Article

Schiff bases derived from drug and their metal Complexes: A review on the history, synthesis, characterization, and applications

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Abstract

The scientific community has given drug-derived Schiff bases metal complexes a great deal of attention due to their special qualities and range of uses in industries, biology, and medicine. These complexes reveal a variety of biological actions, such as antioxidant, antibacterial , cytostatic, antiviral, and anticancer effects. They also have remarkable catalytic properties for a variety of chemicals. With a focus on their biological and catalysis uses, this review offers a thorough analysis of the chemistry, synthesis, history, and uses of numerous drug-derived Schiff bases ligand-based metal complexes. Researchers and professionals working in the subject of inorganic chemistry will find the review to be a significant resource as it outlines the present state of the study and anticipated developments in the field of study.

Keyword: - Shiff Base, Drug, History, Applications

Introduction

When aromatic or aliphatic amines condense with aromatic or aldehydes that are aliphatic or ketones, carbon-nitrogen double bonds (C=N) are formed. These compounds are known as schiff bases. Schiff compounds and related complexes are highly interesting for research since they have several uses in the pharmaceutical and medical industries. Schiff bases are regarded as model compounds and actively contribute to the advancement of coordination chemistry because they form complexes that are stable with transition elements and participate in the chelation process through azomethine linkage. An acid, base, heat, or both can accelerate the reversible process that produces a Schiff base from ketones or aldehydes.[1]. Synthetic organic chemists continue to be interested in creating new molecules that contain the azetidinone component due to the many biological actions of -lactam derivatives.H. Staudinger created e -lactams for the first time in 1907 ,cycloaddition procedure to combine diphenylketene, benzaldehyde, and Schiff base from aniline. Even today, one of the most popular processes for creating azetidinone rings and producing its numerous derivatives is the Staudinger reaction.[2]

Antibiotic: The material that has the ability to inhibit or eradicate other microorganisms at low concentrations; it could also be an active component of antimicrobials, a broad class of antibacterial agents used to treat bacterial infections; or it could be semisynthetic, meaning partially synthesized through a chemical process, or it could be a product that is similar but fully synthesized

(synthetic). However, in everyday medical practice, non-antibiotic antibiotics (such as sulfonamides and antiseptics) are entirely synthetic, while antibiotics (such as penicillin) are naturally created (by an organism that fights the other). The word "antibiotic" can sometimes be used to describe any drug used to combat microorganisms.

The most frequently used cephalosporin antibiotic of the first generation, Cephalexin (INN) or Cefalexin, has been used as a penicillin substitute for infections caused by naturally occurring enterococci and staphylococci. Cephalexin works well against neighboring genes and is a useful treatment for streptococcal pharyngitis. There have been indications that the nucleus of cephalexin has antifungal and antibacterial qualities. Cephalexin is useful in treating infections of the joints, skin, teeth, soft tissues of the respiratory system, bones, and urinary tract. From Levin's classification, cephalexin is used to treat infections (from Klebsiella, staphylococcus, and penicillin-resistant species), respiratory infections (infected and acute bronchitis), acute and chronic infections of the nose, throat, ears, and urinary tract, and sulfonamides are rarely reported. begin taking cephalexin right away, with one non-fatal situation after [3].

Schiff bases are chemical compounds produced when amines combine with aldehydes or ketones. These compounds possess a wide range of biological activities, such as anti-inflammatory, anti-bacterial, anti-fungal, antiviral, and antioxidant actions. Their main application is in the industrial sector. Most of these substances have better catalytic activity. Since Schiff bases mix to form compounds with the metal atoms, they are considered the most versatile ligands. The reason these molecules are so easy to assemble is because they are known as preferred ligands. The majority of these compounds are metallic complexes of copper, zinc, and cadmium. Free radicals are scavengers that Schiff bases and their metallic complexes use to shield living things from the damaging effects of these radicals.

The extensive study of Schiff bases that has been conducted recently has grown into its own field of study within chemistry. Although these compounds have been thoroughly investigated, further study is still required to fully understand their antioxidant potential. In this study, we look at a number of the critical antioxidant roles played by Schiff bases and the synthesis of these bases. We also investigate the impact of some of the most important Schiff base metallic complexes on living organisms. The present work will help provide the groundwork for future investigations into Schiff bases in order to produce high-grade antioxidant molecules and define Schiff bases with regard to antioxidants [4].

Over time, the effectiveness of medicines against Gram-negative and Gram-positive bacteria has significantly decreased due to the alarming development in antibiotic resistance. Therefore, there has always been an imperative need to synthesize innovative compounds with unique mechanisms of action and prospective fields of activity. Innovative medicines based on metals have been developed with the aid of inorganic molecules, especially metal complexes. Isoniazid INH, or isonicotinic acid hydrazide, has long been the first-choice anti-tuberculosis (TB) drug used to cure infection of TB, along with a few other drugs. Unfortunately, since individuals solely depend on this drug, the rate of consumption has been steadily rising over time. Considering that microorganisms resistant to isoniazid are getting same for the long-term extensive use and even misuse, thus it is necessary to

create new medications that have significant activity in a variety of biological areas and have techniques of action beside having anti-tuberculosis capabilities.

Isoniazid derivatives and their metal complexes, especially medicinal inorganic metal complexes, have been considered innovative drugs due to their antimicrobial properties, which include the capacity to bind DNA and exhibit cytotoxic, antiviral, antifungal, and antitubercular properties. The biological activities of several isoniazid-generated metal complexes and their hydrazones—which are more or less effective against microorganisms—are compared in this review. It has been found that INH possesses some quite potent antibacterial qualities [5].

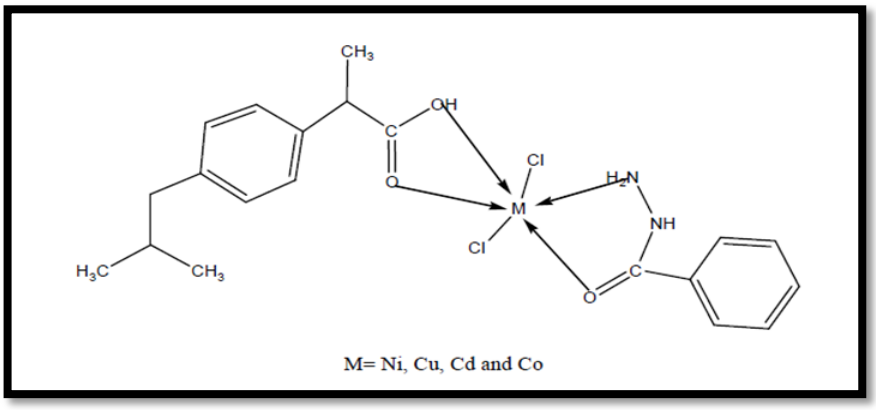


Figure (1): Structure of [Ni (ISO)(IBR)Cl_2], [Co (ISO)(IBR)Cl_2], [Cd (ISO)(IBR)Cl_2] complexes

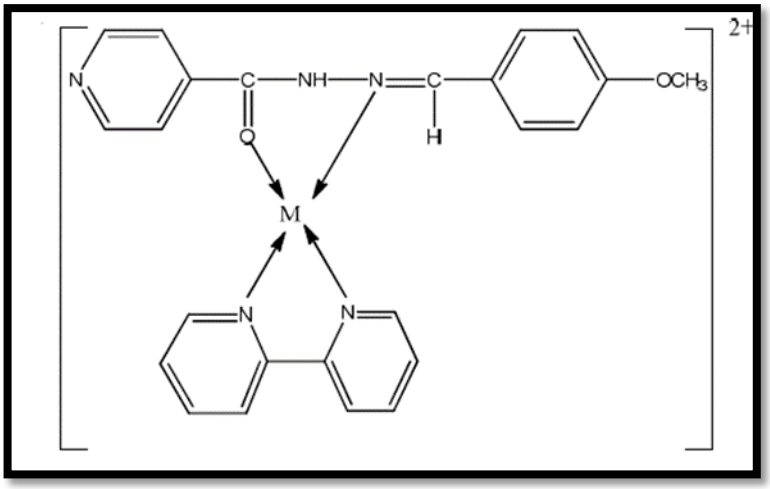


Figure (2): Structure of mixed ligand complexes (where, M= Cu(II) and Ni(II)

Ahmed Abubakar Abdullahi and others Under normal circumstances, a Schiff base ligand was produced via the reaction of 2-aminophenol with benzophenone. $NiCl_2$.6H2O and the Schiff base ligand combined to create a highly hydrated, ash-colored complex that is very thermostable. The characterization was done using both chemical and physical techniques, such as FT-IR, molar conductivity, melting point, and solubility. The results demonstrated the synthesized compounds' solubility in a range of solvents.

Calculations indicate that 2.8% of the crystallization contained water, which is consistent with 1 water molecule. The complex's claimed molar conductance of 2.55 ohm-1 cm2mol-1 proved it is not an electrolyte when subjected to conductivity tests. The ligand's FT-IR spectra shows a band at 1684.88 cm-1 that has moved to a higher frequency and is attributed to νC=N. inside the building complex. This shifting demonstrates how the ligand binds to the Ni $^{(II)}$ ion via the azomethine compound's nitrogen. It was possible to express the complex as [NiL_2] Figure (3) (by spectral analysis.H_2O. The ligand was thought to have a four-coordinate square planar form and function as a monoanionic bidentate ligand, with the phenol oxygen (O) and azomethine nitrogen (N) serving as the coordination sites. [6]

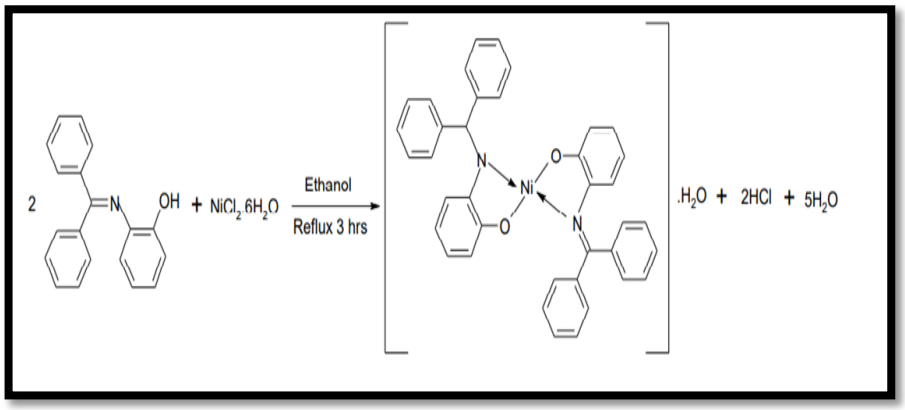


Figure (3): Synthesis of Ni $^{(II)}$ Complex of Benzophenone-2-Aminophenol Schiff Base

Garba, Hussaini, and etal. (2020) This work involved the synthesis and characterization of Mn (II), Fe (III), Co (II), and Ni (II) Metal (II) Complexes Figure (4) with Schiff base ligand derived from Trimethoprim and Cyclohexanone. Elements analysis, conductivity, melting point estimation, UV/Vis and Fourier transform infrared, 1 H-NMR, and solubility were among the many physic-chemical techniques used. For each of the complexes, a six coordinated octahedral geometry has been proposed based on these characterizations.

A pathogenic microbiological isolate was used to assess the antibacterial activity of the Schiff base ligand and its complexes, and the results were compared to the parent drug. The following pattern was shown by the antibacterial activity test results: parent medications > Schiff base ligands > metal compounds. This suggests possible wide-spectrum antibiotics. Additional computational simulations revealed that the trend in the complexes' antibacterial capabilities is due to the M-Cl bond. [7]

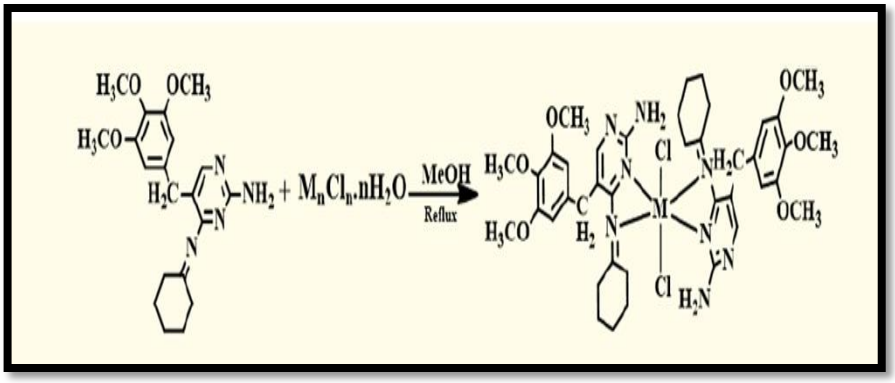


Figure (4): Synthesizing M = Ni (II), Co (II), Mn (II) and Fe (III) and n = 1 - 6.

2020 saw the discovery of a novel beta-lactam at Schiff Base (Sara R. Fisal, Adel S. Orabi, and Abbas M. Abbas). Co(II), Ni(II), Cu(II), Eu(III), and Gd(III) pure complexes of ampicillin acetylacetone Schiff base (HAA) were also produced. Melting point, solvent solubility, conductivity of 0.001 M in DMSO, mass spectra, FTIR, UV-Vis, fluorescence, 1HNMR, DTA, TGA, magnetic susceptibility, X-ray, and AAS are among the properties of the found compounds. The information gathered shows that the target molecules [Co (AA)(H2O)2] are produced.Ni(AA)(H2O)2.Cl.4H2O, [Cu(AA)] and NO3.2H2OEu(AA)(H2O)Cl, Cl2.6H2Ogd(AA)(H2O)(NO3), and Co Cl2.6H2 Ni ONO3.2H2O. and supplied the Oh configuration. Figure (5) .Conversely, Cu provided the square planar form. The crystal field parameters of the target complexes were computed and discussed. Molecular mechanics, molecular modeling, and DFT calculations were performed on the generated compounds. Investigation of x-ray demonstrates the behavior of nanoparticle of the Cu-AA combination with an orthorhombic structure. To study produced compounds with DNA moiety, interactions between spectrometric titration and fluorescence spectroscopy were employed. The disc diffusion method was used to investigate the antibacterial characteristics of the synthesized compounds. Ampicillin did not cause as much effect as HAA and Cu-AA. The FabH protein from Escherichia coli (PDB code: 1HNJ) was utilized in the docking process. Analysis and comparison of the obtained binding energy were done with reference to in vitro tests.[8]

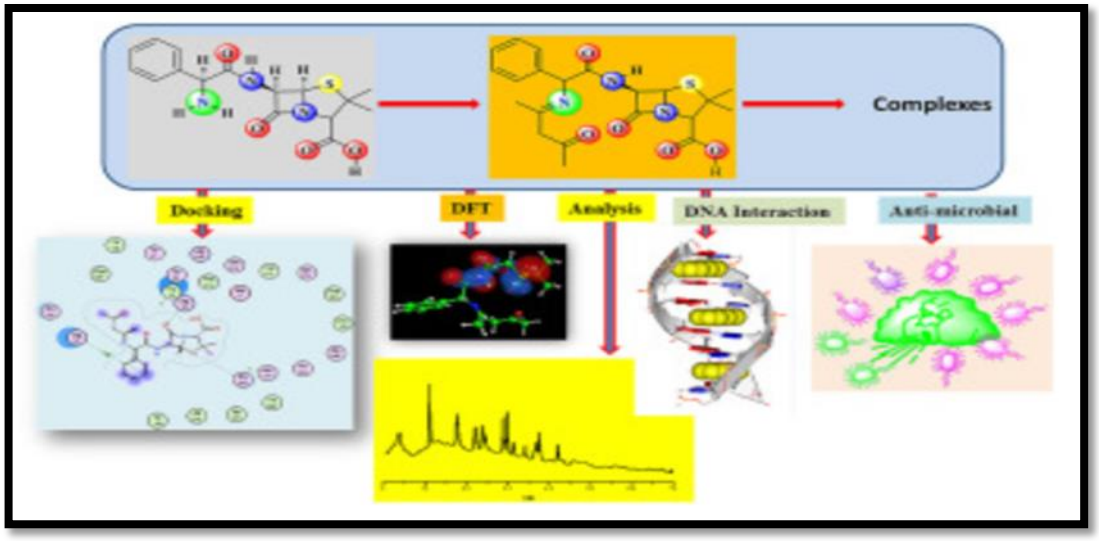


Figure (5): structure complexes from Schiff base

Sahar, S.H and et.al novel ligand synthesis, methyl -6- [2- (diphenyl methylene)amino)[2 [4-hydroxyphenyl] acetamido] -2,2 -dimethyl -5- oxo- 1- thia -4- azabicyclo [3.2.1] hebtan- 3-carboxylate (L) and created fresh complexes with the metal ions cobalt, nickel, copper, and zinc Figure(6) . Different techniques, including FT-IR, magnetic moment, UV-Vis,elemental microanalyses (C.H.N), atomic absorption, and molar-conductance, have been used to analyze the compounds. With the exception of Co complexes, which had a tetrahedral geometry. TThe analysis of the spectrum unequivocally shows that the octahedral geometry of the metal center moieties and the total complexes generated as monomeric structure are two-coordinated. Using the Hyper Chem-8.0.7 program, a geometric shape is suggested after (H°f), (Eb), dipole moment, and FT-IR frequencies have been calculated in gas phase. The bioactivity of the compounds has also been investigated. both antibacterial and antifungal. Additionally, one kind of fungal species, Candida albicans (5 mM, 10 mM), and two doses of the gram-positive bacteria, Staphylococcus aureus and Escherichia coli (5 mM, 10 mM), were introduced. In vitro investigations of cobalt, nickel, and copper complexes have shown an inhibitory activity almost identical to that of the ligand, with the exception of the zinc complexes, which showed a lower level of inhibition than other compounds (2021) [9].

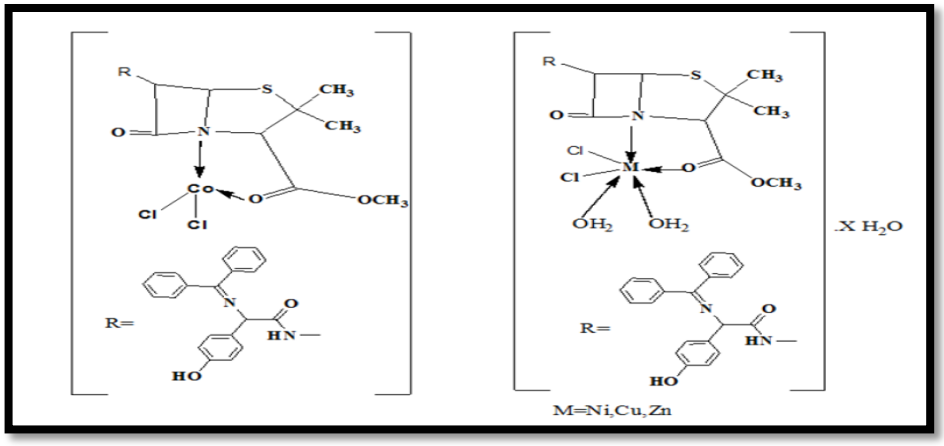


Figure (6): Geometries of complexes

Zaid .M.A: The novel tridentate ligand of Schiff base is produced when cephalexin and sulfadiazine antibiotics react with Cu(II), Co(II), Ni(II), and Zn(II) ions. Its general formula is [MLc(H2O)3] Figure (7), where L = (C26H25N7O5S2). The compounds have been represented by 1H-NMR, UV, mass, FT-IR, and predictions for molar conductivity, magnetic sensitivity, macro-, and TGA studies. Each medication's in vitro efficacy against 2 (+)ive gram and 2 (-)ive gram bacteria is made public. The [NiLc(H2O)3] complex seemed to be more efficient than the free [HLc].

The molar conductance and given analytical results demonstrate that the ligand functions as a tridentate NNO coordinating in the mono complexes. The synthesis of the complexes of Ni(II), Co(II), Zn(II), and Co(II) the same public avenue. Ten mL of an ethanol solution containing 0.001 mmol of HL1 were slowly added while stirring to (0.001 mmol) of the handy M(CHCOO)2 solution made from metals Ni(II), Co(II), Zn(II), and Co(II) in 20 mL of water.

KOH solution was added to this (0.1% in methanol) to maintain the solution's pH at 7-8, and the mixture was then refluxed for 2 hours.[10]

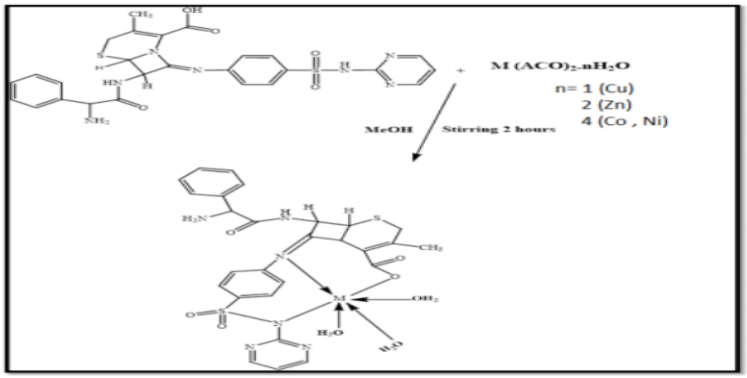


Figure (7): The synthetic route of complexes

Ibtisam. M. Ali et.al. The production of the transition metal ions Fe (II), Cu (II), and Ni (II) in a variety of complexes is accomplished by using this novel ligand (HL). Numerous techniques, including FT-IR, UV-visible, mass spectroscopy, atomic absorption, magnetic moment, and molar

conductivity, are used to investigate the characteristics of these complexes. vessel base A novel Azo-azomethine ligand (HL) "(Z)-3-((3-hydroxybenzylidene) amino) phenol"3, 3 dimethyl-6, oxo-2, thiabicyclo [3.2.0] heptane-4-carboxylic acid" has been created by the reaction of "(Z)-3-((3-hydroxybenzylidene) amino) methyl) phenyl) diazenyl)." with 6-amino pencillanic acid. The ligand (HL) is identified by 1H-NMR, 13 C-NMR, mass spectrometry, CHNs, and FT-IR. The complexes produced by each of these techniques have a 1:2 (M: L) stoichiometry. When sp3d2, d2sp3 hybridization occurs, the azo-azomethine ligand (HL) functions as a tri-dentate ligand to create complexes with an octahedral structure Figure (8). The biological action of these novel ligands and complexes is being examined [11].

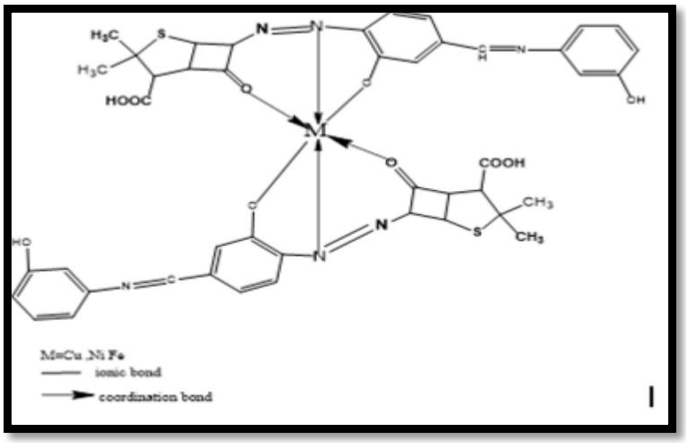


Figure (8): The suggested prepared complexes of(L)

By condensing the ligands in methanol at a 1:1:1 molar ratio operation, Schiff base ligands were created (Figure 9). Co, Cu, Mn, and Fe reacted with the Schiff base and ampicillin to form the transition metal (II) complexes Figure 10. FTIR, melting temperatures, electronic spectra, solubility, and molar conductance were then used to examine them. The complexes' in vitro antibacterial activity was evaluated against 4 bacterial strains: gram-positive (*Staphylococcus pyogenes* and *staphylococcus aureus*) and gram-negative (*Escherichia coli* and *salmonella typhi*). The complexes have a good yield of formation, a range of color colors, and acute melting points. The ligand's HC=N group stretching vibrations of the azomethine produce a new band in the HL's IR spectra at (1651) cm-1; four complexes in this band—[Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB), [Mn(Ampi)(3AMP)Cl], and [Fe(Ampi)(3AMPB)]—have been assigned lower frequencies (1651, 1621, 1651, and 1627 cm-1) during complexation. The coordination of the oxygen atom of the -Lactam group is responsible for the stretching vibration at (1688) cm-1, as demonstrated by the complexes' lowering of the overlap band to a lower frequency at (1370-1425) cm-1.

For compounds of Co, Cu, Mn, and Fe, the band of (525), (526), (524), and (526) cm-1 attributed to (M-O) shows that the oxygen of the ligand's –Lactam group and the carbocyclic oxygen are involved in coordination with metalions. The bands at (659), (669), (660), and (698) cm-1 were found to have their sources in the molecules Co, Cu, Mn, and Fe, in that order. This could mean that nitrogen and metal ions are coordinating. All the complexes appear to have octahedral and tetrahedral geometry based on electronic spectrum data. The molar conductivity indicates that all of the generated

complexes are non-electrolytes and soluble in protic solvents such as methanol and ethanol. In vitro antibacterial tests against the examined pathogens indicated the potential antibacterial activity of Schiff base and its metal complexes (Pindiga Nasiru Y) [12].

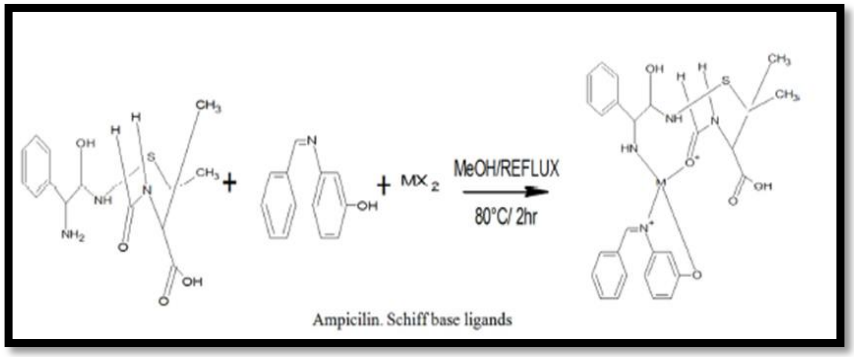


Figure (9) : Synthesis of Schiff base, ampicillin and metal(II)complexes

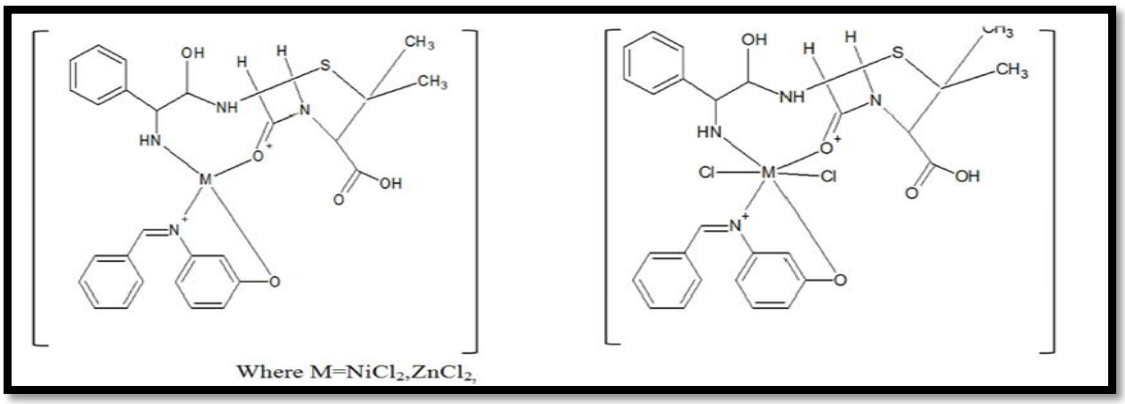


Figure (10): Proposed structure of metal (II) complexes

Khlood, S., Abou Melha et al : Multiple spectrum techniques have been used to characterize N-allyl-2-(2-oxoacenaphthylen-1(2H)-ylidene) hydrazine-1-carbothioamide, a recently synthesized derivative of Schiff's base. It formed 1:1 (M:L) complexes upon contact with the acetates of Co (II), Ni (II), and Zn (II). The keto-thione form of the free ligand was identified by the -e IR and NMR spectra. It exhibited neutral bidentate mode via N1 atom and neutral tridentate behavior via O atom when chelating with Co (II) and Ni (II). The octahedral Figure (11) of all isolated chemicals.

The existence of coordinated water molecules and the suggested formula were confirmed by thermal gravimetric testing. The metal complexes' X-ray diffraction (XRD) patterns show that Ni(II) and Co(II) are both amorphous, whereas Zn(II) has monoclinic crystallinity with an average size of 9.10 nm. The suggested structures were confirmed by DFT modeling of the ligand and complexes. For the ligand complexes with HAAT made of Zn(II), Ni(II), and Co(II), the estimated HOMO-LUMO energy gap, or EH-L, ranged from 1.96-2.49 eV. With 88.6 and 88.5 percent, respectively, the ligand and Zn(II) complexes displayed greater antioxidant activity than the other complexes. Therefore, the anticancer effectiveness of the produced compounds was assessed using the hepatocellular carcinoma

cell line (HepG2). The Zn(II) complex and HAAT both exhibited extremely considerable activity, with IC50 values of 6.39 0.18 M and 6.45 0.25 M, respectively (2021) [13].

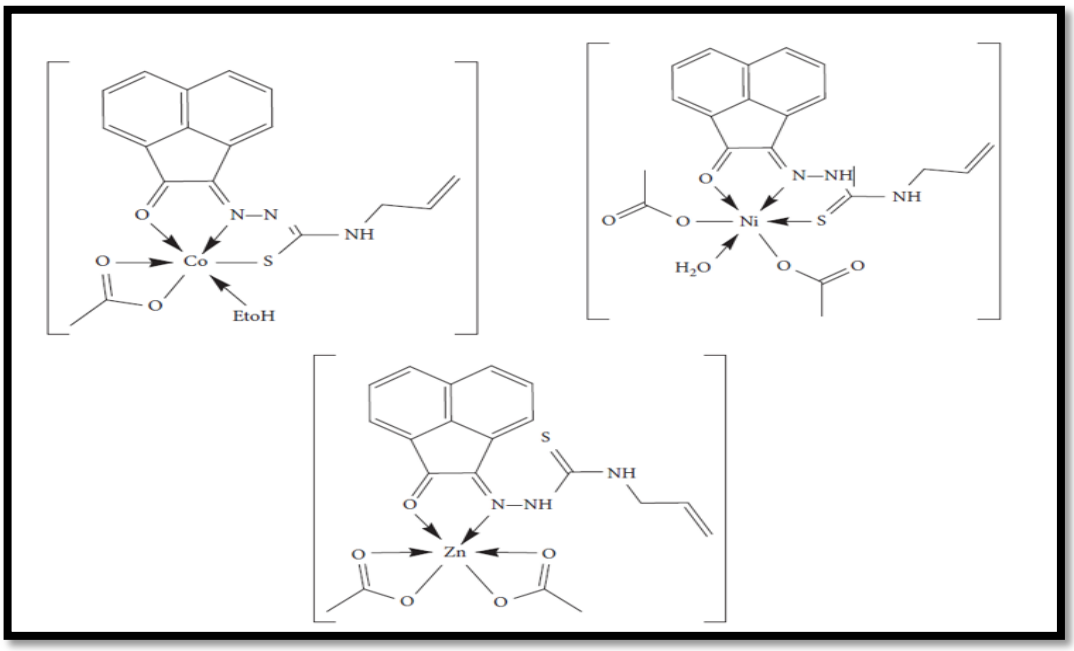


Figure (11) : Suggested structure of complexes .

The synthesis and biological assessment of novel Schiff bases, such as the derivatives of 2-hydroxy-5-methylbenzaldehyde and 2-hydroxy-5-methylbenzaldehyde (sulfisoxazole (S2) and sulfamethoxazole (S1), are detailed here. Alyar, Saliha, and others reported the Pd (II) and Cu (II) complexes. Measurements of conductivity, magnetic susceptibility, 1H-13CNMR, FT-IR, and LC-MS were used to identify the produced compounds. S2M-S1's molecular structure was examined using single crystal X-ray diffraction, and it was found that the compound formed in the monoclinic space group. Additionally, the anticancer properties of recently developed medications were assessed against three human cancer cell lines using the sulfonamide B test and molecular docking studies. In breast (MCF7) cells, the IC50 values for S2M-S1, S1M-S1, and their Cu (II) complexes are 40 M. These substances have demonstrated encouraging cytotoxic efficacy against every type of cell line. Additionally, several novel Schiff bases for sulfa medicines were developed and tested for their antitumor effects in vitro, as well as their Pd (II) Figure (12) and Cu (II) complexes [14].

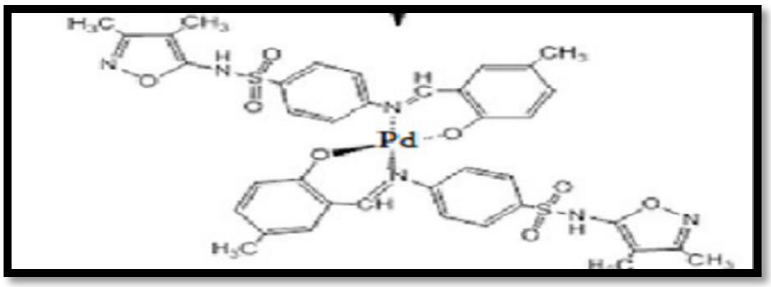


Figure (12): synthesis of new Schiff bases of sulfa drugs and their Pd(II) and Cu(II) complexes was

The researcher, Aurora Reiss, and colleagues (2021), with the help of the Schiff base ligand created via the condensation of sulfathiazole and salicylaldehyde, new Co(II), Ni(II), and Cu(II) complexes were created. Their elements, molar conductance, spectroscopic methods (IR, diffuse reflectance, UV-Vis-NIR), magnetic moments, thermal analysis, and calorimetry (thermogravimetry, derivative thermogravimetry, differential scanning calorimetry) were used to characterize them. Powder X-ray diffraction results explained their morphological and crystal systems.

The IR studies show that the Schiff base ligand consists of two N atoms from the thiazole ring and the azomethine group and one O atom from the phenolic group. It is joined to the metallic ion tridentately. [ML2]nH2O was the composition of the complexes, with an octahedral geometry for the Co(II) complex and a tetragonally deformed octahedral geometry for the Cu(II) complex (M = Co, n = 1.5 (1); M = Ni, n = 1 (2); M = Cu, n = 4.5 (3)). Figure (13) showed this information. T Lattice water molecules were shown to exist through the use of thermal experiments. The powders were polycrystalline and had a monoclinic structure, according to XRD examination. It was discovered that the complexes' unit cell volumes increased in the following orders: (2), (1), and (3). Using SEM, hard agglomerates with micrometric-range diameters were seen for all of the materials (ligand and complexes) that were studied. The N:S and N:M atomic ratios (1.5 and 6.0, respectively) were found to be reasonably close to the theoretical values by EDS analysis. The electrical structures and geometric properties of the Schiff base ligand 4-((2-hydroxybenzylidene) amino)-N-(thiazol-2-yl) benzenesulfonamide (HL) were computationally evaluated using density functional theory (DFT). The expected molecular properties of the chemical reactivity of the HL and Cu (II) combination were determined by a DFT calculation. The Schiff base and its metal complexes were evaluated using the bacterial strains Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus. The results demonstrated that the antibacterial activity of all metal complexes is greater than that of the Schiff base [15].

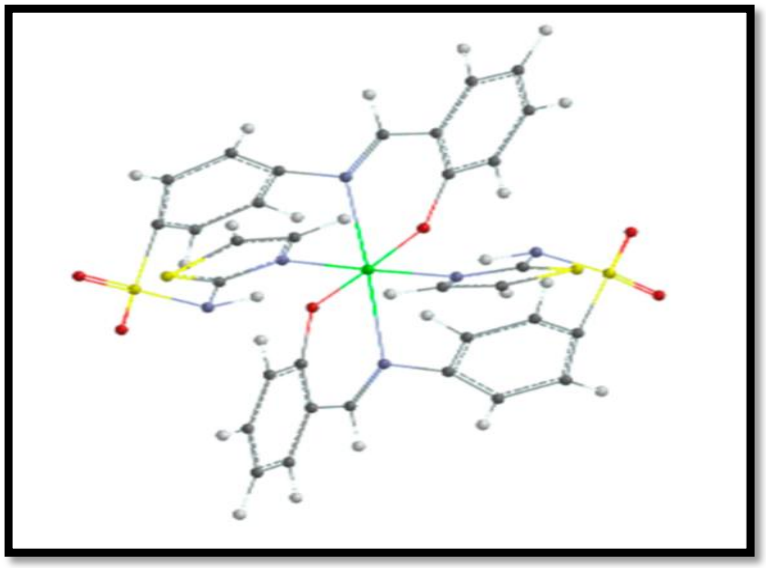


Figure (13). Optimized geometry of copper(II) complex (color codes are white: H; red: O; blue: N;black: C; yellow: S; and green: Cu).

Muhammad Irfan Rana studied the synthesis of new cadmium (II) complexes in 2021. Four cadmium complexes (1-4) with Schiff bases (1 L–4 L) are synthesized, described, and their pharmacological characteristics assessed. The compounds are made of aryl aldehydes and substituted amines. Amantadine forms the Schiff base ligands 1L to 3L by reacting with a range of aryl aldehydes, such as salicylaldehyde, 3-ethoxysalicylaldehyde, and 4-(diethylamino) salicylaldehyde. It also combines with 4-methylaniline to make 4-methylaniline. The complexes were described by spectroscopic, elemental, and thermal analytical methods. X-ray crystallography was used to determine the configuration of three L, or ligand number three. The spectroscopic information demonstrated the cooperation of the ligands and Cd (II).

According to a single crystal XRD investigation, 3 L belongs to the space group P212121 and is orthorhombic. The Cd (II) complexes of the ligands were evaluated for their antibacterial qualities in addition to their ability to inhibit alkaline phosphatase. Comparing cadmium complex 1 to the comparable ligand, the antimicrobial screening findings showed that it has significant antibacterial activity, especially against Staphylococcus aureus. This implies that the antibacterial activity of the complexes is greater than that of their ligands. Upon screening for alkaline phosphatase inhibition, it was shown that the generated cadmium complex 1 more effectively reduced alkaline phosphatase activity compared to the other three complexes [16].

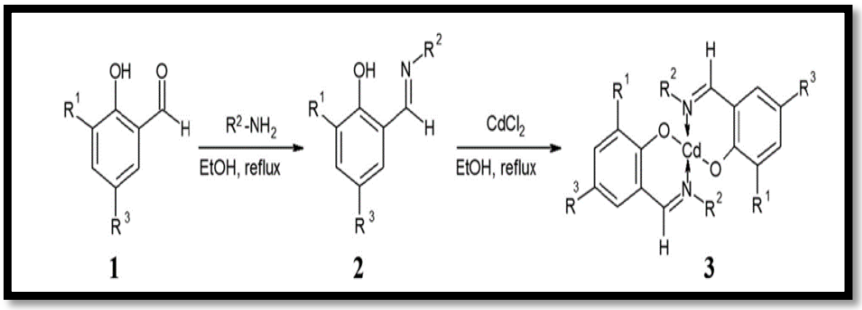


Figure (14) : Synthesis of ligands 2 and their complexes 3 from precursor aryl aldehydes 1upon treating by amantadine. R^1, $R^2$and R^3.

Ampicillin mixed ligand complexes Figure (15), Rajan K. Mohapatra, Taghreed H. Al-Noor, and others (2021) the novel mixed-ligand complexes $[ML_1(L_2)_3]$ seriesThe ligands Schiff base (HL_1), nicotinamide (L2), and the corresponding metal ions in a 1:3:1 molar ratio were used to create Clx [M= Cr (III), Fe (III), Co (II), Ni (II), Cu (II), Cd (II), and Hg (II), n = 2, 3]. The interaction of ampicillin with 4-chlorobenzophenone produced the main ligand, HL1. Utilizing elemental analysis, UV-Vis, FT-IR, 1H-NMR, 13C-NMR, and TG/DTG investigations, the generated mixed ligand complexes were characterized. The Schiff base ligand HL1 exhibited tridentate coordination to the central metal ion via azomethine nitrogen, -lactam ring oxygen, and deprotonated carboxylic groups, whereas the secondary ligand L2 (nicotinamide, Nam) coordinated via pyridine nitrogen atoms in the mixed-ligand complexes. Comparing the complexes to the synthetic compounds, the former showed superior antibacterial activity against S. aureus, B. subtilis, E. coli, and P. pseudomonas infections. DFT studies were also carried out in order to provide additional insight into the bonding inside the structure. Further research was done on the relationships between complexes and potential penicillin binding protein (PBP2) binding sites. Additionally, using molecular docking analysis, evaluations of

the compounds' toxicity and drug-likeness were carried out to determine whether the complexes would be suitable for usage as medications. [17].

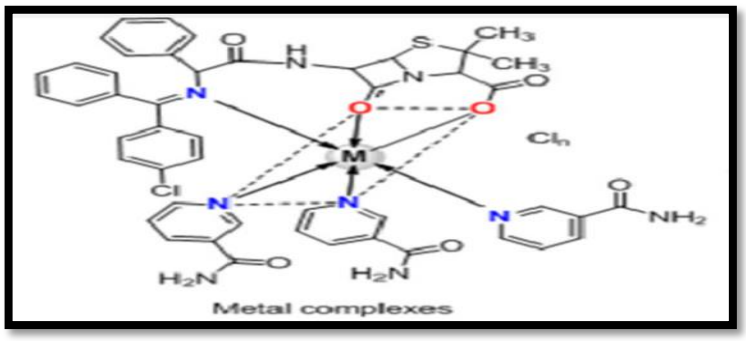
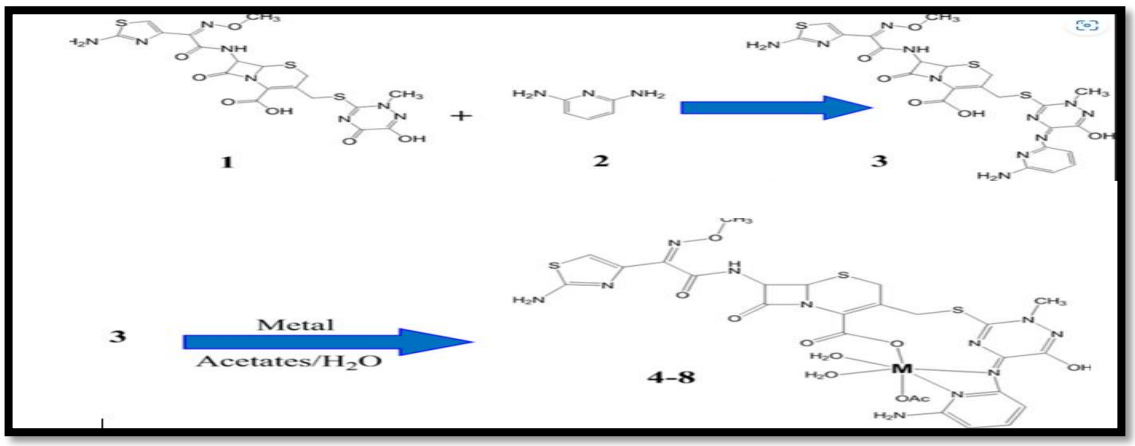


Figure (15): Structure of Mixed ligand with metal complexes

A Schiff base based on ceftriaxone (H2L,3) and its transition metal complexes was produced via the antibiotic ceftriaxone's interaction with 2,6-diaminopyridine 2. Using spectroscopic and physicochemical methods, such as elemental and thermal analyses, density functional theory (DFT) calculations, UV-visible, FT-IR, 1H NMR, EPR, mass spectrometry, molar conductance, and magnetic susceptibility measurements, the binding mode and composition of these complexes were ascertained. The behavior of a monoanionic tridentate N, N, and O ligand is comparable to that of the Schiff base 3 based on ceftriaxone. Since spectroscopic and magnetic data suggests an octahedral geometry, the generic equations [M(HL)(Oac)(H2O)2] (M(II) = Mn2+ 4, Co2+ 5, Ni2+ 6, Cu2+ 7, Zn2+ 8) are provided for all complexes. When it came to E. Coli and S. aureus, Complex 8 had the most promising bactericidal activity (MIC = 0.0048 mol/ml and 0.0024 mol/l, respectively). It works better than the free ligand 1 with MIC values of 0.0140 mol/ml for S. aureus and 0.0560 mol/ml for E. coli. These MIC values were contrasted with those obtained from comparable zinc (II) sources using data that had previously been published. Schiff base complexes Figure (16) shows the outcome of mixing ceftriaxone with silver and gold nanoparticles (NPs). The generated metal complexes showed LC50 values greater than 1000 ppm, suggesting that nauplii of brine shrimp may safely consume them. (Artemia Salina) [18].



A N,N,O tridentate ceftriaxone-based Schiff base 3 was produced by reacting ceftriaxone 1 with 2,6-diaminopyridine 2. Three new transition metal complexes (numbers 4–8) were created, described, and examined for toxicity and antibacterial activity. Zinc(II) complex 8 has a high sensitivity to E. Coli and S. Aureus.

To evaluate the antibacterial activity of these ten new complexes, Eman, R.M., et al. presented a novel Schiff base in 2022 that was formed from cephalexin and isatin. Divalent metal ions (CO, Ni, Cu, Zn, and Mn) were also fully synthesized in ratios of 1:2 for complexes II(a-e) and 1:1 for complexes I(a-e). When the antibiotic cephalexin (Ceph) was refluxed in an ethanolic solution with isatin using an acid catalyst, the -amino group underwent direct nucleophilic addition into a Schiff base ligand. By refluxing in an ethanolic solution, this ligand was coordinated with divalent metal ions in the ratios of 1:1 and 1:2, producing the aforementioned complexes. Complexes were identified using molar conductance, elemental analysis, magnetic susceptibility tests, electronic, FT-IR, and 1HNMR spectrum analysis. The elemental microanalysis, magnetic susceptibility, molar conductivity, and 1HNR, FT-IR, U.V., and electronic spectra were used to confirm the chemical structures of the new ligand Schiff base, as well as the neutral nonelectrolyte octahedral geometry of complexes I (a-e) and electrolyte octahedral geometry of complexes II (a-e).

The Schiff bases ligand was produced from Cephalexin (Ceph) with isatin and complexed with divalent metal ions in molar ratios of 1:1 and 1:2. It was synthesized utilizing simple procedures and demonstrated strong confirmation across all analysis methods. With an octahedra-shaped geometry, complexes I(a-e) are nonelectrolyte, while complexes II(a-e) are electrolyte. As opposed to Pseudomonas bacteria, they haven't shown any antibacterial activity. In particular, complexes Ia and IIe's minimum inhibitory concentration (MIC) (g/ml) against E. coli showed this action at all dosages. [19].

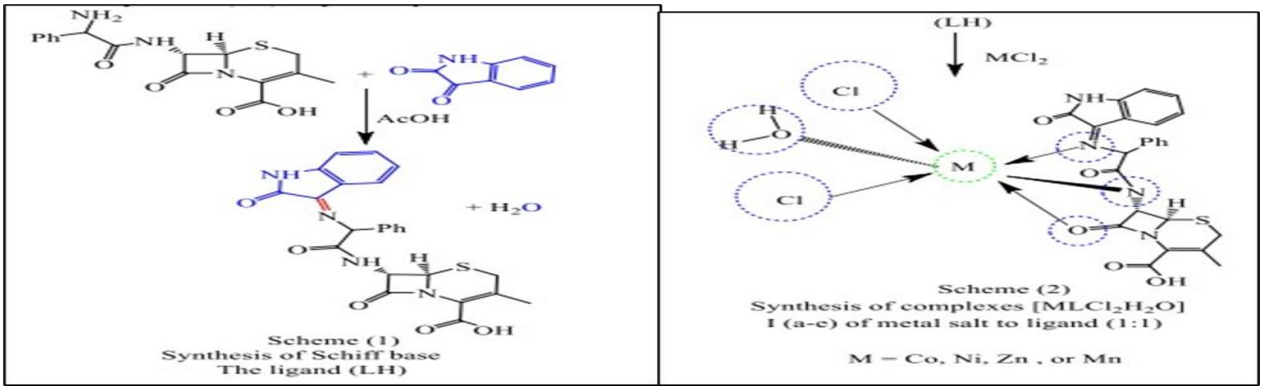


Figure (17): synthesis of Schiff base complexes of metal salt to ligand

Aisha, S.M. Pb (II) in 2022: Using mechanochemical and solution-based methods, cefixime and cefuroxime complexes were created, and their characteristics were assessed for metal analysis, solubility, melting point, conductivity, infrared and ultraviolet spectroscopy, and other aspects. When the complexes formed as white or milky solids with high breakdown temperatures (250–322 °C), Figure (18) shows their thermal endurance. It was found that the complexes had a metal to ligand ratio of 1:1. Sincet the complexes were air stable, largely soluble in DMSO, and insoluble in n-hexane, it seems likely that they were polar.

The complexes are not electrolytes, as evidenced by the low conductivity measurement values (10.4–16.2 Scm2 mol–1) for both approaches. The results of the infrared examination demonstrate that the ligands were produced by the coordination of the Pb (II) ion with the oxygen atom of ν(CO). The disc diffusion method has been used to investigate the in vitro antibacterial and antifungal characteristics of antibiotic medications and their Pb (II) complexes. The results showed that the complexes exhibited strong antibacterial activity against the investigated microorganisms [20].

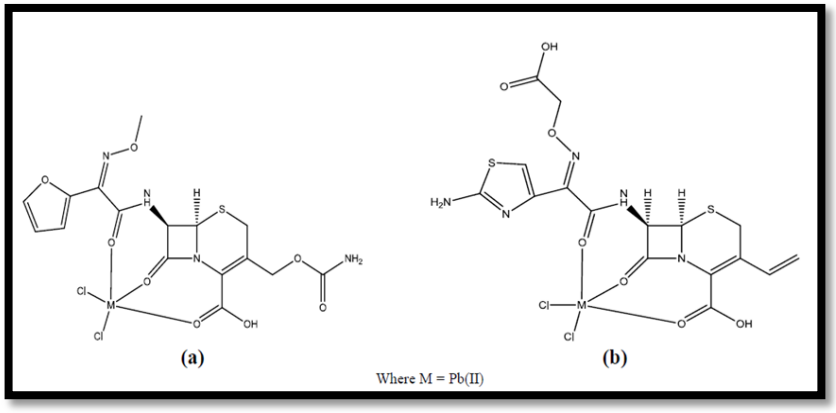


Figure (18): (a) Cefuroxime Pb(II) and (b) Cefixium Pb(II): a proposed structure

Copper complex is made using Schiff base ligand, a new cefotaxime derivative. The composite is described by Mustafa A. Molar conductance, elemental analysis (CHNM%), FTIR, magnetic moment, UV-Vis spectra, and thermal analysis in (2022). The complex stoichiometric ratio is found to be one metal to one ligand. The carboxylate and carbonyl beta lactam groups' oxygen atoms coordinate the copper ion and function as the Schiff base's bidentate, according to the FTIR frequencies.

The Cu-composite's octahedral shape Figure (19) is demonstrated by the ESR spectra, magnetic moment value, and electronic transition. The chemical's water and methanol content are also confirmed by thermal analysis. In the meantime, the Cu-composite is used to test both Gram (+) and Gram (-) bacteria, such as *B. subtilis* , *S. aureus* , *E. coli*, and *P. aeruginosa*. The information gathered indicates the compound's potent antibacterial qualities [21].

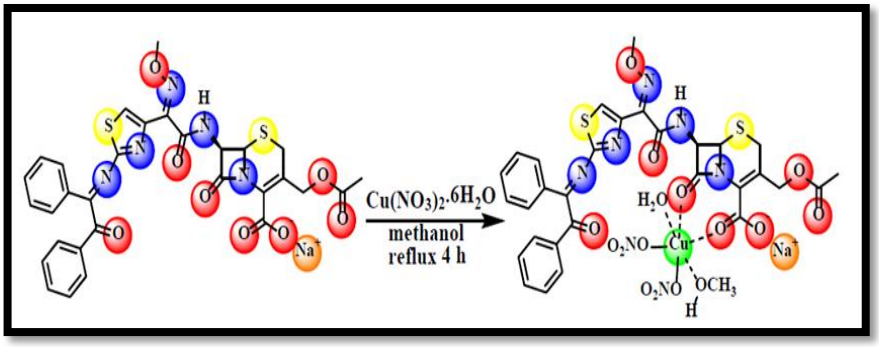


Figure (19): Copper complexes preparation

Combinations of antibiotics and ceftriaxone. In order to investigate the ligational characteristics of ceftriaxone, complexes including magnesium, zinc, iron, copper, and selenium were prepared at a ligand to metal ratio of 1:1. It was found that the complexes comprised coordinated and hydrated water molecules, with the exception of the Se (IV) complex, which contained just hydrated water molecules. The modalities of chelation were clarified using IR, 1HNMR, and UV-Vis spectroscopies.

The distorted octahedral geometry and six-coordinate shape of the Mg (II), Cu (II), Zn (II), Fe (III), and Se (VI) complexes are indicated by the electronic absorption spectra and magnetic moment values Figure (20). Ceftriaxone, with the chemical formula [Mg (CFX) $(H_2O)_2$], connects to the five metal ions as a tetradentate ligand and has four donation sites for nitrogen from NH_2 amino, oxygen from triazine, -lactam carbonyl, and carboxylate $(CFX)(H_2O)_2$, $4H_2OFe(CFX)(H_2O)(Cl)$, and $3H_2OZn(CFX)(H_2O)_2$ in $5H_2O[Se(CFX)(Cl)_2]$ with $6H_2O$ $4H_2O$. Using X-ray diffraction, TEM, and SEM, the morphological surface and particle size of the ceftriaxone metal complexes were assessed.

T In the hepatic tissues of male rats, the study assessed the effects of CFX and CFX metal complexes on oxidative stress and severe tissue injury. The other treated groups received extra CFX metal complexes at the same dose as the CFX-treated group, whereas the second group received 180 mg/kg of CFX orally. Using the TGA(DTG) method, the thermal behavior of the complexes was examined. 56 male rats participated in the test. The antibiotic combination CFX/Zn effectively eliminated Streptococcus pneumoniae, while CFX/Se effectively eliminated Staphylococcus aureus and Escherichia coli. In conclusion, hepatic reactive oxygen species (ROS) and the lipid peroxidation final marker (MDA) increased after repeated exposure to CFX, while levels of antioxidant enzymes dropped. Treatment with the CFX metal complex prevented liver damage in male rats primarily by increasing antioxidant defense enzymes and reducing excessive ROS production. (2022) (Memy.M.E.) [22].

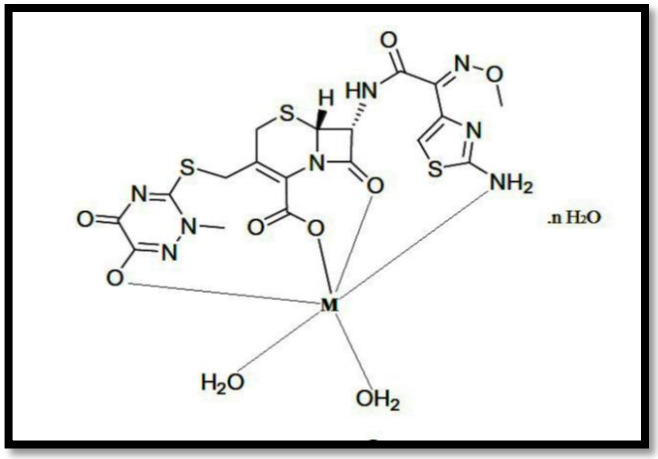


Figure (20): The structure of the prepared CFX complexes. (a) M = Mg, Cu and Zn/ CFX, n = 4,3 and 6respectively. (b) Fe/CFX complex. (c) Se /CFX complex.

G. Malgorzata and colleagues Ampicillin (AMP) and other antibiotics of the b-lactam class Figure (21) have a wide range of applications in the management and prevention of various bacterial illnesses. Multidrug resistance in pathogenic strains is a result of antibiotic overuse. Thus, the biological activity of several significant drugs, including AMP, has decreased. Development of new antibiotic medications, their modification, and their complexation with metal ions, which can enhance their biological properties, appear to be the study areas receiving the most attention at the moment.

Furthermore, due to increased concerns about public health and food safety, penicillin residues in food and the environment have been the subject of a lot of attention lately. Consequently, the creation of innovative sensing agents and methods is essential for the detection of antibiotics. Topics covered in this review include metal complexes, the synthesis of AMP, and the quick and precise detection of AMP. It also outlines current research trends in medicinal chemistry [23].

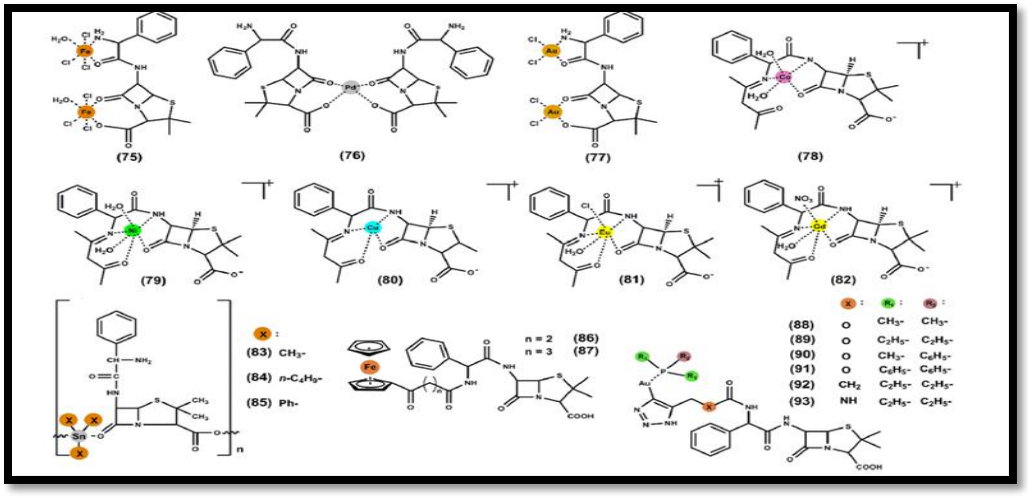


Figure (21): Proposed structures of selected metal complexes with AMP (75e77), its derivatives with acetylacetone (78e82), and organometallic complexes: AMP (83e85), its ferrocenyl bioconjugate (86, 87), and chryso-lactams (88e93). This figure has been prepared based on literature data

Halogenated Schiff base complexes. (2022) Momdouh S, Rehab M. I, and Ahmed M In this contribution, four Ni(II) complexes with bromo or iodo substituents in the salicylidene moiety are constructed using sulfonamide-based Schif bases (SB1–SB5). Significant progress has been made in resolving the chemical structures of these compounds through a multitude of analytical and physical research. All ligands act as bidentate chelators in the ON binding mode, resulting in octahedral, square planar, or tetrahedral geometries. The phenolic OH at 12.80 ppm in the free Schiff base SB2 vanishes in the diamagnetic complex [Ni(SB2 –H)2], allowing the OH deprotonation prior to the chelation with Ni(II) ion. The mass spectrum typically exhibits twin molecular ion peaks when bromine isotopes (79Br and 81Br) are present. The strong thermal stability of each compound was further confirmed by its thermal degradation phases, which yielded NiO residue with a mass ranging from 6.42% to 14.18%. Furthermore, the bactericidal and cytotoxic properties of the ligands and a few selected complexes were evaluated. When it came to the bacteria B. subtilis, E. coli, and A. fumigatus, SB4 fared better than the other ligands, with MIC values of 0.46, 7.54, and 0.95 M, respectively. The combination of different substituents, such as a thiazole ring and two bromine atoms at positions 3 and/or 5 on the phenyl ring, is one explanation for the observed optimal activity. The outcomes of the cytotoxicity screening (IC50), which predicted that the molecules SB2 (16.0 M), SB4 (18.8 M), The breast cancer protein (3s7s), and SB5 (6.32 M), also show a striking degree of agreement with the molecular docking simulation results. Furthermore, [Ni(SB4 –H)2] Figure(22) (4.33 M) is strongly recommended as a promising, potent, and reasonably priced non-platinum antiproliferative agent following additional drug authorization procedures. It has about four times the potency against breast cancer cells (MCF-7) compared to cisplatin (19.0 M). [24]

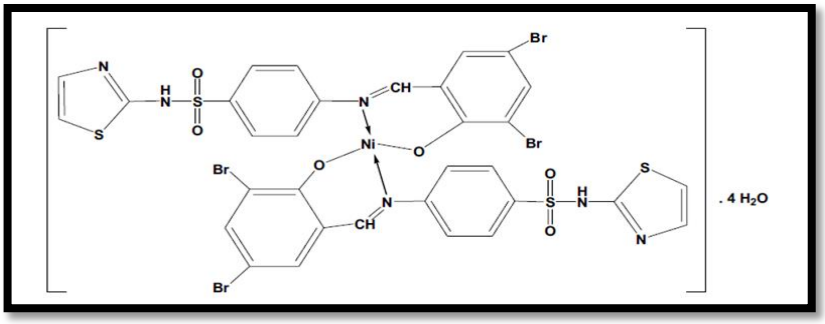


Figure (22): Structure of $[Ni(SB4–H)_2]\cdot 4H_2O$ complex

In 2022, Mohamed Abdel-Hameed and Abdel-Mawgoud M. developed derivatives of ibuprofen, which reacted to generate the ZnL1 and ZnL2 complexes. Two ligands, HL1 and HL2, were produced via the combination of Ibuprofen hydrazide and 2-hydroxy-1-naphthaldhyde, and 5-bromosalicylaldehyde and Ibuprofen hydrazide. Elements analysis (C.H.N.), FT-IR, electronic spectra, magnetic moments, molar ratio measurements, and molar conductance tests were used to characterize the ligands and their complexes. (Figure 23).

The novel ligands' in vitro cytotoxic effects on the breast cancer cell line MCF-7, the liver cancer cell line MCF-8, and the HCT-116 cell line were also investigated. In vitro tests were conducted on ibuprofen Schiff base ligands and their complexes against pathogenic bacteria and fungus. Two Gram-positive bacteria, S. and E. coli, were evaluated in vitro against synthetic materials and the widely used antibiotic Gentamycin. P. vulgaris and E. coli are two more Gram-negative bacteria in addition to S. aureus and B. subtilis. The novel Schiff base ligands and their complexes were evaluated for their in vitro antifungal activity against Aspergillus fumigatus, Candida albicans, and the widely used antifungal medication, Ketoconazole [25].

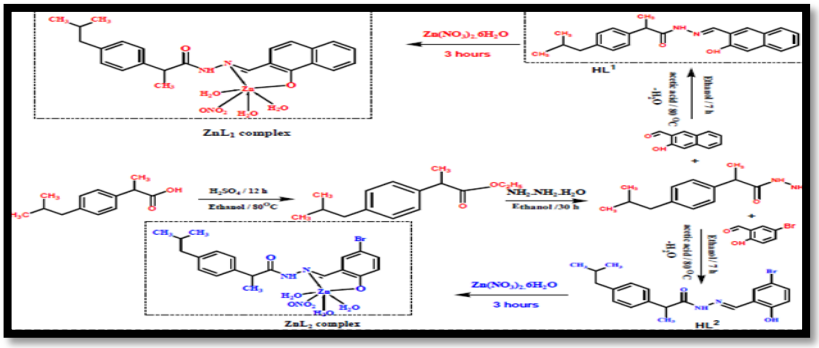


Figure (23) : The scheme of synthesis of the HL_1, HL_2, ZnL_1 and ZnL_2 ibuprofen Schiff base complexes

Alexandra Bargan and Alina Soroceanu: Because of their importance in many interdisciplinary research disciplines, Schiff-base ligands have contributed significantly to the advancement of contemporary coordination chemistry. This nearly all-inclusive review starts with the Schiff-base ligands and covers every facet of complexes. Our research focuses on the most recent advancements and examines the fascinating discoveries produced after 2015. Condensing amino acid

with a carbonyl produces the flexible compounds referred to as effect-base ligands and their complexes. It has been demonstrated that the associated metal complexes possess antiviral, antifungal, antibacterial, and antioxidant qualities. This study is preceded by a brief discussion of Schiff-base ligands and their metal complexes. Among the most noteworthy recent advancements in the field of Schiff-base coordination chemistry is its prospective use as a bioactive core.

Information on the Schiff-base complexes' antioxidant, redox, and catalytic properties is also included in the review; this information will be helpful in the future development of new materials and compounds Figure (24). [26]

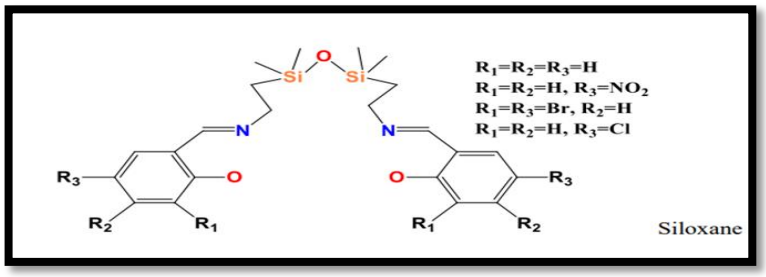


Figure (24): Representative Schiff-bases studied as antibacterial agents

Metal complexes Figure (25) including glutaraldehyde and sulphacetamide sodium (2022), Mohammed Abdullah Mays, et al, we synthesized a Schiff base ligand and used multiple mothed electronic spectra (visible and ultraviolet spectrum) to describe its complexes. Tests for molar conductance, bioactivity, and FTIR magnetic moment all demonstrate the tetrahedral geometry of the compounds. Staphylococcus aureus, Escherichia coli, and Candida albicans were used to investigate the biological activity of the produced ligand and its complexes. The results showed that the complexes had higher levels of activity than the ligand [27].

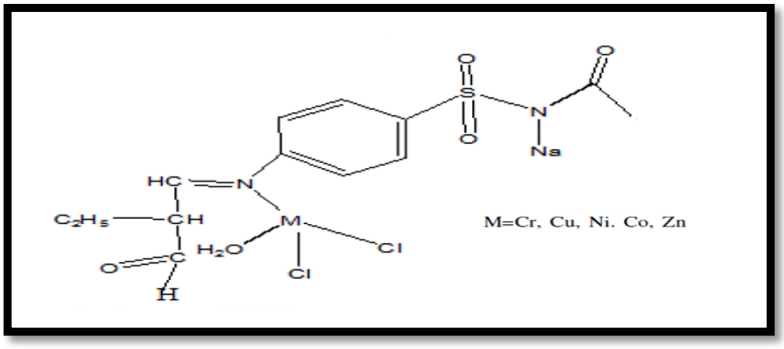


Figure (25): The proposed structural formula of the complexes.

Aiya's S.A. (2023) has developed new metal complexes that are analyzed by various spectroscopic techniques. The ligands used in these complexes are obtained from Schiff's base based on amoxicillin and are coordinated with Pd(II) and Co(II) Figure (26). For the Co (II) and Pd(II) complexes, FT-IR spectroscopy has revealed the production of tetrahedral and square planar geometries, respectively. Atomic force microscopy (AFM) and field emission scanning electron microscopy (FESEM) were used to examine the surface morphology. The metal complexes samples

had a Brunauer-Emmett-Teller surface area of around 6.63 to 8.71 m2/g, pore sizes and volumes of 0.030–0.0501 cm3/g and 18.39–22.98 nm, respectively. Because CO2 is very diffusible at 21.38 and 26.16 cm3, its quadrupole moment greatly influences its adsorption capability. G−1 for the complexes of Pd(II) and Co(II).[28]

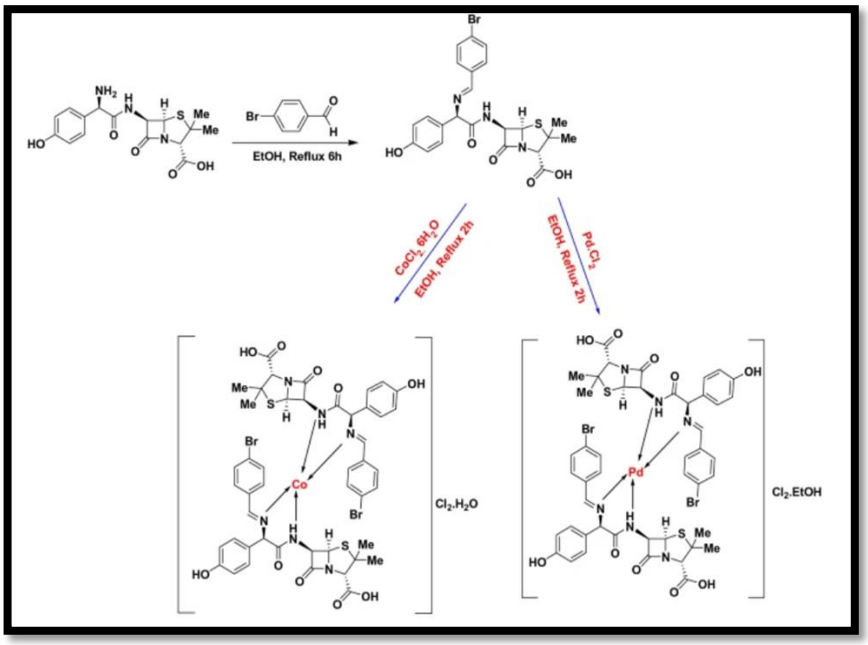


Figure (26): Synthesis of metal complexes

Identification of Synthesis and Antioxidant (2023), Rafid R.A. Condensation methods employing cephalexin) ligand (and) di-organotin (IV) complexes in the presence of sodium hydroxide efficiently created three organotin complexes. To characterize the generated compounds, infrared spectra, elemental analysis, and nuclear magnetic resonance (1H, 13C, 119Sn NMR) were employed. Based on the spectrum data, it was projected that the produced compounds had an octahedral structure. This study used the CUPRAC method and the free radical scavenging activity (DPPH) method to examine the antioxidant activity of tin (IV) compounds. Because of the metal moiety, dioganotin (IV)-cephalexin complexes exhibited more antioxidant activity than ligands, whereas compound (Me2SnL2) Figure (27) shows the stronger antioxidant activity than other complexes [29].

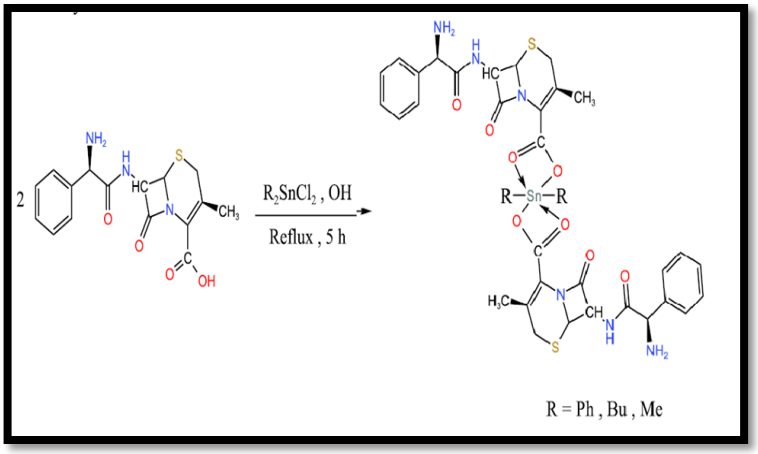


Figure (27): Synthesis of Di-organotin (IV) complexes)

Novel metal compounds derived from Schiff bases created by Samar A. Aly and others (2023).The generic formulas [Cr(H2L)$_2$Cl$_3$. EtOH], [Fe(H2L)(OH)SO4(H2O).2H2O], [Fe(HL)2(OH)].H2O], and [Co(H$_2$L)(HL)2.1/2 EtOH] were used to build new chelates complexes through the use of thermogravimetric analysis and spectrum techniques. analytical thermogravimetric methods that are derivative. The findings verified that the ligand exhibited neutral tetradentate, bidentate, or monobasic tridentate behavior. The carbonyl oxygen (C=O) and N(2)H or (C-S) groups in complex (3) have aided in coordination. Additionally, complex (3) was more stable in comparison to its contemporaries (1-3). As seen in Figure (28), the resultant mononuclear complexes have an octahedral shape. We looked at how the ligand affected the growth of Cr(III), Fe(III), Co(II), and Streptococcus pyogenes, as well as Gram-positive and –negative bacteria. The antibacterial activity of the ligand is not as potent as that of the complexes containing Cr(III), Fe(III), and Co(II), according to the data. The intracellular antitumoractivities further demonstrated the powerful impacts of drugs. It was also demonstrated that most complexes were more efficient than their free ligands. The intriguing potential interactions between the ligands and complexes and the amino acid active sites of the ribosyltransferase moiety were further clarified by molecular docking (PDB ID). [30].

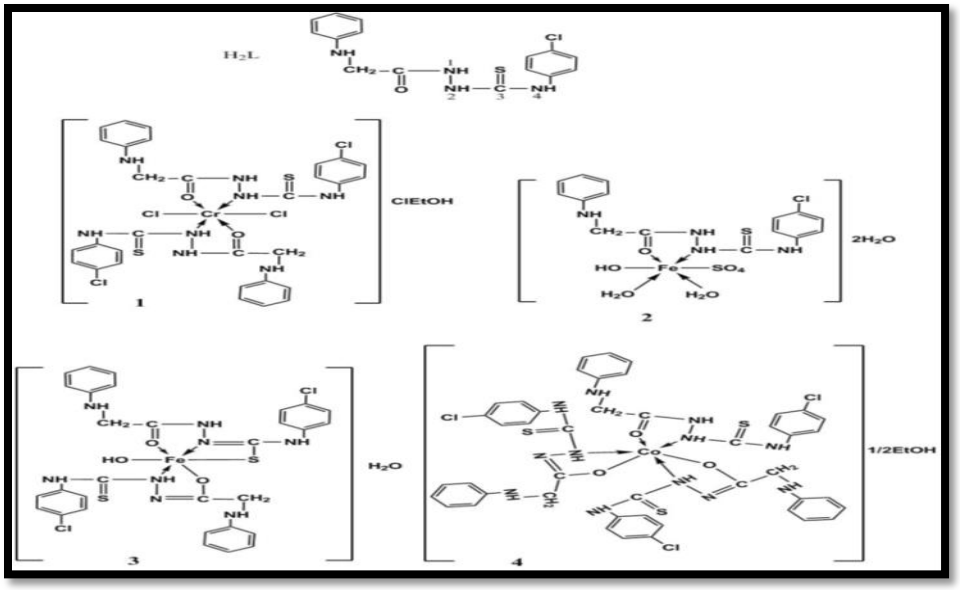


Figure (28) The proposed structure of ligand and its complexes)

By interacting with 2-hydroxy acetophenone (HL1) as the major ligand and L-histidine (L2) as the secondary ligand, 2-aminophenol has created a new series of Fe(III), Cr(III), and La(III) mixed-ligand complexes. Numerous physicochemical methods, including as elemental analysis, mass spectroscopy, molar conductivity, magnetic moment, infrared, UV/Vis, and 1H NMR, have been used to study these compounds. The microanalytical data demonstrated that a 1:1:1 M ratio was produced during the synthesis of the mixed ligand complexes. The octahedral structure of each generated molecule was clearly visible in the electronic spectrum data, as Figure (29) shows. The substances under inquiry were tested using the disc diffusion assay to determine their minimum inhibitory concentration (MIC, g/mL) and disc inhibition zone (IZ, mm) against the development of harmful bacterial strains such as E. coli, S. aureus, P. aeruginosa, and E. faecalis. The cytotoxicity of these medications against human hepatocellular liver cancer (HEPG-2) cell lines was assessed using the MTT test. The medications were assessed using a molecular docking technique against the EGFR tyrosine kinase receptor (PDB code: 1 M17). Examining the interactions in protein-ligand complexes is crucial. Additionally, research on the quantitative structure-activity relationship, or QSAR, was utilized to assess the biological activity of the ligand. as mentioned by Saud I and Al-Rezayes. (2023) [31].

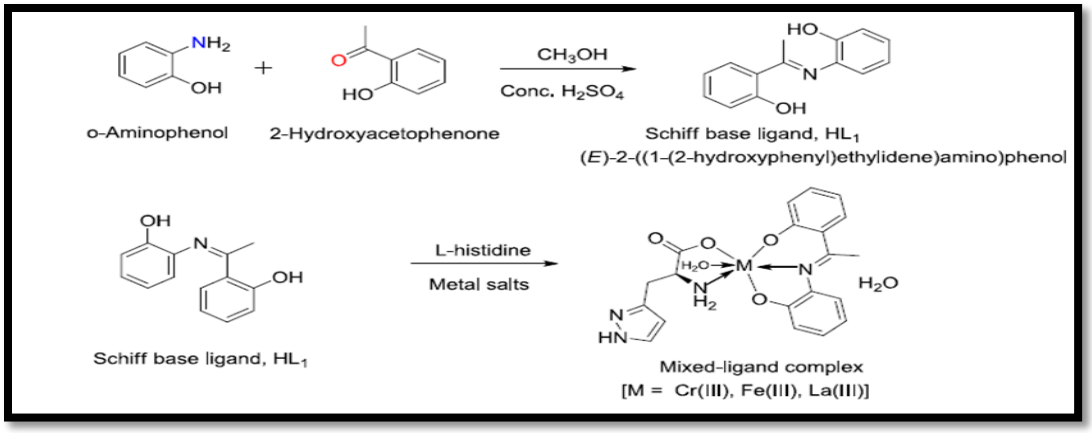


Figure (29): Synthesizing Schiff base ligand & its mixed-ligand complexes

Novel Schiff bases along with their metal compounds. (2023) Ahmed, Sahba A, and others Schiff's foundation complexes are produced by the condensation of 4-aminoantipyrine with 4-(dimethylamino)benzaldehyde and the subsequent condensation with the valine salt amino acid ligand (4-ANdmV), which are arranged via NNO donor sites. For all Co(II), Ni(II), Cu(II), and Zn, spectroscopic (IR, 1H-NMR, ^{13C}-NMR, UV-vis), magnetic, and other studies suggest octahedral geometry (II) Figure (30). The ability of the metal complexes and ligands to inhibit the growth of gram-negative bacteria (Salmonella coli, Pseudomonas aeruginosa), one pathogenic gram-positive bacteria (Staphylococcus aeruginosa), and three gram-positive bacteria (Klebsiella pneumoniaea) varied. These tests were conducted against bacterial starins. [32]

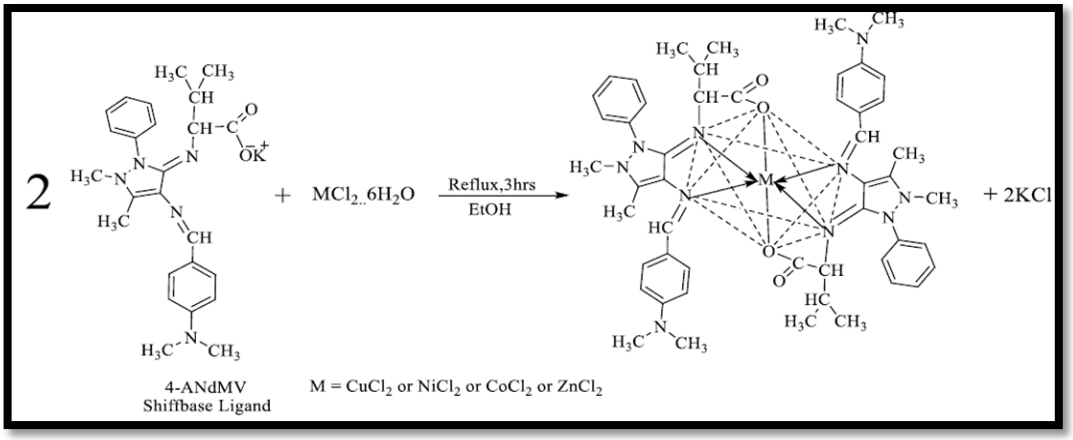


Figure (30): Synthetic pathway of metal complexes

Complexes of Schiff base copper (II). (2023) Masashi, K., and others. A successful production of amino acid Schiff base copper(II) complexes was achieved via a microfluidic technique. The remarkable biological activity and catalytic role of Schiff bases and their complexes make them noteworthy materials. Usually, a beaker-based method is used to manufacture products, with a reaction temperature of 40 C for four hours. In this study, however, we propose to use a microfluidic channel at room temperature (23 °C) to achieve quasi-instantaneous synthesis. The products were inspected using UV-Vis, FT-IR, and MS spectroscopy. Microfluidic channels have the

potential to significantly improve the efficiency of compound manufacturing and material development because of their elevated reactivity, Figure (31) [33].

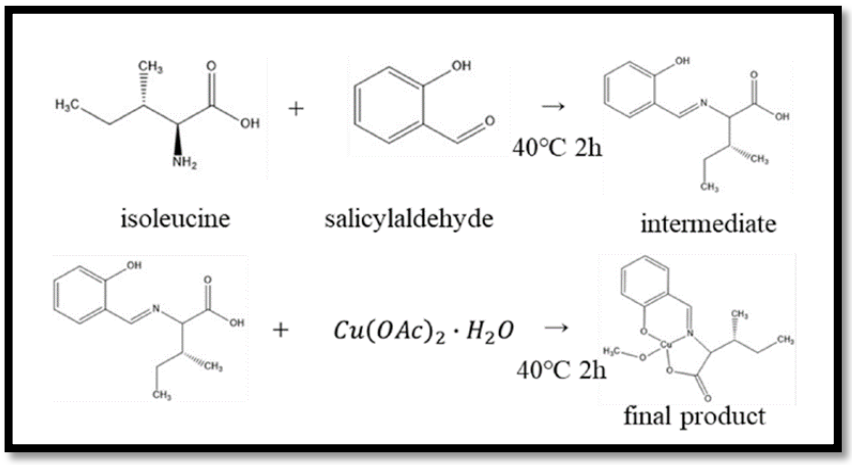


Figure (31): Synthesis reaction of an amino acid Schiff base copper(II) complex

Abdul Jaleel Mohammed Abdul Jaleel: Two novel Schiff base ligands (L1 and L2) were synthesized using vanillin and diamine molecules (ortho phenylene diamine, meta phenylene diamine, and 3,4-diamine toluene). After that, two new complexes were produced by synthesis and treatment with Co (II) chloride at a metal-to-ligand ratio of 1:1:[CoL3(H2O)2]Cl2 and [$CoL_1(H_2O)_2$] Cl_2. These complexes and ligands were described using NMR, IR, atomic absorption, UV visible absorption, molecular weight determination, molar conductance, and magnetic measurement techniques. Based on the data, the ligands were recognized as bidentate ligands with attachments to two azomethine nitrogen sites. It was assumed that these substances would be coordination number four paramagnetic electrolyte materials. The antibacterial properties of the ligands and metal complexes shown in Figure (32) were tested against both gram-positive and gram-negative bacteria, and it was shown that they displayed biological activity. The molecules' shapes were examined through the use of quantum chemical computations. The inquiry includes several quantum chemical features arising from frontier molecular orbitals [34].

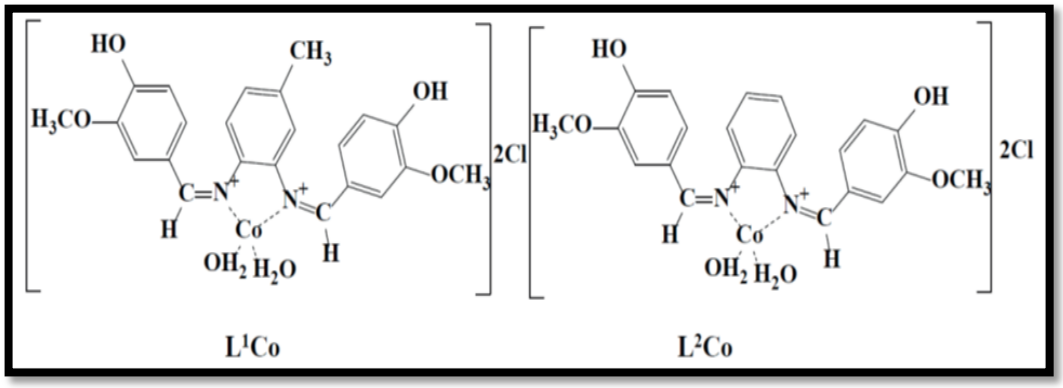


Figure (32): Structure of the prepared complexes

Metal complexes based on drugs Schiff bases are shown in Figure (33). (2023) Kirti Salame and Arun Singh The interaction of isoniazide (IZ) with 5-chlorosalicyladehyde (CSA) and 3,5-dichloro salicylaldehyde (DCSA) yields two novel ligands: N'-(5-chloro-2-hydroxy benzylidene) isonicotinohydrazide (CSAIZ) and N'-(3,5- dichloro-2-hydroxy benzylidene) isonicotinohydrazide (DCSAIZ). Cu^{2+}, Co^{2+}, Ni2+, Mn2+, and Zn2+ metal ions were used to create the transition metal chelates for the CSAIZ and DCSAIZ ligands. Elements such as elemental composition, metal:ligand ratio, magnetic characteristics, and IR spectroscopy were used to characterize each CSAIZ and DCSAIZ ligand and all of its metal chelates. The antibacterial activity of each CSAIZ and DCSAIZ ligand was also observed, along with the activity of its all-metal chelates.[35]

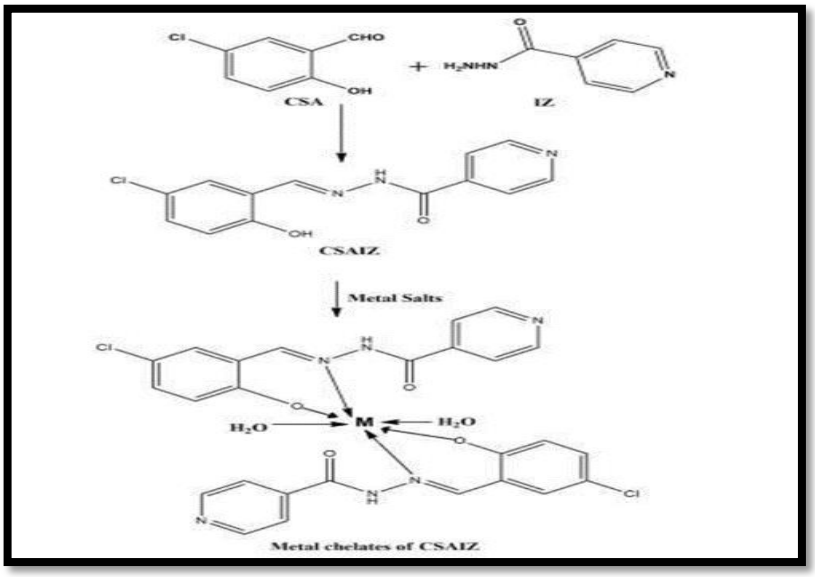


Figure (33): Synthesis of metal chelates of CSAIZ and DCSAIZ

Four unique Mn(II), Fe(III), and Cr(III) complexes were created in this study using two Schif base ligands: 4-bromo-2-[€-[4-(2-hydroxyethyl)phenyl]iminomethyl]phenol (HL1) and 2-[€-[4-(2-hydroxyethyl)phenyl]iminomethyl].It is now known that -4-methoxy phenol (HL2) has been produced. Numerous analytical and spectroscopic methods have been used to describe the ligands and their complexes Figure (34). General formulations of $[M(L)Cl_2(H_2O)_2]$ were proposed for FeL1, CrL_1 and CrL_2, and $[M(L)Cl(H_2O)_3]$ for MnL_2. DFT/B3LYP calculations utilizing the Gaussian 09 program have been used to calculate the electrical characteristics as well as the HOMO and LUMO energies. It is proven that the complexes have optimal lowest energy arrangements. The antibacterial efficiency of the pharmacological activity was evaluated against a range of bacterial and fungal species using the disc effect on approach.

The ligands and their metal complexes' in vitro cytotoxicity was evaluated using the MTT methodon the MCF-7 human breast cancer cell line and the Hep-G2 human liver carcinoma cell line. In comparison to the free ligands, all compounds showed increased activity. The MnL2 complex outperformed the other complexes in terms of activity, with an IC50 value of 2.6 0.11 g/ml against Hep-G2 and 3.0 0.2 g/ml against MCF-7, both of which are lower than the IC50 value of the reference drug cisplatin (4.0 g/ml). The compounds' capacity to bind and cleave CT-DNA has been

investigated through the use of gel electrophoresis and UV-vis electronic spectroscopy techniques. The binding mechanism of the novel complexes has been presented, and it was demonstrated that their binding affinities are in the following order: FeL1>MnL2>CrL2>CrL1.

These are the known binding constants, or Kb, for the interaction. To assess the type A molecular docking research, it was important to ascertain the degree and binding affinity of the drugs being studied with human DNA (PDB: 1bna). The acquired results demonstrated that complexes could be inserted into the DNA molecule to prevent DNA replication and validated the experimentally proposed intercalation binding mechanism. The produced compounds exhibit good bioavailability and conform to the expected range of Lipinski's RO5 in terms of pharmacological, chemical, and physical properties. (Abdel-Rahman, Laila H., and others) [36]

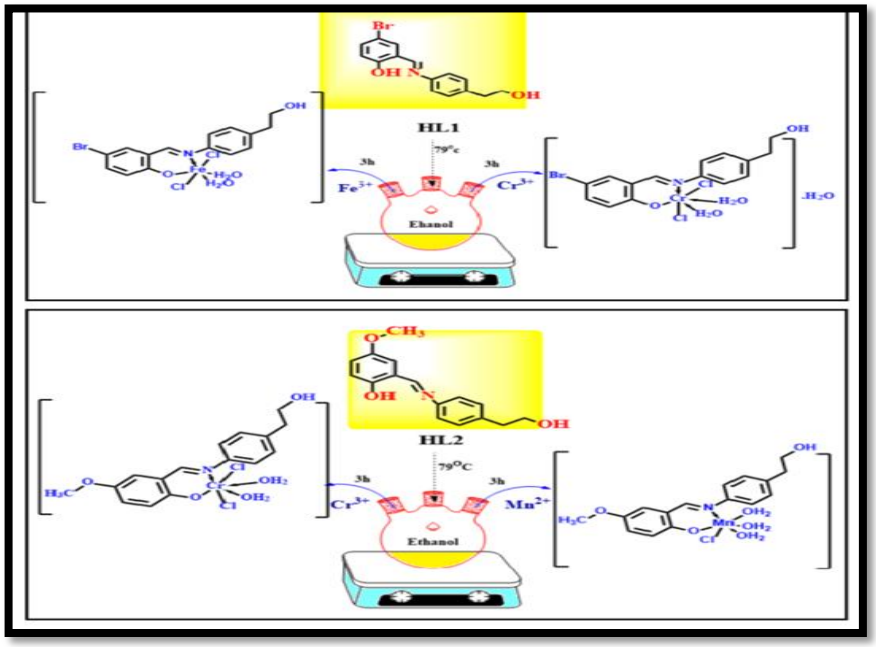


Figure (34): Synthesizing novel ligands , their predicted structure ,and their metal complexes

In 2023, Mona S. Ragab, Randa F. Abd El-Baki, and Shimaa Hosny: This work's main goals were to determine the cytotoxicity of the new H2L ligand and its Cr and Cu nano-complexes Figure (35) and how they affected COVID-19 activities in HEPG-2 cells. In addition, studies on the chemistry of the generated nano-complexes are being conducted. The synthesis of N-(4, 6-dimethyl pyrimidin-2-yl)-4-(((2-hydroxyl naphthalene-1-y l) methylene) amino) benzene—sulfonamidesulfonyl) amide, a new Schif base, is reported in this study. We create new nano- and micro-complexes by utilizing the unique characteristics of $CrCl_2.6H_2O$ and CuCl2.2H2O.

Schiff base H2L. Several spectroscopic methods were employed to interpret the ligand and micro complexes that were produced. Coriandrum sativum (CS) medium extract in ethanol was used to create the environmentally friendly nano-sized Cr and Cu complexes. FT-IR, TEM, and SEM were used to determine the structure, morphologies, and particle sizes of the nano-sized complexes PXRD.

The nano-domain compounds are on the subnano size, according to the results. Additionally, we investigated the impact of heat on the size of freshly synthesized nano-complexes using TGA. DFT calculations were performed to validate the experimental data. According to the findings, the metal complexes under investigation have more stability than H2L, the free ligand. Both before and after the nano-complexes were heated to 200 °C, the anticancer activity was assessed. The findings indicate that the Cr nano combination had potent anticancer activity with an IC50 value of 3.349 µg/ml upon heating. There is good DNA cleavage in the tested Cu nano-complex. Molecular docking analysis was performed on the COVID19 and liver cancer proteins to determine the possible inhibitors' binding energies [37].

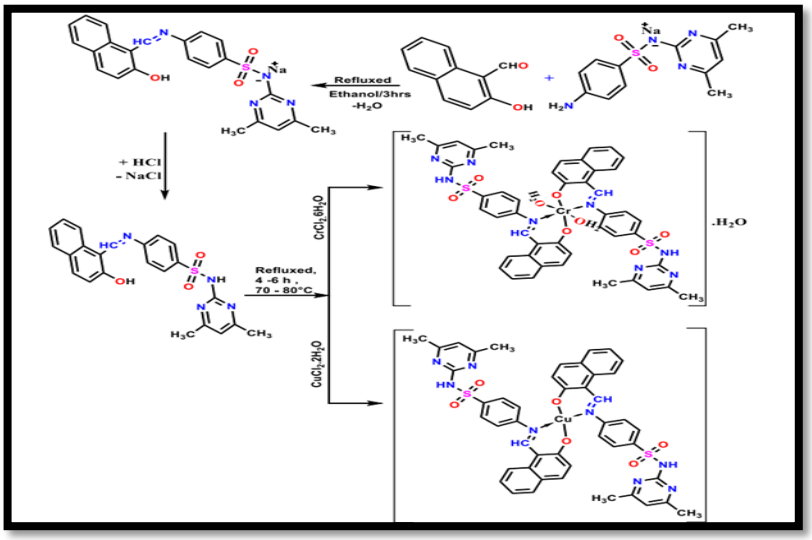


Figure (35): synthesis of ligand and metal complexes

Three novel metal complexes, ions La(III), Ce(IV), and UO2(II), have been made using a Schiff base prepared by condensing anisaldehyde and L-histidine. Density-functional theory (DFT) simulations and a range of spectroscopic methods were used to identify each created molecule. Based on the experiment's findings, an octahedral structure for the complexes was postulated. Figure (36) shows the ideal form, numbering scheme, and dipole moment vector of the Ligand and the La, Ce, and UO2 (1:1) chelates. All of the bacteria that were studied were moderately inhibited by the Schiff base ligand and complexes, with P. aeruginosa, Klebsiella sp., and E. faecalis exhibiting the highest degrees of inhibition (M. El-Barasi and others) 2023 [38].

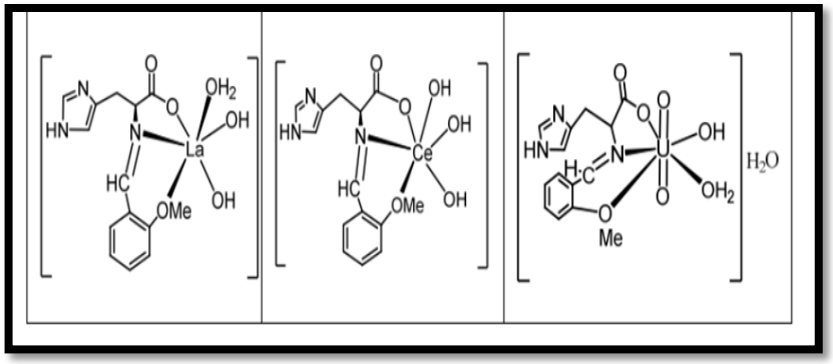


Figure (36): Proposed structure for La(III) , Ce(IV) and UO2(II) complexes

Gopichand Kamble, et al. The Schiff base (2- EBTMCP) of 5- Chloro – 2 – hydroxy benzaldehyde and 6- ethoxy -2-amino benzothiazole was synthesized and characterized by spectroscopic techniques including powder XRD, elemental analysis, SEM, EDX, 1H NMR, and Infrared spectra. It was created, separated into solid compounds, and recognized in its complexes with Ni (II), Co (II), Zn (II), and Cu (III) Figure (37) using a variety of spectroscopic methods. Here, CT (calf thymus) DNA is being used in investigations on the intercalative form of DNA binding to metal complexes. The UV-Vis electron absorption spectroscopy technique has been used to study the capacity of transition metal complexes to bind DNA. To investigate their potential for cytotoxicity in vitro, an MTT experiment was also conducted.[39]

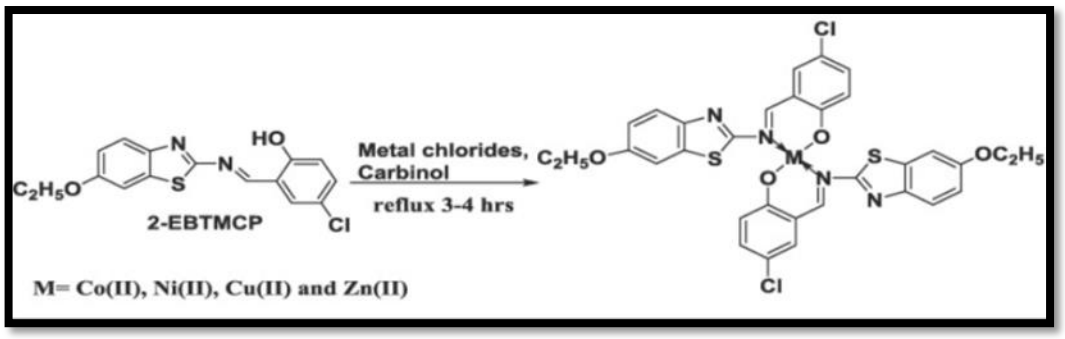


Figure (37): Metal complexes with Benzothiozole Schiff base ligand

β-lactam complexes Figure (38) in 2023 Zabiszak, Michat, and others One of the most often used chemicals in medicine is the -lactam antibiotic due to its potent antibacterial action. Both bacteria (Pseudomonas, Nocardia, Streptomyces, Gluconobacter, Agrobacterium, and Acetobacter) and fungi (Penicillium, Cephalosporium, and Aspergillus) produce these drugs. The strong antibacterial qualities, minimal toxicity, broad spectrum of activity, and excellent therapeutic efficacy of antibiotics make them advantageous. The advantages of these antibiotics stem from their molecular structure, particularly the potential for side-chain changes that could yield a wide variety of antibiotics with distinct broad spectrum of action and clinical pharmacological properties.

All beta-lactam antibiotics work by preventing bacteria from growing their cell walls. Because the antibiotic inhibits the enzymes needed to generate muramin, the primary component of

the bacterial cell wall, it cannot be synthesized effectively.The bacterial cell finally perishes as a result of losing its protective cell wall. The -lactam antibiotic class includes penicillin and its derivatives, cephalosporins, carbapenems, monoamide rings, and enzyme inhibitors that stop penicillin from working on bacteria. However, the development of antibiotic-resistant bacteria poses a significant challenge to modern antibiotic therapy. As their primary defense against medications belonging to the -lactam class, bacteria utilize proteins that generate -lactamase. These enzymes make the antibiotic molecules inactive by employing hydrolases to cleave the amide link in the -lactam ring. The rate of enzyme synthesis, the degree of activity specificity, and the degree of affinity for a particular antibiotic are only a few of the variables that determine how effective -lactamases are. Moreover, -lactamases can interact with metal ions to increase their antibacterial activity. in particular, zinc ions. Because these complexes effectively shield the -lactam ring from hydrolysis, they have significantly greater antibacterial efficacy than other types of antibiotic complexes [40].

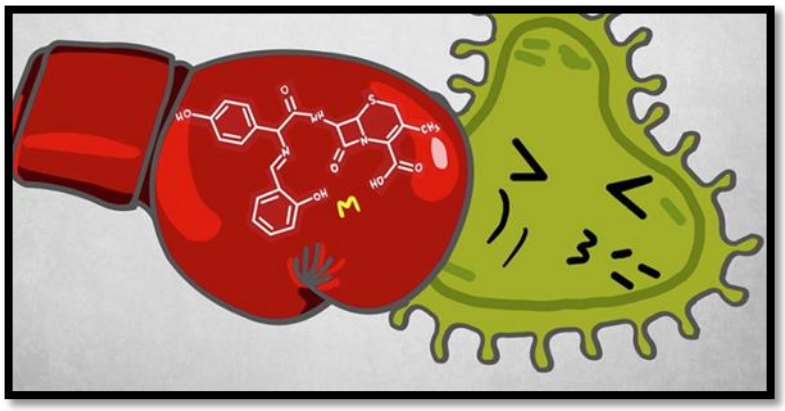


Figure (38): βeta- lactam and Schiff base complexes

Himadri Prya and Gogoi P. Barman synthesized a novel Schiff base ligand in 2023. By reacting 4,5-dichloro-o-phenylenediamine with 5-bromosalicylaldehyde in a 1:2 molar ratio, a novel ligand of Schiff base known as 2,2'-((1E, 1'E)-((4,5 – dichloro – 1,2 – phenylene) bis (azanylylidene)) bis(methanylylidene))bis(4-bromophenol) was produced. We used various spectroscopic and analytical techniques to describe the ligand. Ni(II), Cu(II), and Zn(II) coordination behavior and kind of bonding were inferred by means of 1H-NMR, FT-IR, EI-MS, UV-Visible, and magnetic moment analysis. In addition, the stoichiometry between the ligand and metal ions was determined using Job's approach. Together with their quantum chemistry computations, they also performed computational compound structure optimization.

The Ni(II) and Cu(II) complexes showed square planar geometry, but the Zn(II) complex showed deformed planar four coordinated geometry Figure (39). To determine whether the chemicals created had any antibacterial properties, two strains of each type of bacteria—two Gram-positive and two Gram-negative—were employed as test subjects. Additional bioactivities, such as DNA binding, antioxidant activity, and anti-inflammatory activity, were also performed. To further correlate findings with experimental data, a molecular docking investigation using B-DNA and 6COX enzyme prote receptors was conducted. [41].

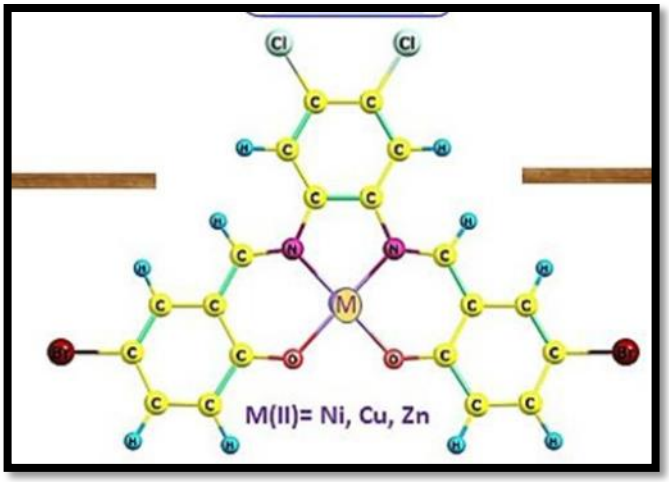


Figure (39): synthesis ONNO Schiff base complexes

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