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Synthesis, Characterization, Antimicrobial, and Antioxidant Studies of New Schiff Base Ligands and Their Complexes with Copper Ion

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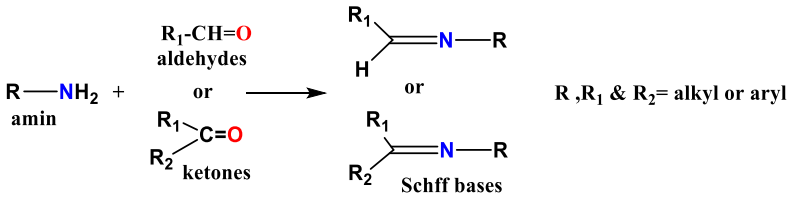
Abstract

The Schiff bases (L1, L2, L3) were prepared by using 2-Aminobenzyleamine with aromatic aldehyde. These ligands were further complexed with Cu(II) ion. The compounds have been characterization on the basis their spectra of H1NMR, mas, Fourier transform infrared (FTIR), as well as magnetic susceptibillty, elemental analysis (CHN) and conductance measurements. Elemental analysis and spectral data of the ligands were found to be in good agreement with their structures, indicating high purity of all the compounds. The program of Hyperchem 8 have been used for theoretical accounts using PM3 method to study the electrostatic potential that provided good information about the complexity site. Of the result obtained we can suggest square planer geometry for Cu(II) complexes. The antioxidant activity of the syntheses compounds was evaluated by DPPH scavenger and these were showed a good antioxidant activity. All ligands and their complexes were screened for antimicrobial activity, and these compounds showed a good antibacterial activity.

Keywords
Schiff base, ligand, complex, characterization, antioxidant, antibacterial

Hugo Schiff (1864-1915) is a German scientist. He discovered some bases and named them Schiff bases [1]. Since 159 years ago, and these compounds are still of high significance for both scientists and researchers due to their applications in different fields [2,3]. Schiff base compounds are synthesized from the reaction of a primary amine with the carbonyl group of aldehyde (RHC=O) or ketone (R2C=O) [4,5] (scheme.1). The Schiff base mechanism is nucleophilic addition reaction throw the carbonyl group (C=O). The nucleophile is the primary amine which is reacts with the aliphatic or aromatic aldehyde or ketone to give an intermediate compound called carbinol amine. This intermediate compound was losing water molecule by hydrolyses process with acidic or basic media as a catalyst [5]. The general function is imine or azomethine (−C=N−) group [6]. Schiff bases are important chemical compounds in various fields such as inorganic, analytical, and medicinal chemistry due to their versatility; they can form numerous, diverse, stable complexes when they are coordinated with different transition-metal ions [7]. The presence of imine linkage (-C=N-) in the Schiff base molecules is essential for exhibiting these compounds' wide spectrum of biological applications like analgesic [8], anticancer [9-11], antimicrobial [12,13], antitumor [14], antioxidant [15,16], antiviral [17,18], and

anti-inflammatory activities [19]. Besides, Schiff bases have various applications in many fields, including analytical chemistry as chemo-sensors [20], corrosion inhibitors [21], dyes [22,23]. Schiff bases are generally being bi, tri, or tetra-dentate chelate ligands and from very stable complexes with metal ions [24]. Many Schiff base complexes show excellent catalytic activity in various reaction at high temperature and in the presence of moisture [25]. The chemistry of metal complexes with Schiff base ligands containing oxygen and nitrogen as donor atoms has continued to attract the attention of researchers [26]. The transition metal complexes of Schiff base ligands bearing O and N donor atoms are very important because of their biological properties [27]. Schiff bases and their copper(II) complexes have been studied extensively [28-30.] due to their vital roles in the coordination chemistry inherent from their simple method of preparation and structural variety [31]. it is confirmed that the coordination of copper(II) ion with bioactive ligands can actually improve their biological activity, for example Cu(II) complexes with hesperetin, naringenin and apigenin have shown higher inhibitory rate than their free ligands against human SGC-7901 (gastric cancer) and HepG2 (hepatocellular carcinoma) cell lines [32].



scheme.1 genral synthesis of Schiff bases

Experimental

All reagents and chemicals used in this study were in the analytical grade and purchased from (Sigma-Aldrich). 2-Aminobenzyleamine 98%, Ortho vaniline, Vaniline, Salicylaldehyde, Diphenyle Picryl Hydrazyl, $CuCl_2.2H_2O$. The melting points of synthesized compounds were measured on the SMP31 melting point apparatus and on the FT.IR affinity (Shimadzu) spectrophotometer using KBr pellets. While their 1H NMR and 13C NMR were recorded in DMSO-d_6 on the Bruker 500MHZ instrument, the internal standard is TMS. Electronic spectral inform were accomplished depending on GERMANY-BG(T60UV). Work mass selective Detector 5973 and elemental micro analysis was done on a perkin_Elmer_automatical instruments.

General procedure for the preparation of Schiff base was by two methods:

Way 1:

A mixture of 2-Aminobenzyleamine (0.01 mol, 1.22 g), aryl aldehyde (0.02 mol), in 5ml ethanol in conical flask was introduced into the microwave oven and irradiated for (2-4) min (400 watt). After cooling, the solid was recrystallized from the ethanol to provide of the title compound as a lamellar crystal [33].

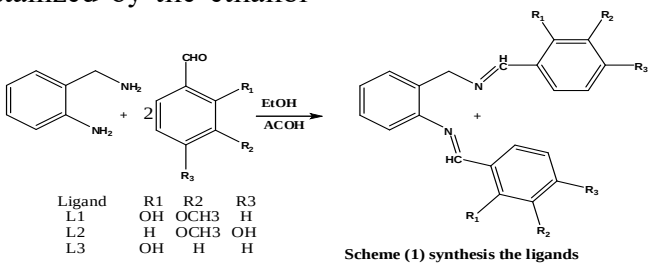
Way2:

A solution of 2-Aminobenzyleamine (0.01 mol, 1.22 g) in ethanol (10 mL) was mixed with a solution of aryl aldehyde (0.02 mol), in ethanol (10 mL) and a few drops of acetic acid was added as a catalyst. The mixture was heated in a reflux temperature for 4 hours, the reaction was followed by TLC (3 hexane: 7 ethyl acetate). Then, the precipitation was filtered, and the residual was recrystallized from the ethanol to obtain the title compound as a crystal [34]. As shown in scheme (2)

Metal complexes synthesis: Copper complex of the obtained Schiff base was prepared using the following approach:

dissolving (0.001 mol) of ligand in 10 mL of MeOH and a drops of DMF. Then, (0.21 g, 0.001 mol) of copper salt (Cu(II) $Cl_2.2H_2O$) were added onto ligand's solution in round flask of 50 mL volume. Thereafter, the mixture was refluxed, heated, and continuously stirred for 2 hours. After completely reflux, mixture was left to perform cooling at room temperature for one hour.

After solvent evaporation, the precipitation was filtered and recrystallized by the ethanol [35].



Scheme (1) synthesis the ligands

Results and Discussion

The ligands (Schiff base) were synthesized by two methods. Compared with way 1 and way2, way 1 has a great virtue which consumes the least time to finish the synthesis of Schiff base. Microwave irradiation synthesis is not only use in the shorter reaction time, but also has the greatest yield. As shown in the table (1)

Table (1) The compare of two way of synthesis of Schiff base.

Ligand	microwave irradiation		reflux	
	time	yield	time	yield
L1	2 min	92	2.5 h	77
L2	3 min	85	3 h	73
L3	4 min	87	3.5 h	70

All the physical properties and elemental microanalysis and (CHNS), atomic absorption and the magnetic momentum data of the ligand and its complexes were gathered in the table (2)

Table (2) Physical properties, elemental microanalysis CHN, molar conductance and magnetic susptibility

compound	Colour	M.P	ʌ.m s.cm^2.mol^{-1}	% C Exp. (cal.)	% H Exp. (cal.)	% N Exp. (cal.)	% m Exp. (cal.)	μeff B.M
$C_{23}H_{24}N_2O_3$ (L1)	orange	161-163		70.8 (70.75)	6.17 (5.68)	8.65 (7.17)		
[Cu(L1)Cl_2]	Deep green	223-225	20				14.39 (12. 11)	1.68
$C_{23}H_{24}N_2O_3$ (L2)	pale yelloish	158-160		71.27 (70.75)	5.92 (5.68)	8.47 (7.17)		
[Cu(L2)Cl_2]	brown	202-204	17				13.89 (12.11)	1.7
$C_{18}H_{16}N_2O$ (L3)	orange	171-173		75.59 (76.34)	4.95 (5.49)	9.15 (4.48)		
[Cu(L3)Cl]	brown	254-256	18				15.71 (14.83)	1.74

FT-IR spectral

FT-IR of the synthesized ligand and its complexes were carried out using KBr disc forto ligands and their complexes and all the data of FTIR were gathered in the table (3). The free ligand (L) exhibited the azomethine bands at (1608)- (1635) cm^{-1}, while the azomethine bands of the complex were exhibited at (1614)-(1627) cm^{-1}. New bands were formed Attributed to the (M- N) and (M- O) bonds appeared at the region (446-456) cm^{-1}and (556-575) cm^{-1} respectively. This indicates that the coordinate occurred through the (N) and (O) atoms. as shown in the table (3) and the figures (6-8).

Table (2) Infrared spectra of Ligand and its metal complexes (υ cm-1)

No.	υ (O-H)	υ (C-H) aromatic	υ (C-H) alaphatic	υ (C=N) azomethane	υ (C=C)	υ (C-O)	M-O	M-N
L1	3454	3055	3902	1635	1570	1273	-	-
(L1)Cu	1462	3053	2965	1614	1554	1292		456
L2	3354	3051	2951	1608	1518	1271	-	-
(L2)Cu	-----	3008	2971	1629	1544	1255		452
L3	3225	3024	2914	1627	1579	1203		
(L3)Cu	3282	3112	2941	1618	1544	1255	575	466

Nuclear Magnetic Resonance

The ^{1}H-NMR spectra of the ligands showed two signals at (2.5 and 3.36) ppm due to The solvent (DMSO), in the 1H-NMR spectra of the ligands L1 and L2 were appeared two signal at (3.74) ppm and 3.83 which due to the proton of methoxy groups, and an anthers signal at (4.94) ppm due to methylene group, melti signals at (6.72-7.47) ppm due to the aromatic group, while two signals of the azomethine groups at (8.17) ppm and (8.93) ppm, the two signals of phenolic groups at (13.04) ppm and (13.53) ppm. while in the ligand (L3) showed two signals of phenolic group appeared at (12.95) ppm and (13.35) ppm. As shown in figure (9-11)

Mass spectra

The mass spectra of the Copper complexes appeared molecular ion peak at 523 m/z for $[CuL_1Cl_2]$, 523 m/z for $[CuL_2Cl_2]$ and 447 m/z for $[CuL_3Cl]$ which is in conformity with the molecular formula $C_{23}H_{22}Cl_2CuN_2O_4$, $C_{23}H_{22}Cl_2CuN_2O_4$ and $C_{21}H_{17}N_2O_2$ respectively. As shown in fig. (12-14).

Conductivity Measurements.

The molar conductance values of the synthesized compounds in 10^{-3}M DMSO were measured at room temperature. The conductance values of the synthesized compounds were below (17-20) $Ohm^{-1}\cdot cm^{2}\cdot mol^{-1}$, indicating their nonelectrolyte nature. This suggested that there were no anions present outside the coordination sphere of the complexes.

Electronic Spectral Analysis

The electronic spectral data of the Schiff base ligand and its metal (II) complexes are given in the table (3). The Schiff base of the ligands showed two bands at (222-267) nm and (257-281) nm due to to π−π∗ transition and the third band at (317-371) nm due to the n−π∗ transition of the azomethane group. While in the UV-Vis spectra of the Schiff base metal (II) complexes Figure (3) displayed similar absorption spectra as the ligand but have either undergone a blue shift or red shift. The band which appeared at (351-371) nm due to charge transfere from metal to the ligand (M→L) as shown in fig. (15-18). The bathochromically or hypsochromically indicated to the coordination [36].

Table (3) The electronic spectral data

(M→L) charge transfere	n−π∗ transition	π−π∗ transition	compound
	267	222	L1
	257	209	L2
371	281	232	[Cu(L1)Cl2]
351	271	229	[Cu(L2)Cl2]

Spectrophotometric determination of DPPH radical scavenging activity

DPPH radical scavenging activity evaluation is a standard assay used in antioxidant activity studies. The antioxidant. The 1mL of an ethanolic solution had 100 µg of synthesized compounds. It was added with an equal concentration of ethanolic solution of DPPH. The prepared solution settled for incubation at room temperature for 30 min and 60 min. The decreases in the concentration of DPPH were measured by noting the absorbance at 517nm. A similar test was performed with ascorbic acid, as an internal standard, instead of Schiff's base. The percentage scavenging of DPPH free radical for each of test compounds had calculated the absorbance of negative control using Eq. (1) [37]. All the synthesized compound is less antioxidant activity than vitamin C, and the complexes were less activity than Schiff base as shown in the fig. (1). The ligands and their metal complexes contain several hydrogen atoms that can be donated. The donating ability of the hydrogen atoms in the complexes was determined by the decolorization of the DPPH reagent. DPPH produces a violet/purple color in a methanol solution, which changes to a yellow color in the presence of antioxidants.

. % scavenging = [(absorbance of control - absorbance of test sample) / absorbance of control)] *100 (1)

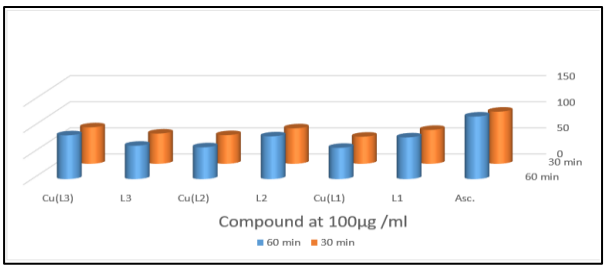


Fig. (1) the antioxidant of the ligands and their complexes with Copper ions

Biological Activity

All the synthesized compounds were screened for them in vitro antibacterial activity against (Escherichia coli, Enterobacter, Pseudomonas aeruginosa, Klebsiella pneumonia and Staphylococcus aureus) bacterial strains by the agarwell diffusion method and recorded in Table (4). Small portion (10 mL) of nutrient broth was inoculated with the test organisms and incubated at 37◦C for 24h.Using a sterile pipette, 0.6mL of the broth culture of the test organism was added to 60 mL of molten agar which had been cooled to 45◦C, mixed well, and poured into a sterile petri dish. Duplicate plates of each organism were prepared. The agar was allowed to set and harden and the required numbers of holes were cut using a sterile cork borer ensuring proper distribution of holes on the border and one in the center. Agar plugs were removed. Different cork borers were used for different test organisms. Using a 0.1mL pipette, 100 μL of the test sample dissolved in an appropriate solvent was poured into appropriately labelled cups and the solvents control were used. The plates were left at room temperature for 2 h to allow diffusion of the sample and incubated face upwards at 37◦C for 24 h. The diameter of the zones of inhibition was measured to the nearest mm. All the compound gave a good activity against the tested bacterial. As shown in Fig. (2)

Table (4). Antibacterial data of ligands and their metal(II) complexes (zone of inhibition in mm).

M3	M2	M1	L3	L2	L1	Type	NO
7	12	22	13	15	14	Pseudomonas	1
17	20	13		7	12	klebsilla	2
9	6	10	18	13	12	E.coli	3
8	12	9	8	7		Enteroccus	4
13	16	16		14	27	staph arues	5

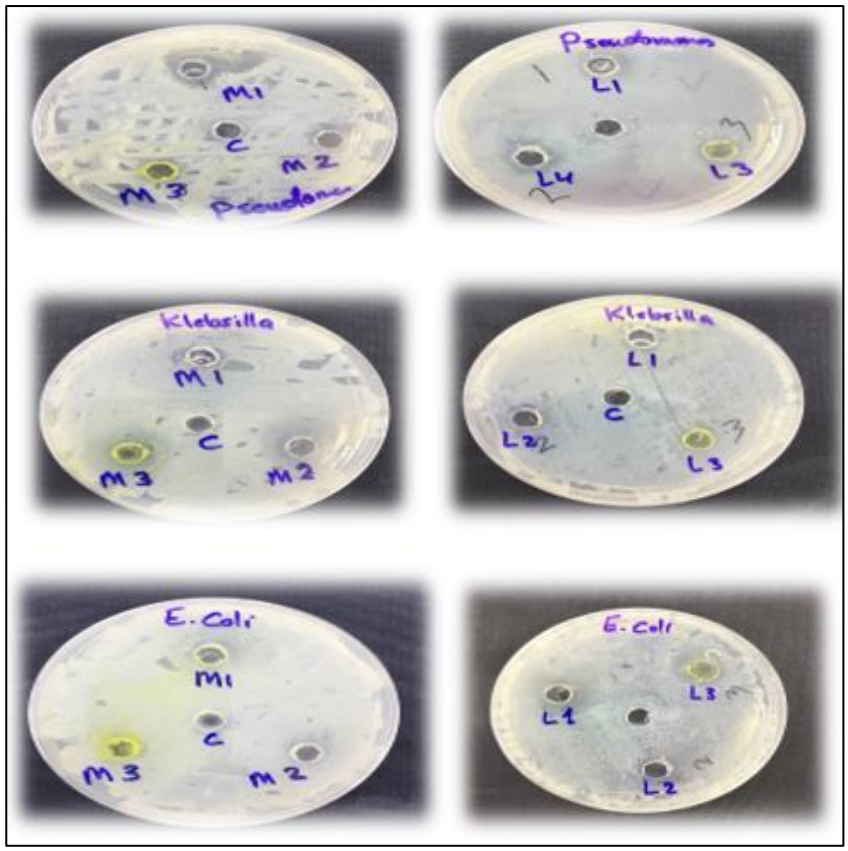


Fig. (2) antibacterial of the ligands and their complexes with Copper ion

M1=[Cu(L1)Cl_2] , M2=[Cu(L2)Cl_2] , M3=[Cu(L3) Cl]

Electrostatic potential(MEP) Molecular

Electrostatic potential is an important in finding the active sites in the molecule system with a positive point charge. The species that have positive charge tend to attack a molecule where the electrostatic potential is strongly negative (electrophilic attack). Electrostatic potential of free ligand was measured and plotted as 2D contour to find the active site of molecule [21] as shown in figures [3-5].

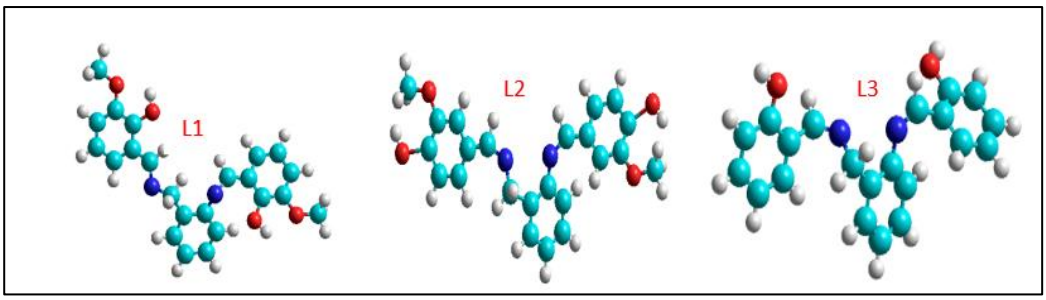


Fig.(3) the geometry othe ligands L1, L2 and L3

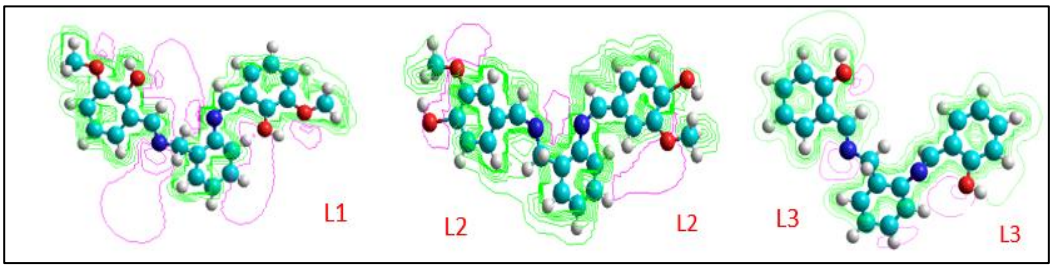


Fig.(4) HOMO Electrostatic Potential as Contours for the ligand L1, L2 and L3

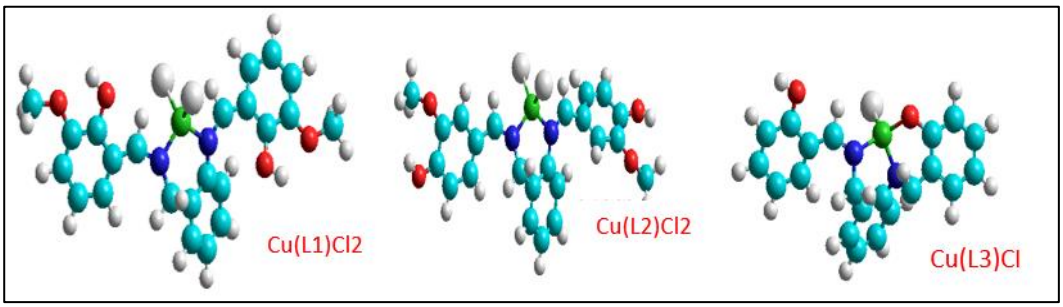


Fig. (5) the geometry of the Copper complexes

Conclusions

The Schiff base ligands and their complexes were successfully synthesized and characterized. The deprotonated bidentate Schiff base ligand coordinated to the Cu (II) ion via the azomethine nitrogen and phenolic oxygen resulting in the formation of a stable six-membered chelate ring. A square planer geometry has been proposed for Cu (II) complexes based on the electronic spectra and magnetic susceptibillty measurements. The complexes formed are neutral with no free anions outside the coordination sphere. The compounds exhibited better antioxidant and antibacterial properties.

Refrences

Qin, W., Long, S., Panunzio, M. and Biondi, S., "Schiff Bases: A short survey on an evergreen chemistry tool". Molecules, 18(10), 12264-12289, 2013.

Khachatryan G.E., Mkrtchyan N.I., Gavalyan V.B., "Antibacterial Ppoperties of new Chitosan-based Schiff-base", Int. J. Adv. Res., 2018, 6:1187

Ghosh, P., Dey, S.K., Ara, M.H., Karim, K.Md.R. and Islam, A.B.M.N., "A Review on synthesis and versatile applications of some selected Schiff bases with their transition metalcomplexes", Egypt. J. Chem., 62 (2), 523-547, 2019.

Mukhtar, S.S., Hassan, A.S., Morsy, N.m., Hafez, T.S, Hassaneen, H.M., Saleh, F.M., "Overview on Synthesis, Reactions, Applications, and Biological Activities of Schiff Bases", Egypt. J. Chem., 64(11), 6541 − 6554, 2021.

Ahmed, A.A., Al-mashhadani, M.H., Hashim, H., Ahmed, D.S., Yousif, E., "Morphological, Color Impact and Spectroscopic Studies of New Schiff Based DerivedFrom 1,2,4-Triazole Ring. Progresss in Color", Colorantsand Coatings, 14, 27-34, 2021.

Kathiresan, S., Annaraj, J., Bhuvanesh, N.S., "Cu (II) and Ni (II) Complexes of Anthracene-Affixed Schiff Base: A Conflict betweenCovalent and Stacking Interactions with DNA Bases", Chemistry Select, 2, 5475−5484, 2017.

Al-Hakimi, A.N., Alminderej, F., Aroua, L., Alhag, S.K., Alfaifi, M., Y., M, S.O., Mahyoub, J.A., Eldin I. Elbehairi, S., Alnafisah, A.S., "Design, synthesis, characterization of zirconium (IV), cad-mium (II) and iron (III) complexes derived from Schiff base 2-mium (II) and iron (III) complexes derived from Schiff base 2-aminomethylbenzimidazole, 2-hydroxynaphtadehyde and evalua-tion of their biological activity", Arab. J. Chem., 13, 7378−7389, 2020.

Yassen, T.M., AL-Azzawi, A.M., "Synthesis and Characterization of New Bis-Schiff Bases Linked to Various Imide Cycles", Iraqi Journal of Science, 64(3), 1062-1070, 2023.

Omer, A.M., Eltaweil, A.S., El-Fakharany, E.M., Abd El-Monaem, E.M., Magda M. F. Ismail M.M.F., Mohy-Eldin, M.S. & Ayoup, M.S., "Novel Cytocompatible Chitosan Schiff Base Derivative as a Potent Antibacterial, Antidiabetic, and Anticancer Agent", Arabian Journal for Science and Engineeri, 1-15, 2023.

Alasadi, Y.K., Jumaa, F.H., Mukhlif, M.G. & Shawkat, S.M., "Preparation, Characterization, Anti-cancer and Antibacterial Evaluation of New Schiff base and Tetrazole Derivatives", Tikrit Journal of Pure Science, 28 (2), 12-19, 2023.

Aroua, L.M, Alhag, S.K., Al-Shuraym, L.A, Messaoudi, S., Mahyoub J. A., Alfaifi, M.Y., Al-Otaibi, W.M., "Synthesis and characterization of different complexes derived from Schiff base and evaluation as a potential anticancer, antimicrobial, and insecticide agent", Saudi J Biol Sci., 30(3), 103598, 2023.

Luis A. Alfonso-Herrera, Sharon Rosete-Luna, Delia Hernбndez-Romero, Josй M. Rivera-Villanueva, Josй L. Olivares-Romero, J. Antonio Cruz-Navarro, Anell Soto-Contreras, "Transition Metal Complexes with Tridentate Schiff Bases (O N O and O N N) Derived from Salicylaldehyde: An Analysis of Their Potential Anticancer Activity", ChemMedChem., 17(20), 1-47, 2022

Awolope, O.R., Ejidike, I.P. & Clayton, H.S., "Schiff base metal complexes as a dual antioxidant and antimicrobial agents", Journal of Applied Pharmaceutical Science, 13(03), 132-140, 2023.

Rezaei, M.T., Keypour, H., Hajari, S., yaghoobi F., Farida S.H.M., Saadati, M. & Gable R.W., "Theoretical and solid-state structures of three new macroacyclic Schiff base complexes and the investigation of their anticancer, antioxidant and antibacterial properties", RSC Adv., 13, 9418-9427, 2023.

Aytac, S., Gundogdu, O., Bingol, Z. & Gulcin, I., "Synthesis of Schiff Bases Containing Phenol Rings and Investigation of Their Antioxidant Capacity, Anticholinesterase, Butyrylcholinesterase, and Carbonic Anhydrase Inhibition Properties", Pharmaceutics, 15(3), 779, 2023.

Abd El-Hamid, S.M., Sadeek, S.A., Mohammed, S.F., Ahmed, F.M., El-Gedamy, M.S, "N_2O_2-chelate metal complexes with Schiff base ligand: Synthesis, characterisation and contribution as a promising antiviral agentagainst human cytomegalovirus", Aplied Organometalic Chemstry, 37(2), 6925, 2023.

Alotaibi, S.H., Amer, H.H., Touil, N., Abdel-Moneim, A.S., Soliman, M.M. & Zaki ,Y.H., "Synthesis, Characterization and Molecular Docking of New Nucleosides and Schiff Bases Derived from Ampyrone as Antiviral Agents to Contain the COVID-19 Virus", 43(3),2023.

Pore, A., Gaikwad, G., Hegade, S., Jadhav, Y., Mane, R., & Kumbhar, R., "Analyzing the Impact of the Substituent on the Quinazolinone Schiff Base and the Interaction of the Fe (III) and Cr (III) with Different Quinazolinone Schiff Base for Antioxidant and Anti-inflammatory Activity", Analytical Chemistry Letters, 13(1), 39-59, 2023.

Krishna, G. A., Dhanya, T. M., Shanty, A. A., Raghu, K. G., & Mohanan, P. V.," Transition metal complexes of imidazole derived Schiff bases: Antioxidant/anti-inflammatory/antimicrobial/enzyme inhibition and cytotoxicity properties", Journal of Molecular Structure, 1274, 134384, 2023.

Ejiah, F. N., Rofiu, M. O., Oloba-Whenu, O. A., & Fasina, T. M. "Schiff bases as analytical tools: synthesis, chemo-sensor, and computational studies of 2-aminophenol Schiff bases", RSC Adv., 13(5), 2756-2767, 2023.

Boulechfar, C., Ferkous, H., Delimi, A., Berredjem, M., Kahlouche, A., Madaci, A. & Benguerba, Y., "Corrosion inhibition of Schiff base and their metal complexes with [Mn (II), Co (II) and Zn (II)]: Experimental and quantum chemical studies", Journal of Molecular Liquids", 378, 121637, 2023.

Ayodhya, D., "Fabrication of SPR triggered Ag-CuO composite from Cu (II)-Schiff base complex for enhanced visible-light-driven degradation of single and binary-dyes and fluorometric detection of nitroaromatic compounds", Inorganic Chemistry Communications, 148, 110295, 2023.

Rajimon, K. J., Elangovan, N., Khairbek, A. A., & Thomas, R., "Schiff bases from chlorine substituted anilines and salicylaldehyde: Synthesis, characterization, fluorescence, thermal features, biological studies and electronic structure investigations", Journal of Molecular Liquids, 370, 121055, 2023.

Dr. A. Xavier1, N. Srividhya2, "Synthesis and Study of Schiff base Ligands", IOSR-JAC., 7(11), 6-15, 2014.

Dalia, S. A., Afsan, F., Hossain, M. S., Khan, M. N., Zakaria, C., Zahan, M. K. E., & Ali, M., "A short review on chemistry of schiff base metal complexes and their catalytic application", Int. J. Chem. Stud., 6, 2859-2866, 2018.

Ommenya, F. K., Nyawade, E. A., Andala, D. M., & Kinyua, J., "Synthesis, characterization and antibacterial activity of Schiff base, 4-Chloro-2-{(E)-[(4-fluorophenyl) imino] methyl} phenol metal (II) complexes", Journal of Chemistry, 2020, 1-8, 2020.

Sumrra, S. H., Ibrahim, M., Ambreen, S., Imran, M., Danish, M., & Rehmani, F. S., "Synthesis, spectral characterization, and biological evaluation of transition metal complexes of bidentate N, O donor Schiff bases", Bioinorganic chemistry and applications, 2014, 1-10, 2014.

Lypez-Gastйlum, K.A., Velбzquez-Contreras, E.F., Garcнa, J.J., Flores-Alamo, M., Aguirre, G., Chбvez-Velasco, D., Narayanan, J., Rocha-Alonzo, F. Mononuclear and tetranuclear copper(Ii) complexes bearing amino acid schiff base ligands: Structural characterization and catalytic applications", Molecules, 26, 7301, 2021.

Pitucha, M., Korga-Plewko, A., Czylkowska, A., Rogalewicz, B., Drozd, M., Iwan, M., Kubik, J., Humeniuk, E., Adamczuk, G., Karczmarzyk, Z., "Influence of complexation of thiosemi-carbazone derivatives with Cu (II) ions on their antitumor activity against melanoma cells", Int. J. Mol. Sci., 22, 3104, 2021.

Al-Shboul, T.M.A.; El-khateeb, M.; Obeidat, Z.H.; Ababneh, T.S.; Al-Tarawneh, S.S.; Al Zoubi, M.S.; Alshaer,W.; Abu Seni, A.; Qasem, T.; Moriyama, H.; et al. "Synthesis, Characterization, Computational and Biological Activity of Some Schiff Bases and Their Fe, Cu and Zn Complexes", Inorganics, 10, 112, 2022.

Yusuf, T.L., Oladipo, S.D., Zamisa, S., Kumalo, H.M., Lawal, I.A., Lawal, M.M., Mabuba, N. "Design of New Schiff-Base Copper(II) Complexes: Synthesis, Crystal Structures, DFT Study, and Binding Potency toward Cytochrome P450 3A4", ACS Omega, 6, 13704−13718, 2021.

Wang, H.; Tan, M.; Zhu, J.; Pan, Y.; Chen, Z.; Liang, H.; Liu, H. "Synthesis, cytotoxic activity, and DNA binding properties of copper (II) complexes with hesperetin, naringenin, and apigenin". Bioinorg. Chem. Appl., 2009, 347872, 2009.

Yang, Z., & Sun, P., "Compare of three ways of synthesis of simple Schiff base", Molbank, 2006(6), M514, 2006.

Kailas, K. H., Sheetal, J. P., Anita, P. P., & Apoorva, H. P., "Four synthesis methods of schiff base ligands and preparation of their metal complex with Ir and antimicrobial investigation", World Journal of Pharmacy and Pharmaceutical Sciences, 5(2), 1055-1063, 2016.

Abou-Hussein, A. A., & Linert, W., "Synthesis, spectroscopic, coordination and biological activities of some organometallic complexes derived from thio-Schiff base ligands, Spectrochimica Acta Part A", Molecular and Biomolecular Spectroscopy, 117, 763-771, 2014.

Vhanale, B., Digambar Kadam, D. & Shinde, A., "Synthesis, spectral studies, antioxidant and antibacterial evaluation of aromatic nitro and halogenated tetradentate Schiff bases", Heliyon., 8, 09650, 2022.

Sumrra, S. H., Ibrahim, M., Ambreen, S., Imran, M., Danish, M., & Rehmani, F. S., "Synthesis, spectral characterization, and biological evaluation of transition metal complexes of bidentate N, O donor Schiff bases". Bioinorganic chemistry and applications, 201, 2014.

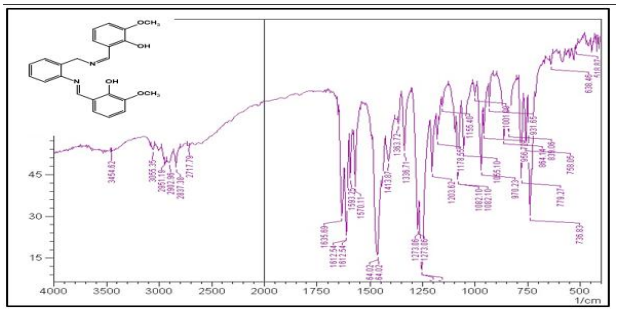


Fig (6) FT.IR Spectrum of the ligand L1

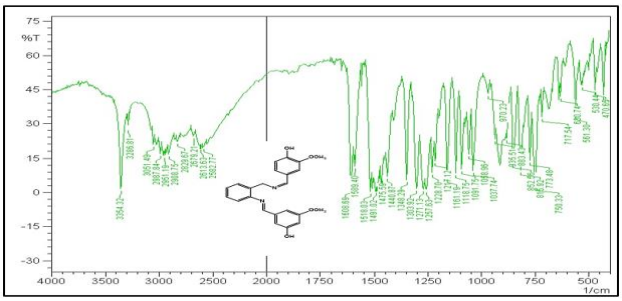


Fig (7) FT.IR Spectrum of the ligand L2

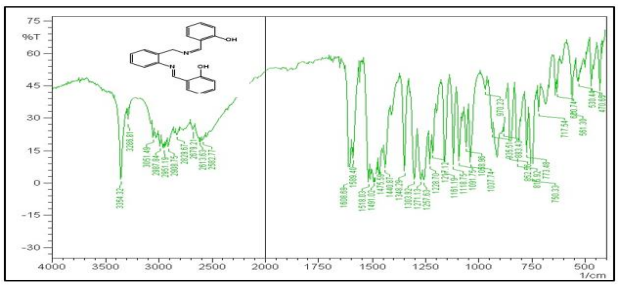


Fig (8) FT.IR Spectrum of the ligand L3

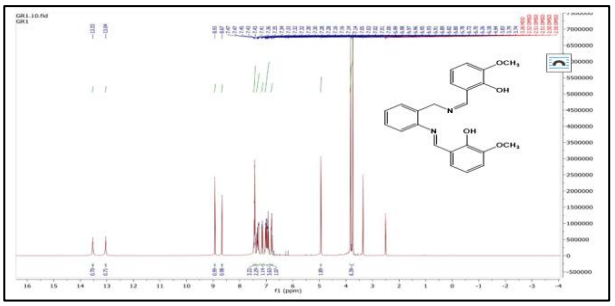


Fig.(9) H1-NMR Spectrum of the ligand L1

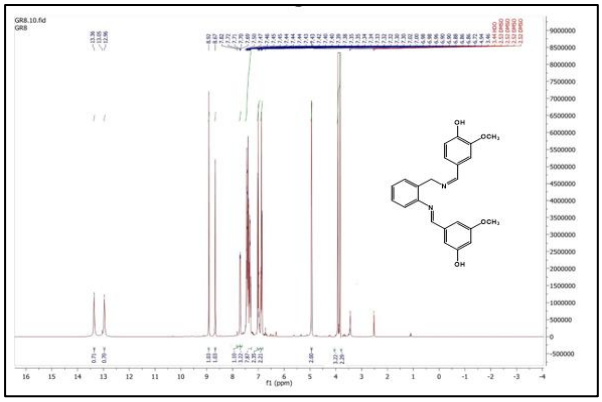


Fig.(10) H1-NMR Spectrum of the ligand L2

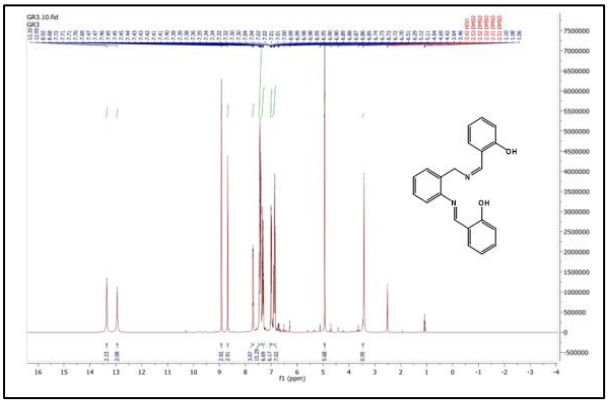


Fig.(11) H1-NMR Spectrum of the ligand L3

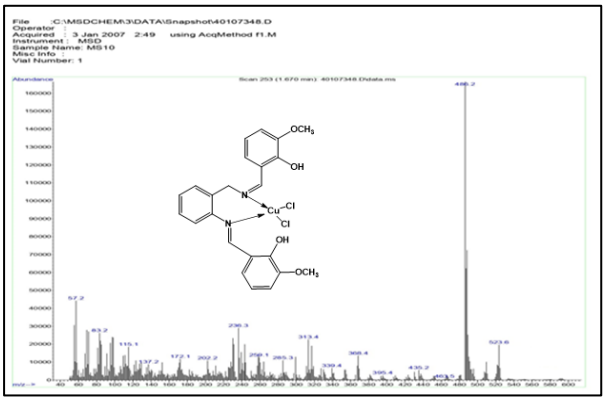


Fig. (12) Mas Spectrum of the complex [Cu(L1)Cl2]

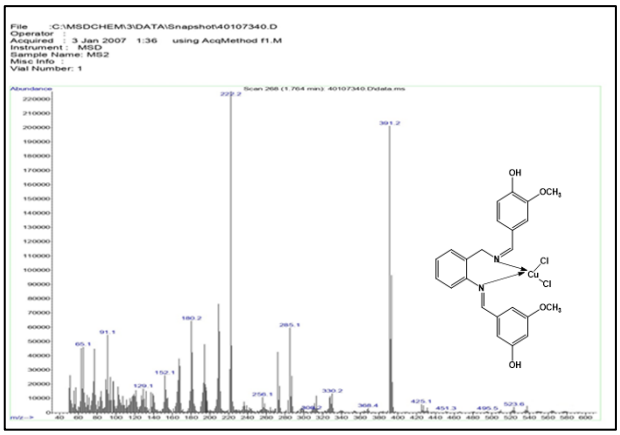


Fig. (13) Mas Spectrum of the complex [Cu(L2)Cl2]

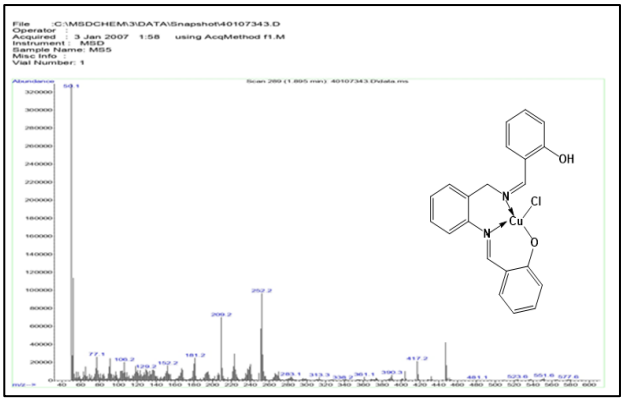


Fig. (14) Mas Spectrum of the complex [Cu(L3)Cl]

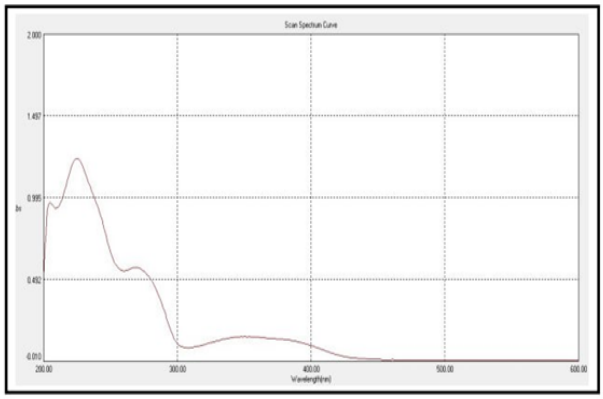


Fig. (15) UV-Visble Spectrum of the ligand L1

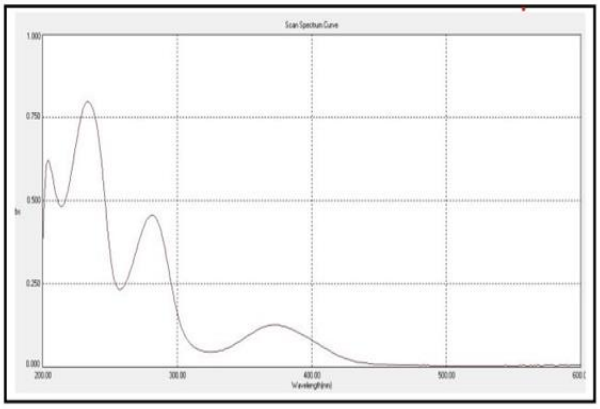


Fig. (16) UV-Visble Spectrum of the complex [Cu(L1)Cl2]

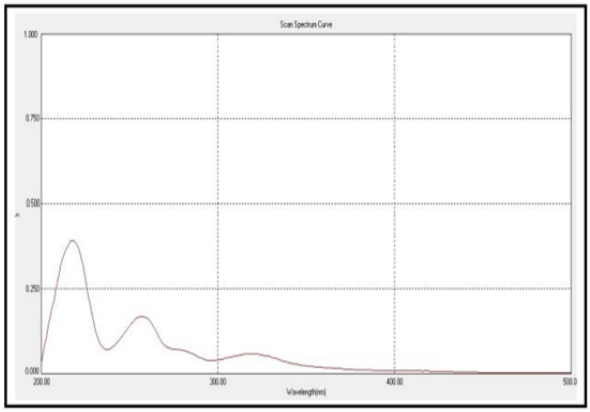


Fig. (17) UV-Visble Spectrum of the ligand L2

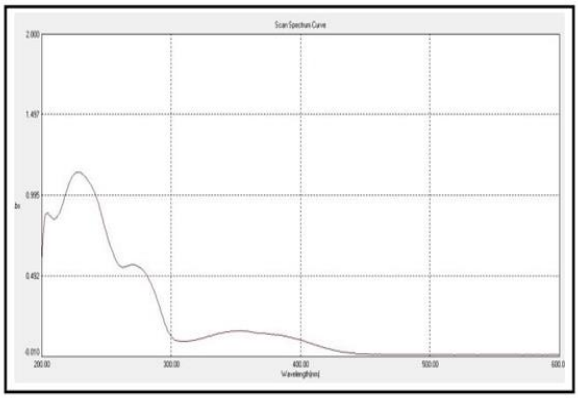


Fig. (18) UV-Visble Spectrum of the complex [Cu(L2)Cl2]