



Chelation of N,O-Donor Attached Schiff Base Ligand Bear Cephalexin Towards Co(II), Ni(II), Cu(II) and Cd(II): Syntheses, Structures, Antimicrobial Activities and Cytotoxic Studies

M. Baidaa and Rehab K. Al-Shemary

Department of Chemistry, College of Education for Pure Science (Ibn Al-Haitham), University of Baghdad, Baghdad, Iraq

Key words: Chelation, cephalaxin, Schiff base, antimicrobial, cytotoxic studies

Abstract: This study comprised the preparation of Schiff base derivatives of cephalaxin antibiotic by condensation reaction with Isatin. Metal complexes of the Schiff base ligands with Co(II), Ni(II), Cu(II), Cd(II) ions were prepared by reacting the ligand with the metal salts in refluxing ethanol. The chemical structure of the ligand, as well as the stereo-chemical structure and arrangements of the synthesized metal complexes were mentioned relying upon the outcomes given from TG analysis and CHN, mass, NMR, atomic absorption and FTIR, spectrophotometry, electronic spectra, measurements of conductivity and magnetic moments. The mole ratio of (ligand: metal ion) was (2:1) with bi-dentate linking demeanors of the chelating ligand with the metal ions. The IR spectra clarified a bidentate ligand which chalets through nitrogen atom of imino from azomethine bond and the oxygen atom of the carbonyl. UV-Vis spectrophotometry showed the characteristic absorption bands conformable to an octahedral arrangement for all metal complexes. The overall form found from empirical values was found to be $M(OADC)_2(H_2O)_2$ where $M = Co(II), Ni(II), Cu(II), Cd(II)$ and $(OADC) = Schiff\ base\ ligand$. This composition was further confirmed by thermal analysis and their thermal constancy in nitrogen atmosphere was carried out. The study of antibacterial appeared that the efficiency of metal complexes is higher than the one established for the free Schiff base ligand. Lastly, the cytotoxicity of $[OADC]$ ligand and its complexes were screened on the cell line of Hep G2. $[OADC]$ ligand appears good efficacy with the cell line of Hep G2 than complexes.

Corresponding Author:

M. Baidaa

Department of Chemistry, College of Education for Pure Science (Ibn Al-Haitham), University of Baghdad, Baghdad, Iraq

Page No.: 15-23

Volume: 16, Issue 2, 2021

ISSN: 1816-3319

International Journal of Tropical Medicine

Copy Right: Medwell Publications

INTRODUCTION

Substantial types of organic components are called Schiff bases, prepared from the condensation of carbonyl

groups with primary amines^[1]. Constitutionally a Schiff base is a nitrogen peer of a carbonyl component in which the carbonyl moiety is superseded by an azomethine or imine moiety^[2]. The imine moiety in these components

is proved to be responsible for deferent biological activities, antibacterial and antifungal being prominent^[3]. The synthesis of new antibacterial agents, through various methods, is, for sure, an emergency^[4]. Isatin (1H-Indole-2, 3-dione) is one of the great optimistic types of aromatic heterocyclic organic components having numerous delightful efficacy profiles and well-tolerated in human subjects^[5]. Isatin and its Schiff base derivatives showed a variety of biological^[6] and pharmacological efficacies^[7] as antimicrobial, antidepressant^[8], cytotoxicity^[9], antileishmanial^[10], insecticides^[11], fungicides^[12], anti-inflammatory^[13], analgesic^[14], anticonvulsant^[15], tuberculostatic^[16], anticancer^[17] and anti-HIV^[18]. Contagious illnesses have been large health trouble for decenniums, particularly in countries the improving and rudimentary. Furthermore, the tendency of microorganisms to enhance impedance to antibiotics moreover presupposes the urge to expand newer drugs^[19]. Isatin, a β -lactam antibiotic belonging to the type of penicillins is an acid steady semi-synthetic drug offered to be active with a large reign of contagions caused by many bacteria strains of (+)ive and (-)I've Grams both in animals and humans^[20].

The preparation of cephalixin-based Schiff base ligand is still restricted parallel with other components of organic^[21]. This is due to the existence of different interacting moieties in the skeleton of these molecules which results in low yields^[22]. In the last years, a distinctive notice has been paid to the chemistry of the metal complexes of the Schiff bases^[23]. This is attributed to the chemical constancy of the complexes in addition to the potential of utilizing them in the great diverse areas. To a great extent, noteworthy prosperities, in this field have been gained resulted in the diverse preparation ways of the complexes^[24]. Recent research focuses more and more on the synthesis of complexes of the transitional metals with ligands of Schiff-base type as a result of the biological properties which they have^[25]. In many cases, the conclusion has been that, through the coordination of the Schiff bases, to the metal ions which are present in the biological systems, the biological activity of the respective Schiff base increases. A large number of Schiff bases and the corresponding metal complexes have proven efficiencies of antileukemia antitumor, antibacterial and antifungal. This work studies the synthesis and characterization of new metal complexes of Schiff base ligand derived from the condensation reaction of cephalixin with (Isatin) and the coordination behavior of the ligand with Co (II), Ni(II), Cu(II), Cd(II) ions.

Synthesis of the Schiff base ligand: Initially, the ligand (OADC) was synthesized from 20 mL ethanol including (1 mM) cephalixin and 10 mL ethanol wherever has been dissolved in present (1 mM) Isatin. For a purpose get data

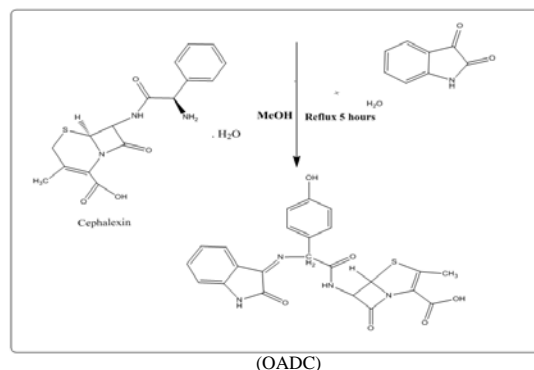


Fig. 1: The structure of Schiff base ligand

of the pH between 7-8, NaOH solution (1.0 M) was added and the solution was refluxed at 3 h. The solution volume was decreased by evaporation to one half when a precipitate was made. It was filtered, washed with ethanol and at room temperature dried in a vacuum under anhydrous CaCl₂. Recrystallization from (50:50) water-ethanol mixture appears the Schiff base (Fig. 1).

Synthesis of the metal complexes: The complexes were synthesized in the same method by mixing ligand (2.0 mM) with 25 mL ethanol including CdCl₂ 6H₂O, CoCl₂ 6H₂O, CuCl₂ 6H₂O and NiCl₂ 6H₂O (1.0 mM). The solutions pH data was regulated to 7-8 by adding NaOH solution (1.0 M) and also they were refluxed at 2 h. Eventually, the volume of solutions was decreased to one half by evaporation and in both states, an appearance of colored products was appeared this being designated to Co(II), Cd (II), Cu(II) and Ni(II) complexes respectively. It was filtered, washed with ethanol and dried in vacuum. Recrystallization from hot ethanol got the metal complexes.

In vitro antibacterial assay: The recently prepared ligand and the complexes were checked for antibacterial efficacy with species of pathogenic bacteria *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* rapprochement s were made. The way of paper disk diffusion relied upon the calculation of antibacterial efficacy. This way is easy and is routinely utilized in laboratories of the hospital. The (30 μ g) ligand/complex in (0.01 mL) DMF was placed on (3 mm) of a paper disk in diameter and used a micropipette. These were put in an incubator at 37°C for 48 h and then were utilized to the bacteria developed on plates of agar. The (50 g) 2% of glucose in the agar of Mueller-Hinton, got from Merck, was suspended in (1 L) of newly distilled water for the synthesis of agar plates for bacterial types). It was let to soak for 20 min and then was boiled till the agar was fully dissolved in a bath of water. The solution was autoclaved at 120°C for 30 min, teeming into dishes of antiseptic

Petri and then stocked at 40°C for pollination. Inoculation was completed with a wire loop from platinum that in a flame was made red hot, cooled and also employed for the application of bacterial strains. Each disk of paper was put on an already inoculated agar plate which was then incubated for 24 h at 37°C. The activity was calculated by determining the diameter of ranges appearing to accomplish inhibition (mm).

Photobiological activity assessment: The physiological efficacy was performed of Isatin, cephalixin derivative, [OADC] ligand and synthesized complexes on mosquito larvae. The (100 mL) 48 flasks of 20 mosquito larvae were utilized in this experience. The 42 beakers are intended for all copies of remedied specimens, 3 beakers for light hegemony (un-handled specimens uncovered to sunlight) and 3 cups for ordinary monitoring. Sample processing was performed by uniformly spreading the shape of the curing agent powder onto the H₂O surface of the therapy cups. The treated specimens were split into two sets. The (21 spheres) of 1st set were uncovered to sunlight throughout the day for 4 consecutive days and the (21 beakers) of 2nd set was kept for the similar interval (dark toxicity) in the dark. The survival proportions of mosquito larvae were calculated every 24 h of the trial interval. All trials were conducted in results of intermediate and triplicates were obtained.

Cell cultures and treatments: Hep G2, cell line of Liver cancer was utilized for experience in lanes from (2-5) cells of Hep G2 were cultured in (medium-modified eagle of Dulbecco) DMEM accomplished with 1% L-glutamine, 10% (serum of fetal bovine) FBS, 100 U mL⁻¹ streptomycin-penicillin. Cells were incubator with 5% CO₂ preserved at 37°C in moisten.

Cell labeling: (Hep G2-cell line) cell line of liver cancer was remedied with [OADC] ligand and diluted complexes at various concentrations in increase modes. Then culture was incubated (full dose) in a full increase medium for 24 h at 37°C in moist air with 5% carbon dioxide. Last, the cells were washed in (phosphate buffered saline) PBS at 3 times and separated 5 min at 300 r min⁻¹. The cells were re-hanged on PBS after centrifugation. Cell count and verve were measured by MTT. Conjoined cells were washed repeatedly with a new PBS to separate the attached extracellular or particles until eluted PBS showed elongated free particles under the light microscope.

Cell viability/cytotoxicity assay: The cellular toxicity of ligand (OADC) and their clusters versus the cell line of Hep G2 were examined by MTT screening. They were incubated together for one day. The cells were then cleaned utilizing PBS. Next, the cells were incubated with solution of MTT for 3 h at 37°C and the dye was solved

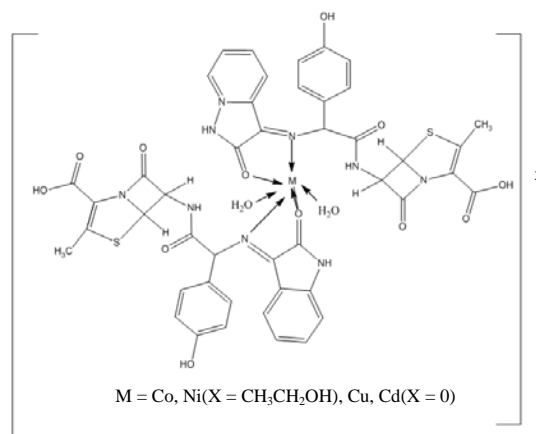


Fig. 2: Suggested structure of [M(OADC)₂(H₂O)₂] complexes

for 20 min by (DMSO). Absorption was assayed at 570 nm and cell viability was calculated as a percentage of control cells without materials and cells tested. Each experience was refined fully 3 times separately.

Physical properties and elemental analyses: The physical features and outcomes got from metal contents and C.H.N. analyses of the prepared component are described in Table 1. The analytical values were almost accepted with determined data with several deviations due to incomplete combustion or technical errors. The molecular formulation of the compounds was proposed corresponding to these values together with those given from spectral and thermal analyses as well as conductivity and magnetic susceptibility of metal complexes. The Schiff base ligand was prepared by refluxing the suitable quantities of Isatin with amoxicillin in methanol and its constructing was founded by microanalytical data and mass, UV-vis, H NMR IR spectrum (Fig. 1). The metal complexes of Schiff base ligand were synthesized by the stoichiometric reaction of the corresponding metal (II) chloride with the ligand in (1:2) a molar ratio. The complexes were obtained as air-stable amorphous solids which are insoluble in water, slightly soluble in ethanol and methanol, entirely soluble in (DMSO) and (DMF). The molar conductivities of the complexes at room temperature determined in 10⁻³ M DMF have low values of 11-19 Ω⁻¹cm²mol⁻¹ referencing their non-electrolyte nature. The elemental analysis above aforementioned for all complexes droves to the next experiential molecular formulation (Fig. 2 and Table 1):



Where:

M = Co(II), Ni(II), Cu(II), Cd(II)
(OADC) = Schiff base ligand

Table 1: The Some of physical properties and micro analysis of products

Compound	Empirical formula	(Formula wt.)	Yield %	Colour	Elemental analyses, Found (Calc.) %(calculated)				
					C	H	N	S	M
[OADC]	C ₂₃ H ₁₈ N ₄ O ₆ S	478	75	Pale brown	57.87 (57.47)	3.26(3.79)	11.10 (11.71)	-	-
[Co(OADC) ₂ (H ₂ O) ₂].EthOH	C ₄₈ H ₃₆ CoN ₈ O ₁₅ S ₂	1115	65	Olive	51.95 (51.71)	4.21 (4.43)	11.15 (11.31)	4.76 (5.75)	5.18 (5.29)
[Ni(OADC) ₂ (H ₂ O) ₂].EthOH	C ₄₈ H ₃₆ NiN ₈ O ₁₅ S ₂	1114	60	Pale green	52.60 (52.72)	4.21 (4.43)	11.17 (11.27)	5.54 (5.75)	5.39 (5.27)
[Cu(OADC) ₂ (H ₂ O) ₂]	C ₄₆ H ₃₃ CuN ₈ O ₁₄ S ₂	1089	75	Greenish brown	51.21 (51.81)	4.04 (4.35)	10.89 (11.57)	5.43 (5.83)	5.27 (5.83)
[Cd(OADC) ₂ (H ₂ O) ₂]	C ₄₆ H ₃₃ CdN ₈ O ₁₄ S ₂	1122	70	Pale yellow	49.11 (49.22)	3.23 (3.86)	11.15 (11.23)	5.40 (5.71)	9.67 (10.01)

Table 2: IR spectral data of the ligand and its metal complexes

Compound	$\nu(\text{OH})$ $\nu(\text{OH}-(\text{H}_2\text{O}))$	$\nu(\text{C}=\text{O})_{\text{isatin}}$	$\nu(\text{C}=\text{O})$ (Amide+ester)	$\nu(\text{C}=\text{N})_{\text{imine}}$	$\nu(\text{M}-\text{OH}_2)$	$\nu(\text{M}-\text{N})$ $\nu(\text{M}-\text{O})$
[OADC]	3352	1690	1750 (1655)	1639	-	-
[Co(OADC) ₂ (H ₂ O) ₂].(EthOH)	3366-3575	1681	1744 (1651)	1620	811	500, 485
[Ni(OADC) ₂ (H ₂ O) ₂].(EthOH)	3387-3586	1677	1749 (1654)	1624	817	512, 495
[Cu(OADC) ₂ (H ₂ O) ₂]	3367-3579	1679	1748 (1650)	1629	820	522, 490
[Cd(OADC) ₂ (H ₂ O) ₂]	3367-3572	1675	1746 (1652)	1626	815	536, 498

Infrared spectra: Table 2 depicts the considerable vibrational styles of (OADC) and its metal complexes. Also this table characterizes the positioning bands for the vibrational patterns of moieties of NH amide, $\nu\text{C}=\text{O}$ from the antibiotic lactam ring segment, the interfering amide carbonyl and the ester for ligand. It has some atoms of the potential donor that assigned to constraints of steric; the ligand may supply an extreme of three atoms of granter to any one center of metal. The ligand (OADC) spectrum displayed the obscurity of bands at (3356, 3283 cm^{-1}) identical to stretching vibrations of amine group of amoxicillin and at 1690 and 1616 cm^{-1} designated to C = O group of Isatin and of NH vibrations of the indole ring system of ligand (OADC) that indicates to the composition of amoxicillin by reaction of condensation between both cephalixin and Isatin with the antibiotic to compose the connection of CH = N azomethine. This was emphasized by the emergence of new bands at 1639 cm^{-1} , respectively that can be designated to $\nu(\text{C}=\text{N})$ from the azomethine moiety. All complexes displayed changes in the bands positions related to carbonyl ($\nu\text{C}=\text{O}$) of Isatin and $\nu(\text{C}=\text{N})$ azomethine moieties that mentions to the chelation of these moieties with the metal ions. This was emphasized by the emergence of new low-density bands at low wavelengths corresponding to the expansion vibrations of the M-N and M-O bonds, respectively. A wide band of approximately 3565 and 3418 cm^{-1} of ligand is realized attributable to vibrational patterns of the OH moiety of hydrogen-related solvent of CH₃CH₂OH and H₂O included in the crystal lattice structure of the ligand. The table also describes the band locations assigned to the amide vibratory modes. These observations indicate that the ligand acted as bidentate ligand in chelation with metal ions.

Electronic spectra, magnetic moments and conductivity measurements

UV-VIS spectra and magnetic measurements: In order to get datum concerning the chelation arrangement of the complexes, the UV-vis spectra were calculated in DMF at

room temperature and the values given were correlated with magnetic sensitivity data and parameters of ligand field: (β) proportion of nephelauxetic, (10 Dq) cleavage energy and (B) parameter of interelectronic disharmony. The ligand spectrum offers two peaks at 42194, 33222 and 28248 cm^{-1} , respectively, attributed to $\pi \rightarrow \pi$ and $n \rightarrow \pi$, respectively, calculated by the C = N and C = O moieties. Then these peaks present in the complexes spectra but they are changed to lower data that evidence the chelation of the central metallic ions to the ligand.

The Co(II) complex spectra present two peaks at 10150 cm^{-1} (ν_1) and 22125 cm^{-1} (ν_3), these are designated to transferences of ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})(\nu_1)$; ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})(\nu_3)$, respectively. These are the distinctive peaks of high spin octahedral Co(II) complexes.

The parameters of the ligand field (β , B Dq) are calculated utilizing E. Koning neutralizations, when only peaks of ν_1 and ν_3 appear in the UV-vis spectra and the values are well within the reign adduced for the octahedral complexes. The magnetic sensitivity values were 5.1 BM for Co(II) complex that mentions three electrons of unpaired in an octahedral arrangement.

The Ni(II) complex spectrum appears two peaks of d \rightarrow d at 20449 and 23310 cm^{-1} in an octahedral arrangement coinciding to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{2g}(\text{F})(\nu_1)$ and ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})(\nu_2)$, transfers. For d⁸ ions in an octahedral arrangement, the energy of ν_1 coincides to 10Dq and the Dq data is gotten from it. The Dq, B, β data are gotten in coinciding with the empirical ones for Ni(II) octahedral complexes. The magnetic sensitivity data of Ni(II) complex is 3.36 BM referencing the existence of two electrons of unpaired on Ni(II) ion and proposing that this complex has an octahedral arrangement. The Cu(II) complex spectrum appeared one wide peak in the zone of the visible designated to the transmission of ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$ of Cu(II) complex has tetragonally distorted octahedral. The magnetic moment of the Cu (II) complex is within the predictable data is 1.88 BM for one unpaired electron. No d-d transmission bands have appeared in the spectrum of the Cd (II) complex that was fully widespread with the complex has d¹⁰ (Table 3).

Analysis of thermal: The complexes analysis was elaborated as curves of TG/DTG/DSC these are clarified in Fig. 3. It may be spotted that, at low temperature up to 200°C, the events may be designated to; the evaporation of the volatiles that were produced during synthesis of complexes or/and elimination of several adsorbed gases; the elimination of ~2.0 moles of chelated water that is in good harmonization with the predictable weight lack. The weight lack gotten for volatiles can be elucidated by the truth which the complexes were ostensibly dried at a temperature below 60°C in warm air to block alteration of complexes composition by fortuitously lack of water. On the curves of DSC, the impacts of endothermic may appear as the shoulders with the upper changed to more temperature data of 200 and 210°C, respectively referencing an interfering with other operations, great potential with the physical evaporation adsorbed ligand on

the complexes particles. The complexes decomposition in range of temperature between 170-400°C takes place with the maximum weight lack with the split of bonds of the chelation between the ligand and metal or with the bonds rupture from inside the ligand pursued by the removal of some by-products with the impacts of exothermic spotted on curves of DSC, at 365 and 360°C, respectively. Furthermore, in this temperature reign equal routes might happen of ligand removal or/and lack of one or the other ligand compound. This would elucidate the occurrence peaks that appeared on the curves of DTG at 225 and 220°C, respectively. Thus, up to 400°C, an analogous proceeding of dissociation happens for the complexes, also the dissociation proceedings do not include other notable notes than those given in Table 4. At more temperature than 450°C, the Co(II) complex dissociated in 2 stages pursued by the influences of exothermic with

Table 3: Electronic spectral data of the ligand and its metal complexes

Compound	μ_{eff}	$\Delta_m, S\ cm^2\ mol^{-1}$	$\lambda\ nm$	$\nu\ cm^{-1}$	Transition	Structure
[OADC]	-	2.12	237 301 354	42194 33222 28248	$(\pi \rightarrow \pi^*)$	-
[Co(OADC) ₂ (H ₂ O) ₂].(EthOH)	5.1	11.90	236 300 350 479 666	42372 33333 28571 20876 15015	$(n \rightarrow \pi^*)$ L.F C.T ${}^4T_{1g(f)} \rightarrow {}^4T_{1g(p)}(u_3)$ ${}^4T_{1g(f)} \rightarrow {}^4A_{2g(f)}(u_2)$	Octahedral
[Cu(OADC) ₂ (H ₂ O) ₂]	3.36	14.43	237 302 351 429 489	42194 33112 28490 23310 20449	L.F C.T ${}^3A_{2g} \rightarrow {}^3T_{1g(p)}$ ${}^3A_{2g} \rightarrow {}^3T_{1g}$	Octahedral
[Ni(OADC) ₂ (H ₂ O) ₂].(EthOH)	1.88	17.34	236 301 350 646	42372 33222 28571 15479	L.F C.T ${}^2T_{2g} \rightarrow {}^2E_{2g}$	Octahedral
[Cd(OADC) ₂ (H ₂ O) ₂]	-	16.65	238 300 355 488	42016 33333 28169 20491	L.F C.T C. T	Octahedral

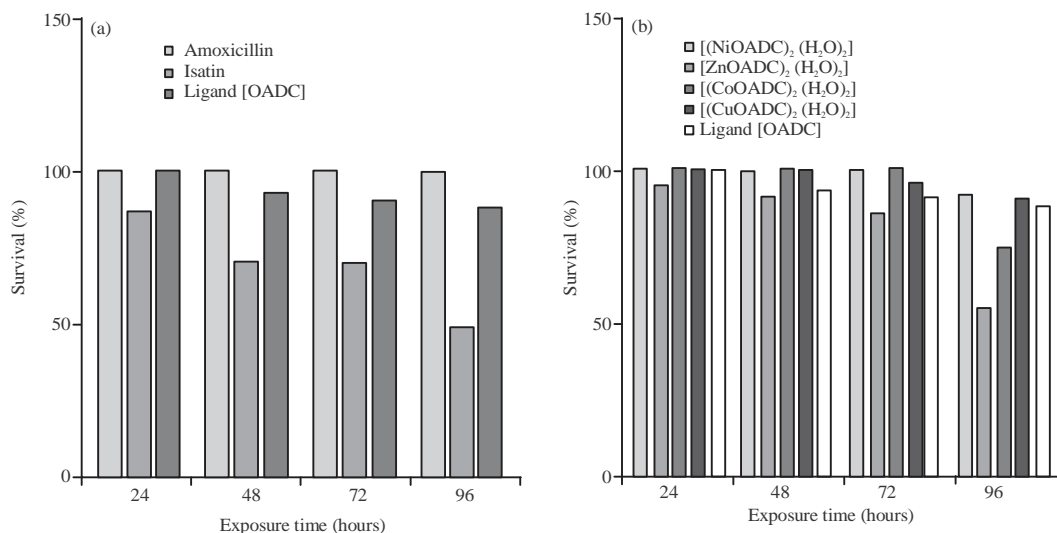


Fig. 3(a, b): (a) Dark toxicity of on mosquito larvae of ligand and its derivatives and (b) Its complexes

Table 4: Thermal decomposition data of some metal complexes

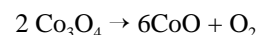
Complexes	Steps	Temperature range (°C)	Thermal effect	Maximum (°C) DTG and DSC	Mass loss (%)	Associated process
[Co(OADC) ₂ (H ₂ O) ₂](EthOH)	1	RT-80	Endo	60	4.5	Loss of adsorbed gases (EthOH) and/or adsorbed volatiles resulted from synthesis
	2	80-170	Endo	Shifted to 210 on DSC curve	3.8	Loss of chelated H ₂ O
	3	170-400	Exo	360	35.1	Ligande decomposition
	4	450-570	Exo	460	45.8	Decomposition of some by-products
	5	570-630	Exo	640	7.43	Decomposition of some by-products
	6	630-900	-	-	2.8	Gradual loss of mass due to elimination of some gases, such as O ₂
			-----Residue-----		25.1	6.56 % C; 16.6 % CoO; 17.8 % Co ₃ O ₄
[Ni(OADC) ₂ (H ₂ O) ₂](EthOH)	1	RT-80	Endo	52	6.2	Loss of adsorbed gases and/or adsorbed volatiles resulted from synthesis
	2	85-180	Endo	shifted to 210 on DSC curve	3.9	Loss of chelated H ₂ O
	3	180-440	Exo	350	38.7	Ligand decomposition
	4	440-606	Exo	560	21.6	Decomposition of some by-products
	5	606-1000	-	-	8.2	Gradual loss of mass due to the elimination of some gases, such as: CO, CO ₂
	6			-----Residue-----		26.8

the maxima temperature in small difference on both curves of DSC and DTG at 460 and 630°C, respectively. After 665°C, piece meal weight lake composed with the small data of 2.6% happen and residing a definitive remain of 25.1%, proposing which this might be contained of an admixture including carbon and MOs, the final being in the status of equilibrium as appears inreaction 1.

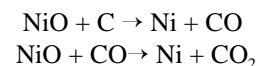
In the several temperatures reigns the dissociation of Ni(II) complex happens through a single step with an influence of exothermic at 576°C being in good approval with the recognized literature values that appeared which the Ni(II) complexes are faster decomposed under high temperature than similar complexes of cobalt. After 620°C the mass loss has a more data than that was recorded for Co(II) complex because in presence of carbon or CO the Ni oxide reduces to metalas reactions II and III show, final residue being of 25.8%; this consists of a mixture containing C, Ni and NiO. Similar events were reported for Cu(II) and Zn(II) complexes of Schiff bases obtained by condensation of Isatin and cephalixin. Other studies showed that cephalixin was thermally decomposed at several stages with a total weight loss of 51.06%, leaving a residual mass at 350°C of 48.94%. Also, distinctive decomposition steps of complexes derived from salicylaldehyde 29 were presented.

Moreover, similar assumptions were reported for residue composition related to thermal decomposition of other transition metal complexes under a nitrogen atmosphere.

M. Lalia-Kantouri showed that the by-products formed after the main degradation step (in our study after 400°C) are not stable and further heating of all the complexes at 700°C leads to a residue consisting in a carbonaceous metal oxide. The details for each studied compound are given in Table 3. Knowing that CoO converts to Co₃O₄ (CoO•Co₂O₃) if it is heated to the next equilibrium characterizes these reactions: around:



So as to appreciate the remains formation of Ni(II) complex the next reactions are utilized:



Depended on the notice that in the reign of the temperature between 900-1000°C, the weight lack is clearly more, attaining a data of 3.8% attributed to the CO₂ removal in the same quantity, it may be spotted which an equal mole (0.080) is due to NiO decreased at metallic Ni.

The identical MWt and the Ni proportion from NiO were utilized to determine the formations of the remains gotten at Ni(II) complex decomposition (26.3%) at 1000°C. Values of Thermal disintegration for all complexes emphasize the existence and the kind of H₂O molecules and the stoichiometry of the purposed complexes. The coordinated molecules of H₂O liberated with the impact of an endothermic and the degeneration operation directly with the impact of an exothermic. Depended on analytical values, UV-Vis and IR spectra and analysis of thermal were suggested synthesis of the complexes (Table 4).

Antibacterial study: The prepared components were screened for *in vitro* antibacterial efficacy utilizing the diffusion way with *E. coli*, *S. aureus*, *P. aeruginosa*. The antibacterial efficacy was evaluated on the foundation of the size of the restraint range made around disks of the paper on the seeded agar plates. Expansion restraint was compared with recognized antibiotics namely ciprofloxacin. The prepared components appeared

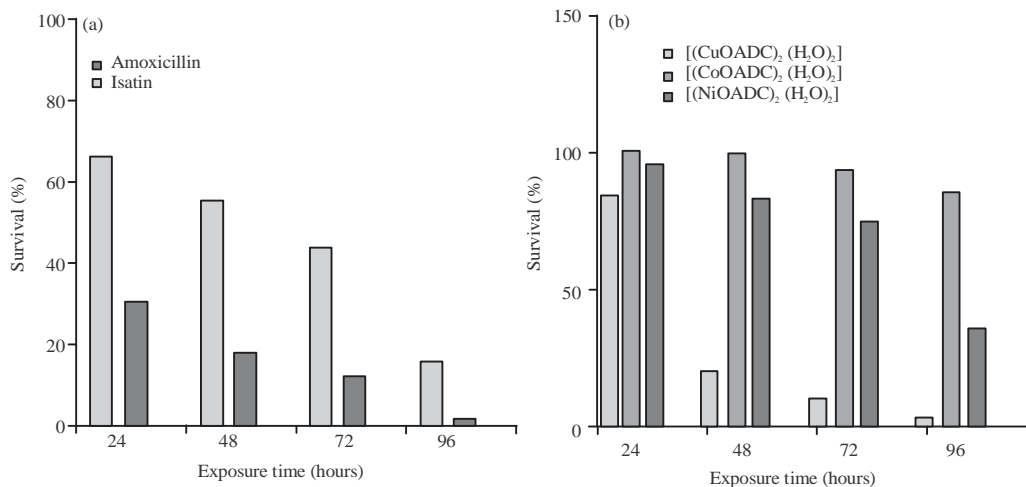


Fig. 4(a, b): (a) Photosensitizing effect on mosquito larvae of ligand and its derivatives and (b) Its complexes

differing grades of restrained impacts on the expansion of species of the screened bacterial. As spotted, the Schiff base (OADC) is sparingly energetic with the bacterial species while the Schiff base efficacy became more pronounced when it is chelated to the metal ions. Referring to complexes, we note that the Cu(II) complex is more active as compared with other complexes. In conclusion, the biological efficacy of the complexes follows the order: Cu(II)>Ni(II)>Co(II) Schiff base ligand. An antibacterial activity of metal complexes better than the one of ligand can be explained on the basis of Overtone's and Tweedy's concepts corresponding to notion of Overtone for permeability of cell, the membrane of lipid which embraces the cell prefers only the transit for materials of lipid-soluble, thence liposolubility is deemed to be a significant agent which dominates the antibacterial efficacy. Drawing on the theory of chelation, the concept of Tweedy elucidates the rise of the lipophilic feature of the metal coordinate. Upon coordination, the (+)ive charge of the metal ion is slightly participated with the granter atom show on the ligand and delocalization of a π -electron over the whole coordinate ring happens. In this method, the lipophilic feature of the metal coordinate increases and prefers its penetration through the layers of lipid for the membranes of bacteria and prevents the metal-binding positions in the bacterial (Table 5).

Photobiological activity assessment: The physiological efficacy of the derivative Isatin, cephalixin and [OADC] ligand and all groups on mosquito larvae has been investigated to examine how well photosensitivity is effective in controlling harmful insects utilizing lineal sunlight (larval impact). The experience was also conducted in the dark (dark toxicity). Figure 4a, b illustrates the influence of photosynthesis of components. Figure 3a, b illustrates the influence of the similar factors

Table 5: Antibacterial activity of compounds

Compounds	Zone of inhibition (mm)		
	<i>E. coli</i>	<i>S. aureus</i>	<i>P. aeruginosa</i>
[OADC]	5.0±1.0	10.0±1.0	5.0±1.0
[Co(OADC) ₂ (H ₂ O) ₂].(EthOH)	22.0±1.5	17.0±1.5	6.0±1.0
[Ni(OADC) ₂ (H ₂ O) ₂].(EthOH)	37.0±1.0	52.0±1.0	23.0±1.0
[Cu(OADC) ₂ (H ₂ O) ₂]	40.0±1.0	50.0±1.0	20.0±1.5
[Cd(OADC) ₂ (H ₂ O) ₂]	17.0±1.0	37.0±1.0	8.0±1.0

Data are the mean±standard deviation of the mean

on dark situations (dark toxicity). Both figures suggest the dark toxicity and the extent of photosensitivity of components. The [OADC] ligand has high efficacy of photosensitivity compared to its dark toxins. In Figure 4a, the [OADC] ligand appears the highest efficacy of photosensitivity as an assignment of the mosquito larval survival rate (0%). [OADC] ligand is more than derivatives of Isatin and cephalixin. Among the complexes, [Cu(OADC)₂(H₂O)₂] has more efficacy of photosensitivity leading to a high rate of larval mortality (100%, Fig. 4b). The efficacy of photosensitization for [Cu(OADC)₂(H₂O)₂] is more than its dark toxicity, Fig. 3b. The arrangement of influence of the larvae of compounds after exposure to sunlight is as follows: [OADC]>Isatin>cephalexin>[Co(OADC)₂(H₂O)₂]>[Ni(OADC)₂(H₂O)₂]>[Cu(OADC)₂(H₂O)₂]>[Zn(OADC)₂(H₂O)₂].

In vitro cytotoxicity studies of schiff base and its complexes: Compounds cytotoxicity was studied with various concentrations on cell line of Hep G2. The data analysis of the cytotoxicity utilizing MTT screening appeared that the screened compounds have favorable efficacy at (25 $\mu\text{mol L}^{-1}$) concentration. In specially, [Ni(OADC)₂(H₂O)₂] 50% prevent from cell line of Hep G2. [OADC] ligand, [Zn(OADC)₂(H₂O)₂] and [Cu(OADC)₂(H₂O)₂] complexes display restraint of 32,

38, 30 and 31%, respectively. On other side, $[\text{Co}(\text{OADC})_2(\text{H}_2\text{O})_2]$ displays the least efficacy of cytotoxic where it prevents only 20% from cell line of Hep G2. Generally, [OADC] ligand displays good efficacy versus cell line of Hep G2 than the complexes.

Also, efficacy of photosynthetic (the influence of larval) of cephalixin and Isatin, ligand [OADC] and all complexes was screened on mosquito larvae to examine how well photosensitivity is effective in controlling harmful insects utilizing immediate sunlight. Ligand [OADC] and $[\text{CuOADC})_2(\text{H}_2\text{O})_2]$ appear the more photosensitivity efficacy as a function of the proportion of mosquito larva mortality (100%). The arrangement of effect of the larvae of the compounds after sun exposure is as follows: $[\text{OADC}] > \text{Isatin} > \text{cephalexin} > [\text{CoOADC})_2(\text{H}_2\text{O})_2] > [\text{NiOADC})_2(\text{H}_2\text{O})_2] > [\text{CuOADC})_2(\text{H}_2\text{O})_2] > [\text{ZnOADC})_2(\text{H}_2\text{O})_2]$. Lastly, the cytotoxicity of [OADC] ligand and its complexes were screened on the cell line of Hep G2. [OADC] ligand appears good efficacy with the cell line of Hep G2 than complexes.

CONCLUSION

The new complexes of Co(II), Ni(II), Cu(II), Cd(II) with the ligand [OADC] derived from cephalixin and Isatin were synthesized and depicted. Data collected from the infrared spectra showed that the [OADC] acts as a ligand [OADC] for chelated ligand in all complexes. The values composed from spectra of IR appeared which the ligand [OADC] exhibits as a bidentate ligand chelated in all complexes. UV-vis spectra and measurements of magnetic suggested an octahedral structure for the metal complexes. Thermal analysis provided pyrolysis data for all complexes which indicates that the chelated water molecules were liberated with an endothermic and followed the procedure of degeneration with a thermal influence. Studies of bacteriological were conducted on three types. The outcomes appeared a grow in the antimicrobial efficacy of complexes compared to the non-composite ligand.

REFERENCES

01. Imran, M., J. Iqbal, T. Mehmood and S. Latif, 2006. Synthesis, characterization and *in vitro* screening of amoxicillin and its complexes with Ag (I), Cu (II), Co (II), Zn (II) and Ni (II). J. Biol. Sci., 6: 946-949.
02. Reiss, A., A. Samide, G. Ciobanu and I. Dabuleanu, 2015. Synthesis, spectral characterization and thermal behaviour of new metal (II) complexes with Schiff base derived from amoxicillin. J. Chil. Chem. Soc., 60: 3074-3079.
03. Joshi, S., V. Pawar and V. Uma, 2011. Synthesis, characterization and biological studies of Schiff bases metal complexes Co(II), Zn(II), Ni(II) and Mn(II) derived from amoxicillin tri-hydrate with various aldehydes. Int. J. Pharm. Bio. Sci., 2: 240-250.
04. Waziri, I., N.P. Ndahi, G.A. Mala and M.B. Fugu, 2014. Synthesis, spectroscopic and biological studies of Cobalt(II), Nickel(II) and Iron(III) mixed antibiotic metal complexes. Der. Pharm. Chem., 6: 118-122.
05. Egorov, N.S., 1985. Antibiotics: A Scientific Approach. Mir Publishers, Moscow.
06. El-Maali, N.A., A.H. Osman, A.A.M. Aly and G.A.A. Al-Hazmi, 2005. Voltammetric analysis of Cu (II), Cd (II) and Zn (II) complexes and their cyclic voltammetry with several cephalosporin antibiotics. Bioelectrochemistry, 65: 95-104.
07. Anacona, J.R. and P. Alvarez, 2002. Synthesis and antibacterial activity of metal complexes of cefazolin. Transition Metal Chem., 27: 856-860.
08. Anacona, J.R. and F. Acosta, 2006. Synthesis and antibacterial activity of cephradine metal complexes. J. Coord. Chem., 59: 621-627.
09. Chohan, Z.H. and M.F. Jaffery, 2000. Synthesis, characterization and biological evaluation of Co(II), Cu(II), Ni(II) and Zn(II) complexes with cephradine. Met. Based Drugs, 7: 265-269.
10. Anacona, J.R. and J. Serrano, 2003. Synthesis and antibacterial activity of metal complexes of cephalothin. J. Coord. Chem., 56: 313-320.
11. Anacona, J.R. and G.D. Silva, 2005. Synthesis and antibacterial activity of cefotaxime metal complexes. J. Chil. Chem. Soc., 50: 447-450.
12. Anacona, J.R. and A. Rodriguez, 2005. Synthesis and antibacterial activity of ceftriaxone metal complexes. Transition Metal Chem., 30: 897-901.
13. Tomi, I.H.R., A.H. Abdullah, A.H.R. Al-Daraji and S.A.R. Abbass, 2013. Synthesis, characterization and comparative study the antibacterial activities of some imine-amoxicillin derivatives. Eur. J. Chem., 4: 153-156.
14. Fisher, J.F., S.O. Meroueh and S. Mobashery, 2005. Bacterial resistance to β -lactam antibiotics: Compelling opportunism, compelling opportunity. Chem. Rev., 105: 395-424.
15. Warra, A.A., 2011. Transition metal complexes and their application in drugs and cosmetics-A review. J. Chem. Pharm. Res., 3: 951-958.
16. Orvig, C. and M.J. Abrams, 1999. Medicinal inorganic chemistry: Introduction. Chem. Rev., 99: 2201-2204.
17. Al Zoubi, W., 2013. Biological activities of Schiff bases and their complexes: A review of recent works. Int. J. Organic Chem., Vol. 3, 10.4236/ijoc.2013.33A008
18. Antonijevic, M.M. and M.B. Petrovic, 2008. Copper corrosion inhibitors. A review. Int. J. Electrochem. Sci., 3: 1-28.

19. Beale, J.M., J.H. Block and R.A. Hill, 2011. *Organic Medicinal and Pharmaceutical Chemistry*. Lippincott Williams & Wilkins, Wolters Kluwer, China, Pages: 501.
20. Karim, L.K.A. and W.A. Jaafar, 2017. Synthesis, characterization and biological activity of schiff bases chelates with Mn(II), Co(II), Ni(II), Cu(II) and Hg(II). *Baghdad Sci. J.*, 14: 390-402.
21. Naji, S.H. and F.H. Musa, 2016. Synthesis and characterization of some anti-bacterial active transition metal complexes of N'-[2-(2-Phenyl hydrazinyl) Phenyl] Benzothiohydrazide. *Al-Nahrain J. Sci.*, 19: 8-15.
22. Numan, A.T., E.M. Atiyah, R.K. Al-Shemary and S.S. Abd-Ulrazzaq, 2018. Composition, characterization and antibacterial activity of Mn(II), Co(II), Ni(II), Cu(II) Zn(II) and Cd(II) mixed ligand complexes Schiff base derived from Trimethoprim with 8-Hydroxy quinoline. *J. Phys. Conf. Ser.*, Vol. 1003, No. 1.
23. Zaidan, B.A.H., N.M. Majeed, R.K. Al-Shemary and A.T. Numan, 2019. Synthesis of some Schiff base metal complexes involving trimethoprim and 2'-amino-4-chlorobenzophenone: Spectral, thermal, DNA Cleavage antimicrobial, antifungal and Cytotoxic activity studies. *J. Pharm. Sci. Res.*, 11: 618-626.
24. Al-Shemary, R.K., J.S. Sultan and S.M. Lateef, 2017. Synthesis and characterization of some new complexes with new Schiff base type (N2O2) derived from Glyoxylic acid and ethylenediamine. *IBN AL-Haitham J. Pure Applied Sci.*, 28: 72-85.
25. Al-Shemary, R.K.R., 2017. Microwave preparation, spectral studies and antimicrobial activities evaluation of Mn(II), Ni(II), Hg(II), Co(II) and Cu(II) complexes with Schiff base ligand. *IBN AL-Haitham J. Pure Applied Sci.*, 30: 58-67.