

Design Synthesis spectroscopic studies and Preliminary Antibacterial Evaluation of Schiff Base derivative from sulfadiazine and cephalixin and its metal complexes

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Abstract: Metal(II) chelation components of new tridentate ligand of Schiff base gotten from the reaction of sulfadiazine and cephalixin antibiotics with Cu(II), Co(II), Ni(II), Zn(II) ions with general formula $[MLc(H_2O)_3]$ where $L = (C_{26}H_{25}N_7O_5S_2)$ have been prepared. The compounds have been depicted by ¹H- NMR, UV, mass and FT-IR spectroscopy and calculations of molar conductivity, magnetic sensitivity, and macro- and TGA analysis. All the compounds have been disclosed both for microbiological efficiency in vitro versus two (-)ive gram and two (+)ive gram bacteria. The $[NiLc(H_2O)_3]$ complex was appeared to be more efficient than the free $[HLc]$. The values of molar conductance and analytical mentioned which the ligand conducts as a tridentate NNO coordinating in the mono complexes.

Keywords: magnetic; spectral; synthesis; cephalixin; tridentate

1. Introduction (12 bold)

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1.1 Subsection (12 bold)

The skeleton of dihydrothiazine, else recognized as the ring of β -lactam, has broadly been known as a helpful constructing prevent in the preparation of fundamental components in biological [1]. The efficacy of renowned antibiotic types like the cephalosporin, cephalixin and penicillin is assigned to the

existence of a ring of a di-hydrothiazine[2]. Regrettably, the broad utilization of the antibiotics fulfilled in the earnest medical difficulty of generic health care and drug impedance [3]. Synthesis of novel artificial derivatives of drugs with a new method of activity has made a significant mission to face drug impedance difficulties [4]. Cephalixin is a very substantial category of β - lactic drugs applied in the remedy of clinical attributed to its specific Schiff bases are vastly utilized in the chemistry of coordination as ligands [5]. The ligands of Schiff base including (RC=N) an azomethine moiety are usually created by the intensification of an energetic carbonyl with a primary amine[6]. They are a substantial category of organic components that chelate to metal ions by N- azomethine with a vast

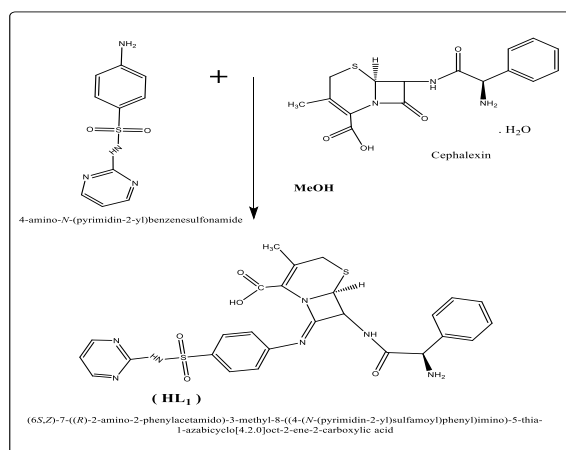
diversity of biological characteristics [7]. In recent years, Schiff bases are acquiring much publicity resulted in naivety in synthesis, versatile, available and consisting of the kind of the starting materials show diverse functionalities and dentities also broad field of enforcements in industrial, medical and biochemical fields [8]. Numerous surveys have been acquainted concerning the biological efficacies of Schiff bases; contain their anticancer [9], antifungal [10], antitumor [11], antibacterial [12], anti-inflammatory [13], herbicidal [14] and antiviral efficacies [15]. The existence of diverse chelation positions makes them advantaged ligands in the chelation chemistry of transition metals [16]. From pursuit with researches of metal-established antibiotics that found if complexation impacts the pharmacological characteristics of Schiff base and to conclude extra-essential cognition about activity of antibiotic [17]. Lately, metal established drugs are acquiring great importance in the sciences of medicine, attributed to their raised potentiality that vigorously interrupts the growth eager mechanism of microorganisms [18]. The central metal ion in it is the clef characteristic of the technique of activity. Various medical problems that arise related to free metal ion toxicity can be battlemented by coordinating agents as Schiff bases [19]. Furthermore, the number, nature, and the proportional sit of the granter atoms of a ligand let a good dominance over the stereochemistry of centers of the metallic, add to over the figure of the ions within hetero- and homo-polynuclear complexes [20]. All these features make Schiff bases better nominees in the attempt to preparation metal complexes of attention in chemistry of bioinorganic, encapsulation, separation, transport and catalysis procedures, we study here the synthesis and description of complexes including ligand derived from the condensation of cephalixin antibiotics with sulfadiazine.

2. Materials and methods

Cephalexin monohydrate and Sulfadiazine (DSM, Spain) and all other chemicals (Merck, Germany) were utilized without more refining. Spectra of Ultraviolet-visible were registered listed on a spectrophotometer of Ultra Violet-Visible (UV-60A, Shimadzu). whilst metal contents for the complexes were calculated by technique of (A.A) atomic absorption employing spectrophotometer of atomic absorption a Shimadzu AA 620G. IR-spectra were estimated on (FTIR-8400S, Shimadzu) Spectrophotometer of Fourier Transform Infrared (4000- 400) cm^{-1} with specimens synthesized as discs of KBr. ^1H NMR Spectrum of Nuclear magnetic resonance for ligand was registered in DMSO- d_6 employing instrument of Bruker 300 MHz with (TMS) as an interior standard. The examples were listed at Al-Albeit university, Queen Mary, Jordan, Amman. Micro-analysis of Elemental for the ligand was completed on a 2400 Perkin Elmer (C.H.N.S.O). Conductivities were determined at 25°C in DMSO for 10-3M of complexes employing (conductivity meter, model 4070, Jew wary). The offered structure of molecular for the complexes was sketching by employing prog. of chem. office, 3DX (2006). Magnetic measurements were registered on an apparatus of Bruker BM6 at 25°C . Then melting points were acquired employing (Stuart Melting Point Apparatus).

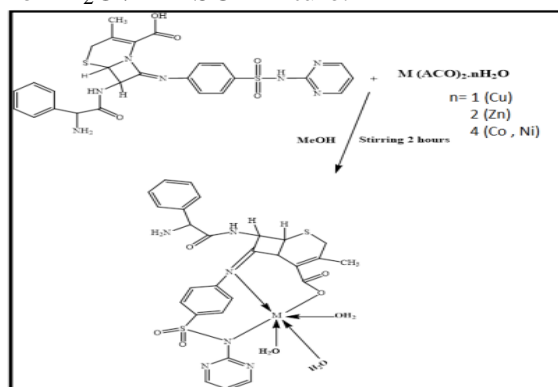
Synthesis of Schiff base

Initially, the ligand was prepared from 25 mL methanol including 0.419 g (1mmol) cephalixin and 15 mL methanol where has been dissolved in anticipation of 0.61 g (2.113mmol) sulfadiazine. So as to get the pH data at (7 – 8), 1.0 M solution of KOH was gathered and the solution was refluxed for 4hrs. The volume of the solution was decreased to semi by vaporization when an output was composed. It was cleaned with methanol after filtered and desiccated in a vacuum under anhydrous CaCl_2 at room temperature. A product was recrystallization by water-ethanol (50:50) obtain the ligand

Scheme (1): The preparation path of HL_c

Preparation of Coordination Compounds

The complexes of Ni(II), Co(II) Zn(II) and Co(II), were synthesized by the similar public way. To (0.001 mmol) of the convenient $M(\text{CHCOO})_2$ solution from metals of Ni(II), Co(II) Zn(II) and Co(II), in 20 mL of water were tardily added with stirring in 10 mL of an ethanol solution of 0.001 mmol of HL¹. To this (0.1% in methanol) of KOH solution was gathered to regulate the pH at 7–8 of the solution and the solution was then refluxed for 2 h. and product created. The complexes were isolated from the reaction as unorganized products and washed various times with ether, H₂O and MEOH and dried under reduced pressure at room temperature. They were refined by recrystallization from H₂O / DMSO mixture.



Scheme (2): The synthetic route of complexes

Antibacterial activity

In vitro technical was performed for investigating antibacterial efficacy versus the (+)ive gram bacteria as (*Staphylococcus aureus*), and (-)ive gram bacteria as (*Escherichia coli*) were applied DMSO solvent as a control, for this technicality, the concentrations of the compound in 10^{-3}M of the solvent. This method was to get the sensibility of each micro-organism to the new metal complexes by measuring the minimal inhibitory concentration (MIC) that was obtained by utilizing the Tube Dilution Method. The (MIC) of the new compounds for each bacteria was measured at the minimum concentration of the component obtained to restrain the increase of these bacteria, these tubes including diverse concentrations of the new components were brooded at 37°C for 45hr. Moreover, two of the know antibiotics (cephalexin and sulfadiazine), were gotten as standard.

Results and discussion

The complexes under investigation were isolated by refluxing in methanol $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$, $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$, $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ and $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ with the ligand. The separated complexes were insoluble in popular organic solvents and complexes were separated perspicuous in appropriate yields. They have melting temperatures more than 200°C ; they did not melt/decompose. Endeavor to made complexes of a clear-cut stoichiometry They are of diverse colours. The complexes are insoluble in popular solvents of organic such as benzene, methanol, ether dichloromethane acetonitrile, chloroform, petroleum ether and acetone and water, but soluble in DMSO and DMF. The data of molar conductance determined change from 2.12

| Compounds | Empirical Formula | (Formula wt.) | Yield % | Colour | Elemental Analyses | | | | |
|--|--|---------------|---------|--------------|-----------------------------|----------------|------------------|------------------|----------------|
| | | | | | Found (Calc.) %(calculated) | | | | |
| | | | | | C | H | N | S | M |
| [HL _C] | C ₂₆ H ₂₅ N ₇ O ₅ S ₂ | 579 | 78 | Yellow | 53.12 (53.87) | 4.02 (4.35) | 16.54 (16.92) | 10.47 (11.06) | - |
| [CoL _C (H ₂ O) ₃] | C ₂₆ H ₂₉ CoN ₇ O ₈ S ₂ | 690.61 | 80 | Redish Brown | 41.88 (45.22) | 4.13 (4.23) | 14.31 (14.20) | 9.09 (9.28) | 7.39 (8.53) |
| [Ni L _C (H ₂ O) ₃] | C ₂₆ H ₂₉ NiN ₇ O ₈ S ₂ | 690.37 | 76 | Green | 44.95 (45.23) | 4.34 (4.23) | 14.17 (14.20) | 8.89 (9.29) | 8.65 (8.50) |
| [Cu L _C (H ₂ O) ₃] | C ₂₆ H ₂₉ CuN ₇ O ₈ S ₂ | 695.23 | 73 | Dark Green | 44.17 (44.92) | 4.11 (4.20) | 10.97 (14.10) | 9.27 (9.22) | 9.30 (9.14) |
| [Zn L _C (H ₂ O) ₃] | C ₂₆ H ₂₉ ZnN ₇ O ₈ S ₂ | 697.06 | 71 | Pale brown | 44.49 (44.80) | 4.00 (4.19) | 14.27 (14.07) | 7.88 (9.20) | 9.19 (9.38) |

to 17.34 S cm² mol⁻¹ in DMSO at room temperature, suggestive the kind of non-electrolytic for the complexes. The preparation path of HL_C ligand is shown in Scheme (1).

Elemental analysis and physical Data: The compounds were presented to micro-elemental. The outcomes of micro-elemental with some physical values and molecular formulae such as color alteration and melting points of the compounds are presented in Table 1. Consequently, the universal form [ML_C(H₂O)₃] where M(II) is Ni(II), Co(II) Zn(II) and Co(II) has been specified to the complexes and at room temperature they are solids of air-stable and for a long time without decomposition. The molecular masses determined mass spectrometrically also assured the [ML_C(H₂O)₃] composition[2].

The outcomes are in better correspondence with the mentioned form of molecular. The compounds have a sharp melting point signalizes the pureness of the intended components. The alteration in color of the compounds from the standard

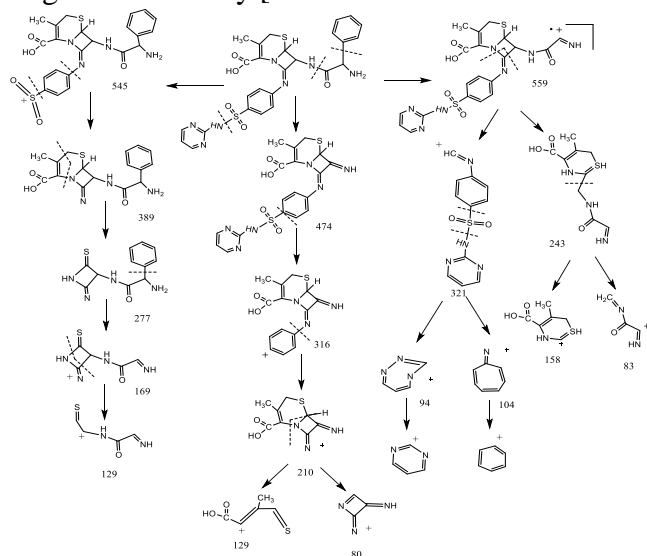
material components applied for their synthesis is the good designation of fashioning by a reaction of chemical [3]. In complexes showed a drop-down of pH data assigned to the de-protonation of ligand.

Table 1: Physical, Elemental Analyses Data and Coloures of the Metal (II) Complexes

Mass Spectrum of Ligand

The ligand spectrum displayed a peak at m/z 579 amu conformable to its peak of molecular

ion $[M^+]$ the fractions and it emphasizes the suggested molecular form of the ligand. Also the peaks of HLC at m/z 559, 545, 474, 389, 321, 316, 276, 243, 210, 169, 158, 129, 104, 94, 83 and 79 amu are the peaks assignment and proposed routes, Scheme (3). The important fragments and their chemical shifts concerned with in spectra of 1H NMR for the ligand. Their intensities supply the conception of the fragments' stability [4]



Thermal analysis

Thermal analyses for the complexes of Ni(II), Cu(II), (Zn(II) and Co(II) were achieved between 25°C - 800°C that displays almost the same manner. Determined and empirical weight lacks are similar by this analysis, an acquaintance on their characteristics, kind of final and intermediate produces of their thermal dismantling may be acquired. From curves of TGA, the weight lack was determined for the various stages and resembled those determined in theory for the referenced form founded on the products of molar conductance determinants add to macro- analyses [5].

TGA elucidated the fashioning of MO as the final output from that content of the metal may be determined and resembled with that acquired from a calculation of analytical. Thermal graphs of the hydrated complexes point out endothermic dismantling in two stages and add

to detect that the complexes are steady without solvent molecules and hydration water. The 1st stage from 140 to 220°C reign is designated to lack of molecules of chelated H₂O (Table 2). The last dismantling stage contains the entire vaporization of the ligand adds to the fashioning of MO as last produce from that content of the metal was get to be in better correspond with the values acquired from analyses of complex-metric. So, the comprehensively thermogravimetric outcomes are compatible with these complexes formula [6]. The remains acquired during the thermal dismantling of complexes are appropriate MO: CuO CoO, ZnO and NiO. The patterns of diffraction of acquired remains have resembled patterns of reference.

Table 2: Thermal decomposition compounds values

| Comps. | Temp. rang °C | Wt. loss % found (calculate) | Fragments loss | Residue % Found (calcd) |
|---|-----------------------------|------------------------------|--|-------------------------|
| [CoL _C (H ₂ O) ₃] | 145–200 200–570 > 570 | 7.5(7.6) | Loss of 3H ₂ O Loss of L metallic residue CoO | 10.4 (10.5) |
| [NiL _C (H ₂ O) ₃] | 150–210 210–580 > 580 | 7.7 (7.8) | Loss of 3H ₂ O Loss of L metallic residue NiO | 10.2 (10.3) |
| [CuL _C (H ₂ O) ₃] | 140–200 200–575 > 575 | 7.6 (7.5) | Loss of 3H ₂ O Loss of L metallic residue CuO | 10.4 (10.3) |
| [ZnL _C (H ₂ O) ₃] | 155–220 220–590 > 590 | 7.2 (7.3) | Loss of 3H ₂ O Loss of LC metallic residue ZnO | 10.6(115) |

1H -NMR

1H NMR spectrum of ligand (HLC) in DMSO-d₆ figure (5) displayed signal at 9.67 ppm which assigned To proton of OH of carboxylic group, signal at 9.0 ppm attributed To proton of NH, and a signals at 8.6 ppm which imputed to proton of azomethin group CH=N, as well as signals were appeared in range 68– ppm which assigned To proton of aromatic rings in addition To signal absorbed at 4.96 ppm was attributed

To protons of NH_2 . While a signal of proton of CH β -lactam ring appeared at 3.9 ppm [8], also a assigned of protons of CH_2 appeared at 2.8 ppm [170]. Finally was absorbed at 1.2 ppm which assigned To protons of methyl group CH_3 and as shown in the Table (3).

Table (3) shows chemical shifts of the ligand HLC

| Compound | Factional groups | δ (ppm) |
|----------|--|----------------|
| HLC | proton of OH of carboxylic group | 9.67 |
| | proton of NH | 9.0 |
| | proton of azomethin group $\text{CH}=\text{N}$ | 8.6 |
| | proton of aromatic rings | 6-8 |
| | protons of NH_2 | 4.96 |
| | proton of CH β -lactam ring | 3.9 |
| | protons of CH_2 | 2.8 |
| | protons of methyl group CH_3 | 1.2 |

FT-IR Analysis: The complexes spectrum were registered down to the FT-IR range of $400\text{--}1000\text{ cm}^{-1}$ and analogized with those of sulfadiazine and cephalixin. The complexes spectra included all the bands from the ligand and some new bands symptomatic of chelation through nitrogen and oxygen of the ligand with metal ions. The great considerable IR spectral bands are offered in Table 4. Values of the IR spectral comparison the adduced complexes with those of the un-complexed ligand supplies worthy datum about the chelation positions of the ligand. The β -lactam $\nu(\text{C}=\text{O})$ absorption show at 1753 cm^{-1} in the cephalixin spectra. The Schiff base antibiotic spectrum appears no band that may be indicated to $\nu(\text{C}=\text{O})$ of β -lactam vibration of cephalixin [9]. The non-attendance this absorption together with the occurrence of a new absorption at 1664 cm^{-1} imputed to $\nu(\text{C}=\text{N})$ vibration, is appropriate with the product being the predictable ligand. The complexes spectra display bands in the $1653\text{--}1647\text{ cm}^{-1}$ zone that can be assigned to the $\text{C}=\text{N}$ stretching vibrations of the chelated ligand (HLC), robustly referencing non- participation of this moiety in coordination. Three frequencies of the ligand at $(3218\text{--}3345)\text{ cm}^{-1}$ related to $\nu(\text{NH})$ and $\nu(\text{NH}_2)$

as yet exist in the complexes, robustly mentioning nonparticipation of these moieties in chelation [10].

Tentative frequency assignments of several distinctive absorption frequencies of ligand were made by comparing with anoth attached structures. The strong bands appeared at $(1323)\text{ cm}^{-1}$, $(1151)\text{ cm}^{-1}$ and $(943)\text{ cm}^{-1}$ were related to asymmetric $\nu_{\text{as}}(\text{SO}_2\text{--N})$ and symmetric $\nu_{\text{s}}(\text{SO}_2\text{--N})$ of the $(\text{SO}_2\text{--N})$ group and $\nu(\text{S--N})$ stretching vibration respectively appear significant changes upon complexation[11]. The first division into two frequencies in the ranges $(1340\text{--}1350)\text{ cm}^{-1}$ and $(1310\text{--}1303)\text{ cm}^{-1}$ and the second appears in the ranges $(1142\text{--}1130)\text{ cm}^{-1}$. The band at 943 cm^{-1} coinciding to $\nu(\text{S--N})$ is changed to more wavenumbers (978 cm^{-1}) upon complexation for Cu(II) , Co(II) , Ni(II) and Zn(II) complexes respectively. All these shifts mention back up the chelation of the nitrogen for sulfonamide to the center of metal. Moreover, the occurrence of new frequencies in the ranges $(490\text{--}450)\text{ cm}^{-1}$ imputed to $\nu(\text{M--N})$ stretching modes, appeared in the complexes spectra (missing in the ligand) supply reference that the metal ion might be linked with the N--SO_2 group through the atom of N [12].

Transfer in the sites of two vibrations at $(1571)\text{ cm}^{-1}$ and $(1390)\text{ cm}^{-1}$ related to asymmetric $\nu_{\text{as}}(\text{COO}^-)$ and symmetric $\nu_{\text{s}}(\text{COO}^-)$ modes of (COO^-) carboxylate moiety for ligand to lower in ranges $(1553\text{--}1548)\text{ cm}^{-1}$ and $(1375\text{--}1368)\text{ cm}^{-1}$ in the complexes [13]. This truth is moreover adduced that ligand has reacted. when the metal ion may chalet to the carboxylate (COO^-) moiety as monodentate or bidentate structure, the " $\Delta\nu$ criterion" [$\Delta\nu = \nu_{\text{asym}}(\text{COO}^-) - \nu_{\text{sym}}(\text{COO}^-)$] < 200 was utilized to calculate the chelation vibration of (COO^-) moiety related to $\nu(\text{COOH})$ in the ligand and in the complexes occurrence new ν_{as} and ν_{s} vibrations of the (COO^-) moiety designates that the ligand has reacted[14]. The $\Delta\nu$ data in the reign of $(178\text{--}169)\text{ cm}^{-1}$ in these complexes are analogous to that adduced for the complexes with bidentate $\mu^2\text{-O}$, O'' carboxylate moiety, consequently referencing the carboxylate moiety conducts as a

bidentate ligand. The residual carboxylate frequencies, namely $\rho(\text{COO})$, $\omega(\text{COO})$ and $\gamma(\text{COO})$, formerly at 538 cm^{-1} , 612 cm^{-1} and 794 cm^{-1} , respectively, also change as a result of

values a reference that the carboxylate-O and N-SO₂ moieties with the bidentate structure have participated in chelation in the complexes and that the ligand conducts as a tri-dentate mono-

| Compound | $\nu(\text{NH})$ $\nu(\text{NH}_2)$ | $\nu(\text{OH})$ $\nu(\text{OH}-(\text{H}_2\text{O}))$ | $\nu(\text{C}=\text{N})$ imine | $\nu(\text{C}=\text{O})_{\text{asym}}$ | $\text{C}=\text{O})_{\text{sy}}$ $\nu(\text{m})$ | $\Delta\nu$ | $\nu \text{O}_2-(\text{S})$ $\text{N})_{\text{asym}}$ sym | SO_2- N_{sym} | ν (S O ₂) | $\nu_r(\text{H}_2\text{O})$ $\nu_w(\text{H}_2\text{O})$ | ν (M- N) ν (M- O) |
|--|--|---|-----------------------------------|--|---|-------------|--|---|------------------------------------|--|--|
| [HL _C] | 3218-3345 | 3352 | 1664 | 1571 | 1390 | - | 1323 | 1151 | 93 9 | - | - |
| [CoL _C (H ₂ O) ₃] | 3220-3343 | - 3428 | 1649 | 1550 | 1369 | 174 | 1346 1310 | 1140 | 98 4 | 876 547 | 480 430 |
| [Ni L _C (H ₂ O) ₃] | 3217-3340 | - 3422 | 1647 | 1548 | 1373 | 169 | 1342 1308 | 1137 | 97 8 | 894 550 | 476 447 |
| [CuL _C (H ₂ O) ₃] | 3220-3343 | - 3431 | 1650 | 1553 | 1375 | 178 | 1350 1305 | 1142 | 98 2 | 848 552 | 463 443 |
| [ZnL _C (H ₂ O) ₃] | 3219-3340 | - 3439 | 1253 | 1548 | 1376 | 172 | 1348 1303 | 1133 | 98 0 | 890 545 | 450 437 |

coordination. The frequencies in the $430\text{--}447\text{ cm}^{-1}$ range designated in the complexes are tentatively designated to $\nu(\text{M-O})$ vibrations. Also, the complexes appear mods in the regions $(1555\text{--}1427)\text{ cm}^{-1}$, $(1110\text{--}1078)\text{ cm}^{-1}$ and $(745\text{--}726)\text{ cm}^{-1}$ that may be designated to phenyl ring mods[15]. Medium intensity frequency showing in the range $(2848\text{--}$

Table (4): IR spectral data of the synthesized compounds

2950 cm^{-1} coincides with $\nu(\text{C-H})$ aliphatic, while $\nu(\text{C-H})$ aromatic stretches show in the

range $(3104\text{--}3021)\text{ cm}^{-1}$. Broad frequencies centered at $(3439\text{--}3422)\text{ cm}^{-1}$ for the complexes may be designated to the $\nu(\text{OH})$ stretch of chelated molecules of H₂O. The coordinated water exhibited, in addition to these modes, the $\nu_r(\text{H}_2\text{O})$, rocking near $848\text{--}894\text{ cm}^{-1}$, $\nu_w(\text{H}_2\text{O})$, wagging near $545\text{--}552\text{ cm}^{-1}$. These overall

Magnetic is the magnetization grade of a material in restraint to a magnet. The technique determines the Boltzmann equation of all energy grades. Rectified magnetic moments were determined to utilize constants of Pascal from the molar magnetic sensitivity data. The quantities of the magnetic moments for the complexes of paramagnetic fall within the scopes connected with high spin (spin-free) ions in octahedral arrangements. The magnetic moment for cobalt(II) complex $5.10\text{ }\mu_{\text{eff}}\text{ B}$ that is higher than the spin-only values and a normal data of a d^7 arrangement with 3 unpaired electrons signaling a quartet state in an Oh system around the metal, as resembled with the adduced data for Oh complexes of cobalt(II) $(4.7\text{--}5.2\text{ }\mu_{\text{eff}}\text{ B})$ [16]. The variance between values of calculated and measured consequences to spin-orbital coupling. A magnetic moment of the nickel(II) complex of $3.36\text{ }\mu_{\text{eff}}\text{ B}$ distinctive of 2 unpaired electrons and higher than the spin-only data, potentially related to the orbital involvement consequence from the shift of an electron from the $dx^2\text{--}y^2$ orbital to the d_{xy} orbital. Therefore the complex supposedly has a

anionic NO₂ coordinating agent [16].

Magnetic properties
Sensitivity of

distorted octahedral system. A magnetic moment for copper (II) complexes of $1.88 \mu_{\text{eff}} \text{ B}$ that is lower than the spin-only values and a normal data of a d^9 arrangement with 1 unpaired electrons signaling a quartet state in an Oh system around the metal, as resembled with the adduced data for Oh complexes of copper (II) ($1.9\text{--}2.2$) $\mu_{\text{eff}} \text{ B}$ at room temperature is usually noted in any case mononuclear copper (II) complexes system. Zinc(II) complex is diamagnetic as predictable for the d^{10} system[17].

Electronic spectra

A long-range UV–Vis study was investigated to confirm the stability of new complexes in the DMSO solution. Compared with the ligand, it is considered to observe that the absorption wavelengths of new complexes barely diverse, significance that the complexes were stable in the DMSO solution. The UV–Vis spectra of the ligand in 10^{-3} M DMSO solution observed three broad peaks at 237 and 300 nm. The previous two absorptions are related to the $\pi \rightarrow \pi$ and $n \rightarrow \pi^*$ transformations within ring of the aromatic and the chromophore $>\text{C}=\text{N}-$ attribute to the chelation of N-azomethine to the metal atom. This peak changes lightly to the higher energy range in the complexes spectra attributed to the polarization within the chromophore $>\text{C}=\text{N}$ happened by the interaction of electron for ligand-metal [189]. The complexes spectra appear in which the peaks around 400–800 nm are related to charge transfer of ligand to metal and d–d transmission peaks of the metal in the complexes. The nickel(II) complex spectrum shows two main peaks maxima, at 428 and 489 nm related to d-d bands that can be designated, an observance that the immediate chelation field of the metal is Oh symmetry, to the transmissions $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{P})$ and $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{F})$ respectively. The copper (II) complex spectrum appears a broad absorption concentrated at 646nm designated to the $^2\text{E}_g \rightarrow ^2\text{T}_{2g}$ transmission in a distorted Oh symmetry around the copper (II) ion. The Zn(II) complex spectrum does not include d \rightarrow d transmissions but shows only one band at 488 cm^{-1} , that can be designated to an $\text{M} \rightarrow \text{L}$ charge transfer.

Coordination sites

The chemistry of chelation for antibiotics with metal ions such as cefepime, ceftriaxone, ceftazidime and cefotaxime has been adduced. In our study, the ligand of Schiff base-antibiotics including both sulfadiazine and cephalexin has several atoms of possibility which could be implicated in chelation granter with the metal ions forming complexes, but, assigned to steric hindrances, the ligand may supply a most of three atoms of donor to anyone center of metal [23]. It shows that each metal ion locates from the values in a distorted octahedron chelation sphere and the Schiff base would act as an efficient pseudo-encapsulating ligand, with O-carboxylate moiety with bi-dentate system and N-sulfonamide, perhaps restricted to ions of the octahedral. So, metal ions in formula complexes of $[\text{ML}_\text{C}(\text{H}_2\text{O})_3]$ containing $3\text{H}_2\text{O}$ molecules at the headers of an octahedron are hexa-chalet[24]. The same linking mode, out of a distorted trigonal system of the imido- nitrogen, was noticed with sulfadiazine when modes mononuclear complexes of Zn(II), Ag(I), Hg(II) and Cu(II), whose crystal compositions were calculated. We have tried to expand single crystals of the metal coordinates but in no status have we had any prosperity, attributed to their insolubility in widespread solvents of organic. The complexes only shape unorganized materials as detected by their XRD manners [25]. So far there are no crystals structures for complexes including a cephalexin-based Schiff base have been adduced. These researches appear an involvement in outlook analyses of crystallographic, which are intricate by the awkwardness in giving crystals of X-ray quality for complexes derived from cephalosporin. Though complexes crystal structures are not recognized, the chelation medium of mononuclear may temporarily be suggested [26].

Antibacterial efficacy

In vitro biological efficacies were determined from the diameter of obvious discouraging scopes reasoned by specimens under the conformable empirical stipulations and versus the same bacteria. As per the color estimate, the complexes stay undamaged in antimicrobial screening. So as illustrate the role of DMSO in any contributing and $M(OCA)_2$ salts in the antimicrobial testing, independent researches were investigated with the free metal salt and DMSO solutions alone and they have been gotten that they have no impact on the increase of any bacteria given[27].

The biological efficacies of compounds were screened on with bacteria of *E. coli* and *S. aureus* and resembled sulfadiazine and cephalexin applied as standards. As predictable, the ligand is sufficiently more toxic with *S. aureus* than *E. coli* bacteria, which can be attributed to the various cell wall frameworks of the screened bacteria, while the indication components sulfadiazine and cephalexin appear nearly equal efficacy versus both chains checked [28].

The rate outcomes are displayed in Table 5, where maybe estimated that compounds have various conduct resembled standard antibiotics with the same bacteria. So: (1) $Cu(II)$ and $Zn(II)$ complexes were established to have more efficacy than cephalexin and sulfadiazine versus the bacteria strains elaborated under the screen stipulations, appearing which they have a better efficacy as bactericides. (2) The biological efficacy of $Ni(II)$ and $Co(II)$ complexes appear to be lower toxic than the cephalexin and sulfadiazine and ligand[29]. Approbating to the theory of Tweedy, coordination could promote the lipophilic description of the focal metal atom, which thereafter prefers its penetration through the layers of lipid of the cell velum and preventing the metal linking positions on bacteria enzymes. In our study, the in vitro biological efficacies explained that complexes of $Zn(II)$ and $Cu(II)$ have greater biological efficacy in rapprochement with that ligand[30]. But in contradiction with these outcomes, ligand displayed highly biological efficacy versus the screened chains liken to the complexes of $Ni(II)$

and $Co(II)$. Thus, biological efficacy must be affected by other agents beyond the permeability of the membrane [31].

The aims for antibiotics have β -lactam are cell wall- proteins linking synthesizing enzymes (PBPs) penicillin that are got as both cytoplasmic enzymes and membrane- restricted which catalyze reactions of cross-linking. The antibiotics have β -lactam; intervene by linking covalently with cell wall synthesis to the position of the PBPs catalytic. All bacteria almost have PBPs, but they differ from categories to categories vary in affinity, molecular weight, an amount for enzymatic function (e.g., endopeptidase, carboxypeptidase or transpeptidase) and β -lactam antibiotics [32]. The outcomes may be comprehended deeming that the enzyme supposedly avails foremost to contract moieties of the substrate or catalytic in the appropriate sites and is potential to anticipate that ligand- metal complexes can shift the arrangement obtained in reactions of solvolytic on a surface of the enzyme. The required consequences can highlight that the efficacy of the compound is most supposedly regarded to their

(morphological modification, counting on the nature and the complexes size and restrictions of the geometrical concluded by intra-molecular hydrogen bonds. So, the bactericidal efficacy of cephalexin Schiff base and its complexes liken to cephalexin antibacterial efficacy can consider a various mechanistic passageway by that they react with the PBP energetic positions to realize fashioning of a steady adduct of PBP-inhibitor. The resistance level to β -lactam complexes is calculated by kinetic features of nature and amount [33].

Conclusion

In this study, we attributed chelation chemistry of Schiff base as new ligand and its complexes with $Co(II)$, $Ni(II)$, (Zn) and $Cu(II)$ which have been derived from cephalexin and sulfadiazine (HL_c), effectually in an medium of an alcoholic suspension utilizing alkali

catalyst with good yields under and characterized by diverse spectral and physicochemical analyses. The chelation to metal happens via the carboxylate-O and N-SO₂ moieties with bi-dentate structure. The Schiff base solubility and its metal complexes in H₂O and widespread solvents of organic on complexation are minimized. The ¹H-NMR values reference that the ligand deprotonated after complexation. The thermo-gravimetric data displayed the degeneration paradigm of the complexes. Also, thermal values elaborated on the complexes assisted to distinguish the complexes. The un-complexed cephalixin and the sulfadiazine were

| Compound | Zone of inhibition (mm) in doses 400 µg /disc | |
|--|---|-----------------------|
| | E.C. Escherichia coli | Staphylococcus aureus |
| cephalexin | 12 | 14 |
| Sulfadiazine | 7 | 8 |
| [HLC] | 15 | 14 |
| [CoLC(H ₂ O) ₃] | 5 | 6 |
| [NiLC(H ₂ O) ₃] | 4 | 5 |
| [CuLC(H ₂ O) ₃] | 17 | 19 |
| [ZnLC(H ₂ O) ₃] | 15 | 20 |

mentions to have less bactericidal efficacy than Zn (II) and Cu (II) complexes versus strains of the bacteria, appearing that they have good activity as bactericides. The complexes of Ni(II) and Co(II) displayed to be minimal toxic than the ligand and two allusion drugs. Apart from membrane permeability, at most biological efficacy of ligand derived from cephalixin and its metal complexes counts on the metal ion and the kind of bacteria.

Table (5): Electronic spectral data of the ligand and its metal complexes

| Compound | μ_{eff} | λ_{max} nm | ϵ cm ² mol ⁻¹ | λ nm | ν cm ⁻¹ | Transition | |
|--|--------------------|---------------------------|--|--------------|------------------------|---------------------------------|-------------|
| [HLC] | - | 2.12 | | 237 | 42194 | ($\pi \rightarrow \pi^*$) | |
| | | | | 301 | 33222 | ($n \rightarrow \pi^*$) | |
| [CoLC(H ₂ O) ₃] | 5.1 | 11.90 | | 236 | 42372 | L.F | Octahedra 1 |
| | | | | 300 | 33333 | | |
| | | | | 350 | 28571 | C.T | |
| [NiLC(H ₂ O) ₃] | 2.9 | 14.43 | | 237 | 42194 | L.F | Octahedra 1 |
| | | | | 302 | 33112 | | |
| | | | | 351 | 28490 | C.T | |
| | | | | 429 | 23310 | $^3A_2g \rightarrow ^3T_1g(P)$ | |
| | | | | 489 | 20449 | $^3A_2g \rightarrow ^3T_1g$ | |
| [CuLC(H ₂ O) ₃] | 1.71 | 17.34 | | 236 | 42372 | L.F | Octahedra 1 |
| | | | | 301 | 33222 | | |
| | | | | 350 | 28571 | C.T | |
| | | | | 646 | 15479 | $^2T_{2g} \rightarrow ^2E_{2g}$ | |
| [ZnLC(H ₂ O) ₃] | - | 16.65 | | 238 | 42016 | L.F | Octahedra 1 |
| | | | | 300 | 33333 | | |
| | | | | 355 | 28169 | | |

Table (6): of HL_C Antibacterial activity of the Compounds

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Figure (1): FT-IR spectrum of [HL_C]

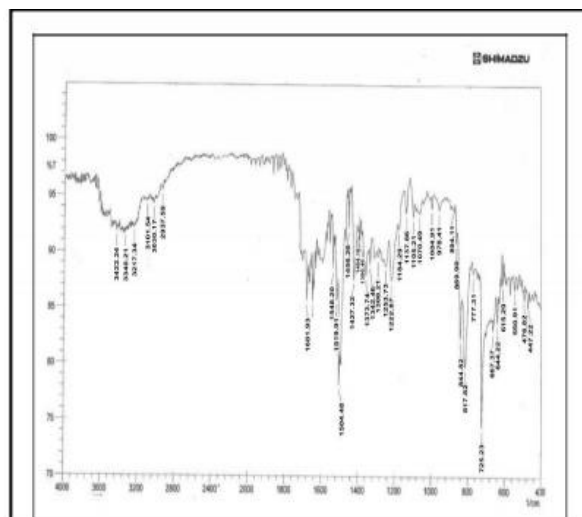


Figure (4): U.V-Vis spectrum of [Cu L_C(H₂O)₃]

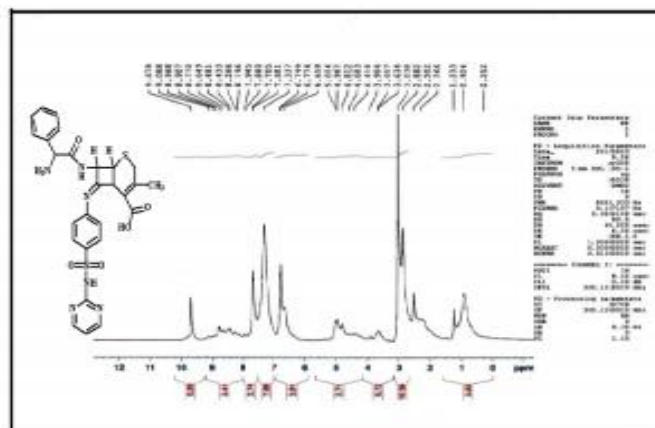


Figure (5): ¹H NMR spectrum of the ligand (HL_C) in DMSO-d₆

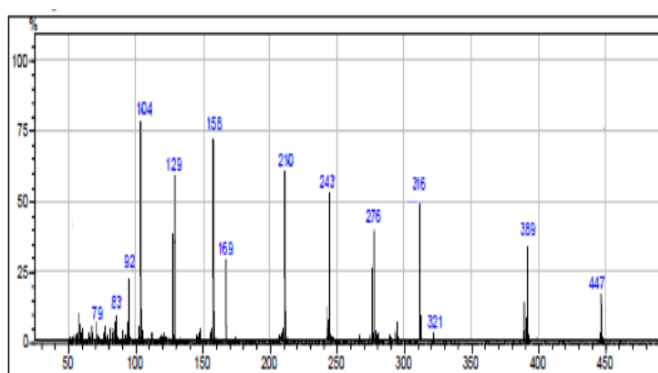


Figure (6): ES(+) mass spectrum

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