



**Theoretical, Spectroscopic and Biological Studies of  
Some Hydrazone Schiff-Base Derivatives and  
their Metal Complexes**

*Thesis Submitted By*

**Manal Ahmed Mahmoud Afifi**

**M. Sc. in Chemistry (special Chemistry), Fayoum University. 2010**

**A thesis Submitted in Partial Fulfillment**

**of**

**The Requirements for the**

**Ph.D. of Science**

**In**

**Inorganic Chemistry**

**to**

**Department of Chemistry**

**Faculty of Science, Fayoum**

**Fayoum University**

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**Supervised by**

**Prof. Dr. Samir Moustafa Hasan El-Medani**

**Professor of Inorganic Chemistry, Faculty of Science – Fayoum University**

**Signature .....**

**Prof. Dr. Abdelmoneim Abdelsalam Makhoul**

**Professor of organic Chemistry, Faculty of Science – Fayoum University**

**Signature .....**

**Prof. Dr. Mohamed Said Abu El Ghar**

**Vice Dean of Postgraduate Studies and Research, Fayoum University.**



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**Thesis Advisors**

**Prof. Dr. Samir Moustafa Hasan El-Medani**

Professor of Inorganic Chemistry,  
Faculty of Science – Fayoum University.

**Prof. Dr. Abdelmoneim Abdelsalam Makhloof**

Professor of organic Chemistry,  
Faculty of Science – Fayoum University.

**Thesis Approval**

.....

.....

Head of Chemistry Department

**Prof. Dr. Soha Hamdy**

**2020**

## **Title Sheet**

**Name of Researcher: Manal AhmedMahmoud Afifi**

**Date of Birth: 1/7/1989**

**Place of Birth: Fayoum**

**First University Degree: B.Sc. & amp; Ed., May 2010 (Excellent with Honor).**

**Name of University: Fayoum.**

## SUMMARY

This thesis includes the study of complexes resulted from the reaction of (E)-N'-(2-hydroxybenzylidene)-2-phenylacetohydrazide(**HL1**), (E)-N'-(1-(2-hydroxyphenyl) ethylidene)-phenylacetohydrazide(**HL2**) and (E)-N'-((1-hydroxynaphthalen-2-yl)methylene)-2-phenylacetohydrazide (**HL3**) as ligands with Cu(II), Ni(II) and Co(II) metal ion. Acid catalyzed reaction of HL2 gave a dimer that probably formed via radical mechanism. The (C=O) group, (C=N) group and phenolic –OH group are the possible bonding sites in the ligands. The importance of the ligands and their metal complexes refers to the variety of their application as models in biological, biochemical, analytical, antimicrobial system, anticancer, antibacterial and antifungal activities. In this work, the ligands and their metal complexes were characterized by elemental analysis, spectroscopic studies mass, IR, <sup>1</sup>H NMR, molar conductance, and magnetic moment. Electron spin resonance (ESR) of [(CuL2)<sub>2</sub>] and [(CuL3)<sub>2</sub>] is also carried out. X-ray crystallography for **HL1**, **HL2**, the **dimer** and [(CuL2)<sub>2</sub>] is reported. The spectroscopic characterization of the reported complexes was confirmed by theoretical studies. Density Functional Theory (DFT) calculations, the B3LYP/6-311++G\*\* level of theory have been carried out to investigate the equilibrium geometry of the ligand. The optimized geometry parameters of the complexes were evaluated using DFT-B3LYP/GENECP level of theory. Furthermore, the thermogravimetric analysis and Biological studies including, antimicrobial and antioxidant activities of the complexes along with fluorescence quenching studies and viscosity measurements are carried out. Also the interaction of the complexes with calf thymus DNA was studied by different techniques.

**This thesis consists of four chapters:**

**I- Literature Survey,**

**II- Experimental and Theoretical Background,**

**III- Results and Discussion.**

**III- biological activity and molecular docking of the ligands and complexes**

Chapter III is divided into four parts;

**Part one,** Spectroscopic studies and molecular Orbital Calculations of **HL1** and its complexes.

Thermal reaction of  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$ ,  $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  and  $\text{Co}(\text{NO}_3)_2$  with L1 resulted in the formation of  $[\text{Cu}(\text{L1})_2] \cdot 2\text{H}_2\text{O}$ ,  $[\text{Ni}(\text{L1})_2]$  and  $[\text{Co}(\text{L1})_2]$ , respectively. X-ray analysis of **HL1** confirms the structural and indicates that the structure is not planer and the molecule as a whole is unsymmetrical ( $C_1$  system). The elemental analysis and mass spectroscopy proved that the complexes are structurally formulated in 1:2 [Metal]:[Ligand] ratio. It is confirmed the presence of two hydrated water molecules in Cu complex. The IR spectrum confirm that M(II) coordinated to two L1 via three coordinated site oxygen of the phenolic–OH group, oxygen of (C=O) group and nitrogen of (C=N) group. Also, indicates the presence of a water molecule in the Cu complex.

In the complexes,  $[\text{Cu}(\text{L1})_2] \cdot 2\text{H}_2\text{O}$ ,  $[\text{Ni}(\text{L1})_2]$  and  $[\text{Co}(\text{L1})_2]$ , the metal ions coordinated to one ligand forming a five-membered ring, namely, M44N2N1C47O62 and six-membered ring, namely, M44O39C26C25C24N23, forming octahedral structures. The HOMO-LUMO and energy gap used in studding the chemical reactivity, softness, hardness, chemical potential and electro negativity. Natural charge distribution of the

complexes was studied which indicated the electronic charge distribution in the complexes. The calculated dipole moment and first order hyperpolarizability results showed that the complexes have a good non-linear optical behaviour.

**Part two,** Spectroscopic studies and molecular Orbital calculations of **HL2** and its complexes and the dimer.

Thermal reaction of  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  and  $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  with L2 resulted in the formation of  $[(\text{Cu L2})_2]$  and  $[\text{Ni}(\text{L2})_2]$ , respectively. X-ray analysis of **HL2** confirm the structural and showed that it crystallized with a water molecule, and indicate that the structure of the ligand is not planer and the molecule as a whole is unsymmetrical ( $C_s$  system). X-ray analysis of the dimer confirms the structural and indicates that the molecule has the symmetry point group  $S_2$  ( $C_2 + \sigma_v$ ). The elemental analysis and mass spectroscopy proved that the Cu complex is structurally formulated in 2:2 [Metal]:[Ligand] ratio, while the Ni complex is structurally formulated in 1:2 [Metal]:[Ligand] ratio. The IR spectrum confirm that the two Cu(II) coordinated to two L2 via three coordinated site oxygen of the phenolic-OH group, oxygen of aromatic -OH group and nitrogen of (C=N) group. The IR spectrum confirm that Ni(II) coordinated to two L2 via three coordinated site oxygen of the phenolic-OH group, oxygen of (C=O) group and nitrogen of (C=N) group. X-ray analysis of  $[(\text{CuL2})_2]$  confirm the structural and indicate that two ligands coordinated as tridentate (two oxygen and one nitrogen) to form five- and six-membered chelates with two Cu ions. It is obvious that the complex has the symmetry point group  $S_2$  ( $C_2 + \sigma_v$ ). The copper atom is occurred in a distorted square planar coordination geometry.

In the two complexes,  $[(\text{CuL2})_2]$  and  $[\text{Ni}(\text{L2})_2]$ , the metal ion coordinated to one ligand forming a five-membered rings, namely, Cu1N12N11C9O10 for

Cu complex and Ni<sup>2+</sup>O<sup>9</sup>C<sup>8</sup>N<sup>10</sup>N<sup>11</sup> for Ni complex and six-membered rings, namely, Cu<sup>1</sup>O<sup>19</sup>C<sup>15</sup>C<sup>14</sup>C<sup>13</sup>N<sup>12</sup> for Cu complex and Ni<sup>2+</sup>N<sup>11</sup>C<sup>12</sup>C<sup>14</sup>C<sup>19</sup>O<sup>20</sup> for Ni complex, forming tetrahedral structure for Cu complex and octahedral structure for Ni complex. The HOMO-LUMO energy gap used in studying the chemical reactivity, softness, hardness, chemical potential and electro negativity. Natural charge distribution of the studied complexes was studied which indicated the electronic charge distribution in the complexes. The calculated dipole moment and first order hyperpolarizability results showed that the complexes have a reasonable good non-linear optical behaviour.

**Part three,** Spectroscopic studies and molecular Orbital calculations of **HL3** and its complexes and the dimer.

Thermal reaction of Cu(CH<sub>3</sub>COO)<sub>2</sub>.H<sub>2</sub>O, Ni(CH<sub>3</sub>COO)<sub>2</sub>.H<sub>2</sub>O and Co(NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O with L3 resulted in the formation of [(CuL3)<sub>2</sub>], [(NiL3)<sub>2</sub>] and [Co(L3)<sub>2</sub>].2H<sub>2</sub>O. The elemental analysis and mass spectroscopy proved that the Cu and Ni complex is structurally formulated in 2:2 [Metal]:[Ligand] ratio, while the Co complex is structurally formulated in 1:2 [Metal]:[Ligand] ratio. They also confirm the presence of two hydrated water molecules in Co complex. The IR spectrum confirm that the two Cu(II) and two Ni(II) coordinated to two L3 via three coordinated site oxygen of the phenolic-OH group, oxygen of aromatic -OH group and nitrogen of (C=N) group. The IR spectrum confirm that Co(II) coordinated to two L3 via three coordinated site oxygen of the phenolic-OH group, oxygen of (C=O) group and nitrogen of (C=N) group.

In the complexes, [(CuL3)<sub>2</sub>], [(NiL3)<sub>2</sub>] and [Co(L3)<sub>2</sub>].2H<sub>2</sub>O, the metal ion coordinated to one ligand forming a five-membered rings, namely, M<sup>2+</sup>N<sup>11</sup>N<sup>10</sup>C<sup>8</sup>O<sup>9</sup> and six-membered rings,



namely, M<sub>24</sub>N<sub>11</sub>C<sub>12</sub>C<sub>13</sub>C<sub>18</sub>O<sub>23</sub>, forming tetrahedral structures for Cu and Ni complexes and octahedral structures for Co complex. The HOMO-LUMO energy gap used in studying the chemical reactivity, softness, hardness, chemical potential and electro negativity. Natural charge distribution of the studied complexes was studied which indicated the electronic charge distribution in the complexes. The calculated dipole moment and first order hyperpolarizability results showed that the complexes have a reasonable good non-linear optical behaviour.

**Part four**, Electron spin resonance (ESR) of [(CuL<sub>2</sub>)<sub>2</sub>] and [(CuL<sub>3</sub>)<sub>2</sub>].

The values of  $g_{\parallel}$  and  $g_{\perp}$  indicated that Cu(II)-ligand bonds have a considerable covalent properties, and the unpaired electron is mainly localized in the  $d_{x^2-y^2}$  orbital of the copper(II) ion. The calculated G factors for the present complexes indicated that there is a significant exchange interaction between the copper ions.

## Chapter IV

### (A) Biological activity studies

#### 1- Antimicrobial activity

The activity of the studied ligands against different microorganisms is generally enhanced by chelation with the biological active metal. The complexes of Cu(II) with the three ligands showed the highest biological activity.

#### 2- Antioxidant activities by DPPH<sup>·</sup> radical scavenging activity.

The complexes can use as antioxidants; they could facilitate the scavenging of DPPH<sup>·</sup> radical. The IC<sub>50</sub> of the complexes follows the order [(CuL<sub>2</sub>)<sub>2</sub>] <

$[(\text{CuL3})_2] < [\text{Cu}(\text{L1})_2] \cdot 2\text{H}_2\text{O} < [\text{Co}(\text{L3})_2] \cdot 2\text{H}_2\text{O} < [\text{Co}(\text{L1})_2] < [\text{Ni}(\text{L2})_2] < [\text{Ni}(\text{L3})_2] < [\text{Ni}(\text{L1})_2]$ .

### 3- Fluorescence quenching studies.

It was clear that, the addition of the complexes to CT-DNA pretreated with EB caused a reduction in emission intensity, indicating that the complexes bind to DNA at the sites occupied by EB. the order of binding strength follows  $[(\text{CuL3})_2] > [(\text{CuL2})_2] > [(\text{NiL3})_2] > [\text{Cu}(\text{L1})_2] \cdot 2\text{H}_2\text{O} > [\text{Co}(\text{L3})_2] \cdot 2\text{H}_2\text{O} > [\text{Co}(\text{L1})_2] > [\text{Ni}(\text{L2})_2] > [\text{Ni}(\text{L1})_2]$ .

### 4- Viscosity measurements.

The result showed an increase in the relative specific viscosity of DNA  $(\eta/\eta_0)^{1/3}$  solution with increasing concentration of complexes. This indicates that complexes bind to CT-DNA through an intercalation binding mode. The increased degree of viscosity, which may depend on its affinity to DNA, follows the order of  $[(\text{CuL3})_2] > [(\text{NiL3})_2] > [(\text{CuL2})_2] > [\text{Cu}(\text{L1})_2] \cdot 2\text{H}_2\text{O} > [\text{Co}(\text{L3})_2] \cdot 2\text{H}_2\text{O} > [\text{Co}(\text{L1})_2] > [\text{Ni}(\text{L2})_2] > [\text{Ni}(\text{L1})_2]$ .

### (B) Molecular docking of the ligands and complexes.

Molecular docking explains the compound-DNA interactions and the potential binding mode and energy. The docking studies determine the way by which the docked compounds fundamentally fit in the DNA minor groove and comprise of hydrophobic, ionic, and hydrogen bonding interactions with the DNA bases.