41.5 – 231.7 °C, corresponding to the loss of 3.02% (calc.3.3%) for two water molecules (Lattice and coordinated) and at the temperature range 232.2 – 369 °C, another loss of 23.8% (calc.23.6) % for another one coordinate water with 2HCN and C8H16N2O4S as apart from the ligand. At higher temperature range 397 - 778 °C a loss of 59% (Calcd. 58%) corresponding to C23H19N3S4O4 decomposition of the compound then it gives NiO.

For the Cu (II) complex, a mass loss occurred within the temperature range 34 – 200° corresponding to the loss of 20.4 % (calc.20.9%) for two molecules of lattice ethanol with C6H12N2. At the temperature range 225 – 300 °C another loss of 24.5% (calc.25.6) % for C6H12N2SO4. In the temperature range 305 – 400 °C a mass loss of 9.2% (calc.9.8) % corresponding to C6H12N. At higher temperature range 400.5 – 799°C a loss of 35.8% (35.8%) corresponding to C27H13N2O2 from the compound, then it forms CuO.

The order of the subsequent ligand will be lower than that of the reactants and / or the reactions are fast [38].

The other thermo kinetic parameters (∆H*, ∆S*, ∆G*) were calculated. The order (n) and thermo kinetic parameters of the decomposition steps for the chosen complexes are listed in Table 2. From the obtained data, the following remarks can be pointed out:

1-The ∆S* values for complexes were found to be positive. This indicates that the activated complex is less ordered than the reactants and / or the reactions are fast [38].

2-The values of ∆G* increase significantly for the subsequently decomposition stages due to increasing the values of ∆S* from one step to another which override the values of ∆H*. This increase reflects that the rate of removal of the subsequent ligand will be lower than that of the precedent ligand [39]. This may be attributed to the structural rigidity of the remaining complex after the expulsion of one and more ligands, as compared with the precedent complex, which requires more energy for its rearrangement before

![Fig. 4. TGA - DrTGA curves of Co (II), Ni(II) and Cu(II) complexes](image-url)
undergoing any compositional change.

3-The positive values of $\Delta H^*$ means that the decomposition processes are endothermic.

| Complex | step | n  | R            | $E^*$ (kJmol$^{-1}$) | $\Delta H^*$ (kJmol$^{-1}$) | $A^*$ (S$^2$) | $\Delta S^*$ (kJmol$^{-1}$K$^{-1}$) | $\Delta G^*$ (kJmol$^{-1}$) |
|---------|------|----|--------------|----------------------|-----------------------------|---------------|--------------------------------|--------------------------------|
| [Co(L)$_2$(H$_2$O)$_4$]H$_2$O | 1$^a$ | 1  | 0.9933      | 0.03213              | 0.909300                    | 3.52055       | 0.06348                         | 6.28267                       |
| [Ni(L)$_2$(H$_2$O)$_2$]H$_2$O | 1$^a$ | 1  | 0.9933      | 0.03213              | 0.909300                    | 3.52055       | 0.06348                         | 6.28267                       |
| [Cu(L)$_2$]2EtOH | 1$^a$ | 1  | 0.9933      | 0.03213              | 0.909300                    | 3.52055       | 0.06348                         | 6.28267                       |

3.6. Magnetic Properties

The magnetic moment values obtained at room temperature were listed in Table 3. The magnetic measurements for all Co(II) and Ni(II) complexes showed magnetic moment values of 4.3-5.3 and 2.88-3.6 BM respectively, suggesting consistency with their octahedral environment [35]. The Cu(II) complexes 7, 8 and 9 showed magnetic moment values of 4.3-5.3 and 2.88-3.6 BM respectively expected for one unpaired electron, which offers the possibility of a distorted octahedral or square planer geometry [39]. The measured effective magnetic values for the Cu-complexes, some what higher than spin-only value. Such divergence is not uncommon Cu(II) complexes due to mixing-in of some angular momentum from the closely lying excited state via spin-orbit coupling [40].

3.7. Electronic Spectral Studies

The electronic spectra of the Co(II), Ni(II), and Cu(II) complexes were recorded in freshly prepared DMF solution (10$^{-3}$ M) at room temperature and the spectral data were presented in Table 3. The electronic absorption spectra of the Co(II) complexes namely, 1,! and 3 show bands at 658, 665 and 650 nm respectively corresponding to $^4T_{1g}(F)$ $\rightarrow$ $^4A_2g(P)$ and $^4T_{1g}(F)$ $\rightarrow$ $^4T_{1g}(P)$ transitions indicating octahedral structure [41]. The Ni(II) complexes 4, 5, 6 exhibited 2 absorption bands, at 630-645 and 740-768 nm ranges, assignable to $^3A_{2g}(F)$ $\rightarrow$ $^3T_{1g}(F)$ ($\nu_3$) and $^3A_{2g}(F)$ $\rightarrow$ $^3T_{2g}(P)$ ($\nu_4$) transitions, respectively, in an octahedral environment [42]. The Cu(II) complexes 7, 8 and 9 exhibited a single broad asymmetric band in the region of 630-658 nm ranges corresponding to $^2E_g$ $\rightarrow$ $^2T_{2g}$. The broadness of the band may have been due to dynamic Jahn-Teller distortion. All of these data suggested a distorted octahedral geometry around the Cu(II) ion in case of complex 8 or distorted octahedral leads to square planer geometry around the Cu(II) ion in case of complexes 7 and 9 [42]. As expected, the electronic spectra of the Zn(II) complexes do not furnish any relevant data towards stereochemistry, but on the basis of analytical, conductance, and infrared spectral data, a square planer geometries were proposed for the complexes 10 and 12 of the Zn(II) complexes and octahedral for the complex 11.

In case of Cu-nano complex, the mole ratio 1:30 provided an absorption peak at 560 nm (Table 4) with no residual absorption at 800 nm (corresponding to Cu$^{2+}$ ions), and no shoulder at 630 nm which disappeared at later stages of addition. The latter absorption band may due to the formation of a transient complex between terminal ammmonium ion of CTAB and Cu$^{2+}$ ions in IPA which may be converting to Cu$^{0}$ (peak at 560 nm) at latter stages, confirming formation of pure spherical copper particles [34]. Also, this change is related to the complex formation between Schiff base ligand (HNMBSQ) and colloidal Cu-nanoparticles.

| No. | complexes | $\lambda_{max}$(nm) in DMF solution | d-d assignment | $\mu_{eq}$ B.M. | g$_{eq}$ |
|-----|-----------|-----------------------------------|----------------|----------------|---------|
| 1   | [Co(HNMBSQ)$_2$(H$_2$O)$_4$]H$_2$O | 658 | $^4T_{1g}(F)$ $\rightarrow$ $^4A_2g(P)$, $^4T_{1g}(F)$ $\rightarrow$ $^4T_{1g}(P)$ | 5.1 |       |
| 2   | [Co(HNMBSQ) Phen (H$_2$O) (NO$_3$)$_2$] | 665 | $^4T_{1g}(F)$ $\rightarrow$ $^4A_2g(P)$, $^4T_{1g}(F)$ $\rightarrow$ $^4T_{1g}(P)$ | 4.3 |       |
| 3   | [Co(HNMBSQ)$_2$(HQ) (H$_2$O)$_4$]H$_2$O | 651 | $^4T_{1g}(F)$ $\rightarrow$ $^4A_2g(P)$, $^4T_{1g}(F)$ $\rightarrow$ $^4T_{1g}(P)$ | 5.3 |       |
| 4   | [Ni(HNMBSQ)$_2$(H$_2$O)$_4$] : H$_2$O | 630, 740 | $^4A_2g$ $\rightarrow$ $^4T_{1g}(F)$, $^4A_2g$ $\rightarrow$ $^4T_{1g}(P)$ | 2.8 |       |
| 5   | [Ni(HNMBSQ) Phen (H$_2$O) NO$_3$] | 640, 768 | $^4A_2g$ $\rightarrow$ $^4T_{1g}(F)$, $^4A_2g$ $\rightarrow$ $^4T_{1g}(P)$ | 3.6 |       |
| 6   | [Ni(HNMBSQ)](HQ) (H$_2$O)$_2$] EtOH | 645, 765 | $^4A_2g$ $\rightarrow$ $^4T_{1g}(F)$, $^4A_2g$ $\rightarrow$ $^4T_{1g}(P)$ | 3.3 |       |
| 7   | [Cu(HNMBSQ)$_2$] 2EtOH | 658 | $^2E_g$ $\rightarrow$ $^2T_{2g}$ | 2.05 | 2.1 |
| 8   | [Cu(HNMBSQ) Phen (H$_2$O) NO$_3$]EtOH | 665 | $^2E_g$ $\rightarrow$ $^2T_{2g}$ | 2.2 | 2.05 |
| 9   | [Cu(HNMBSQ)](HQ) EtOH | 651 | $^2E_g$ $\rightarrow$ $^2T_{2g}$ | 2.1 | 2.05 |
3.8. ESR Spectra of Cu (II) Complexes

ESR spectra of Cu (II) complexes, and nano Cu-HNMABSQ Complex were recorded at room temperature as shown in Fig. 5. The $g_{\text{eff}}$ values were calculated and recorded in Table 3. The shape of ESR signals and the $g_{\text{eff}}$ values for Cu (II) complexes 7, 8 and 9 respectively, indicated square planer for complexes 7 and 9 or distorted octahedral geometries for complex 8 around Cu (II) ions in these complexes, where two anisotropic signals were observed. From the observed $g$-values of the Cu (II) complexes, it is clear that $g_{\perp} > g_{\parallel}$ which indicates that the unpaired electron is predominantly in the $d_{x^2-y^2}$ orbital [43] giving $^2B_1g$ as the ground state. The observed data showed that the $g_{\text{eff}}$ values are > 2.0023 for complexes and hence the metal-ligand bonding in these complexes is essentially covalent character [44].

In case of nano Cu-Schiff base complex, X- band ESR spectrum showed four anisotropic lines due to phenoxide of naphthyl moiety [34, 45] as seen in Fig 6.

![Fig. 5. X-band ESR spectra of Cu, L and nano Cu L complex](image)

3.9. 3D Molecular Modeling Study

3D modeling of the ligand and its metal complexes were studied by PM3 method to confirm the geometry of the ligand and its complexes using Hyperchem 7.52 program [46-47]. The 3D-optimized molecular structures of the Schiff base ligand and some complexes namely 1, 4, 7 and 10 were shown in Figs 7, 8.

3.9.1. Molecular Parameters

The molecular parameters: total energy, binding energy, electronic energy, heat of formation, dipole moment, energy of the lowest occupied molecular orbital ($E_{\text{HOMO}}$) and energy of the highest unoccupied molecular orbital ($E_{\text{LUMO}}$) were calculated and represented in Table 4. Additional parameters, such as separation energy, $\Delta E$ (the gap between the HOMO and LUMO energy levels, ($E_{\text{gap}}$), electrophilicity index ($\chi$), chemical potential ($\mu$), absolute hardness ($\eta$), absolute softness ($\sigma$) and additional electronic charge ($\Delta N_{\text{max}}$) were calculated [48] and listed in Table 4.

From the obtained data, we can conclude the following:

a) Absolute hardness ($\eta$) and softness ($\sigma$) are important properties to measure the molecular stability and reactivity. A hard molecular has a large energy gap and a soft molecule has a small energy gap. Soft molecules are more reactive than hard ones because they could easily offer electrons to an acceptor. In a complex formation system, the ligand acts as Lewis base while the metal ion acts as Lewis acid. Metal ions are soft acids and thus soft base ligands are most effective for complex formation [47-48]. Accordingly, it is concluded that the ligand HL with proper $\sigma$ values has a good tendency to
we observed that there is an elongation in the bond s of the C-OH phenolic) of the ligand and their some metal complexes

c) The LUMO - HOMO energy gap (ΔE) is an important stability index that should be considered. As the LUMO – HOMO energy gap decreases, interactions between the reacting species become stronger and as a result the stability of the formed metal complexes increases [50]. The values of ΔE indicated that the ligand under investigation has high inclination to bind with the metal ions. From the calculated values of binding energy we notice that there is an increase of the values of binding energy of the complexes compared to that of the ligands which indicates that the stability of the formed metal complexes is higher than that of the free ligand. The calculated heat of formation values indicated a large stabilization of the formed metal complexes compared to the free ligand, since they have heat of formation values lower than that of the free ligand. The metal complexes have higher values of the dipole moment than that of the free ligand.

A comparison between the selected bond lengths (C=N and C-OH phenolic) of the ligand and their some metal complexes is illustrated in Table 6. From the data obtained we observed that there is an elongation in the bonds of the active group of the ligand taking part in coordination with the metal ions after complexation, which correlates with the experimental IR frequencies. As there is an elongation in the bonds a lower energy of the vibration frequency is needed

3.9.2. BondLengths Calculations

Table 6. Calculated bond lengths of the ligands and some of their metal complexes

| Compound          | (C=N) asymmetric | (C-O) asymmetric |
|-------------------|------------------|------------------|
| HL                | 1.298            | 1.36053          |
| [Co(L)2H2O]4H2O   | 1.4558           | 1.2916           |
| [Ni(L)2H2O]4H2O   | 1.4528           | 1.30576          |
| [Cu(L)2]2EtOH     | 1.4069           | 1.3049           |
| [Zn(L)6]3H2O      | 1.43839          | 1.28845          |
|                   | 1.43956          | 1.28204          |

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Table 4. The calculated quantum chemical parameters of the ligand (HL) and its complexes

| Compound          | E_HOMO   | E_LUMO   | ΔE     | Z     | η      | σ      | Pl     | ΔN_{max} |
|-------------------|----------|----------|--------|-------|--------|--------|--------|----------|
| HL                | -8.8042  | -1.38107 | 7.4231 | 5.092 | 3.71156| 0.2694 | -5.026 | 1.372    |
| [Co(L)2H2O]4H2O   | -5.794   | -1.42102 | 4.372  | 3.607 | 2.186  | 0.457  | -3.607 | 1.65     |
| [Ni(L)2H2O]4H2O   | -8.67798 | -1.445752| 6.97112| 5.061 | 3.4855 | 0.2869 | -3.4855| 1.4522   |
| [Cu(L)2]2EtOH     | -8.41687 | -1.35331 | 7.06356| 4.885 | 3.532  | 0.2831 | -4.885 | 1.383    |
| [Zn(L)6]3H2O      | -3.89373 | -1.68822 | 6.70911| 5.042 | 3.354  | 0.2982 | -5.0425| 1.5034   |

Table 5. Theoretical parameters of the molecular modeling of (HL) and its complexes

| The assignment of the theoretical parameters | (HL) | [Co(L)2H2O]4H2O | [Ni(L)2H2O]4H2O | [Cu(L)2]2EtOH | [Zn(L)6]3H2O |
|---------------------------------------------|------|----------------|----------------|--------------|--------------|
| Total energy (Kcal / mol)                   | -11420.04156 | -257709.2 | -266127.4688 | -255073.156 | -228333.531 |
| Binding energy (Kcal / mol)                 | -5863.44 | -12823.608 | -12303.703 | -11786.97 | -11623.7509 |
| Electronic energy (Kcal / mol)              | -928708.37 | -328718.5 | -331873.1 | -302134.4 | -2868327.2 |
| Heat of formation (Kcal / mol)              | 43.72 | -347.79 | -267.459 | 3.843611 | 117.5409 |
| Dipole moment (Debye)                       | 7.691 | 8.933 | 6.412 | 2.061 | 3.705 |
| E_HOMO (ev)                                 | -8.8042 | -5.794 | -8.67798 | -8.41687 | -8.39733 |
| E_LUMO (ev)                                 | -1.38107 | -1.421 | -1.445752 | -1.35331 | -1.383 |

4. Biological Activities

4.1. Antibacterial and Antifungal Assays

The biological activities of synthesized Schiff base (HNMBSQ), its Co(II), Ni(II), Cu(II), Zn(II) complexes and nano Cu- HNMBSQ complex were studied for antibacterial and antifungal properties by the agar diffusion method in DMF solvent against Escherichia coli, Staphylococcus aureus, Bacillus subtilis and Salmonella typhi bacteria , Candida albicans and, Aspergillus fumigatus fungi. The results of antibacterial and antifungal activity of tested
compounds were discussed as follows:

A comparative study of the ligand and complexes indicated that most complexes exhibited higher antimicrobial activity than the free ligand. Such increased activity of the complexes can be explained on the basis of Overtone’s concept [52] and Tweedy’s chelation theory [53]. These complexes also disturb the respiration process of the cell and thus block the synthesis of the proteins, restricting the further growth of the organism. Furthermore, the mode of action of the compound may involve the formation of a hydrogen bond through the azomethine group with the active center of the cell, resulting in interference with the normal cell processes. In general, metal complexes are more active than ligands because metal complexes may serve as a vehicle for the activation of ligands the principle cytotoxic species [50]. Nano-Cu-complex showed higher antimicrobial activity than the free ligand and its metal chelates, this is due to their high surface to volume ratio are very reactive, can easily interact with other particles and increase their antimicrobial efficiency [54]. Also, this difference in activities is related to the complex formation between Schiff base ligand (HNMABSQ) and colloidal Cu- nanoparticles, leading to super strong materials increase their antimicrobial efficiency.

Generally, the orders of antimicrobial activity are:

\[
\text{Cu-nano complex} > \text{Zn(II) complex} > \text{Co(II) complex} > \text{Ni(II) complex} > \text{Cu L,}>\text{L}
\]

4.2. Anticancer Evaluation

This study aimed to evaluate the growth inhibitory on human cancer liver cells. In this work, three compounds, namely sulpha drug ligand (HNMABSQ), [Cu(HNMABSQ)\textsubscript{2}] 2EtOH, and nano Cu- HNMABSQ Complex were chosen as representative examples to evaluate their cytotoxic activity against carcinoma cell line(HePG-2). Doxorubicin was used as a reference drug. The percent inhibition of cell viability was determined using Eliza Tecan Sunrise 570 nm filters with reference to the control values (without test compound). The data was subjected to linear regression analysis and the regression lines were plotted for the best fit. The IC50 (inhibition of cell viability) concentrations were calculated using the respective regression equation. According to the obtained results, the examined carcinoma cell lines appeared to be sensitive to all of the tested compounds. The data showed that high cytotoxic activity against (HePG-2) carcinoma cells lines, so all tested compounds inhibited the growth of the liver cancer cell.

5. Conclusions

Copper- nano complexes were prepared and characterized. These compounds have a great interest recently due to unique physical and chemical properties and low cost of preparation in which have great applications as antimicrobial and anticancer materials.

The newly synthesized sulphal drug Schiff base acted as a mono-negative bidentate ligand. The metal ion was coordinated through the phenolic oxygen and the nitrogen of the azomethine group.

Based on the above results gained from elemental and thermal analyses, conductance measurements, IR, UV/Vis, ESR spectra as well as magnetic moments studies, the geometric structures of the complexes under investigation can be formulated as follows:
Complex (7) \[ M = \text{Cu}, \quad y = 2 \text{EtOH}, \quad X = \text{amine} \]

Complex (10) \[ M = \text{Zn}, \quad y = 6\text{H}_2\text{O}, \quad X = \text{amine} \]

Complex (3) \[ M = \text{Co}, \quad y = \text{H}_2\text{O}, \quad X = \text{amine} \]

Complex (6) \[ M = \text{Ni}, \quad y = \text{EtOH}, \quad X = \text{amine} \]

Complex (9) \[ M = \text{Cu}, \quad y = \text{EtOH}, \quad X = \text{amine} \]

Complex (12) \[ M = \text{Zn}, \quad y = 2\text{H}_2\text{O}, \quad X = \text{amine} \]
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