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Synthesis and Applications of Mixed Drugs Metal Complexes: A Review

Mamman Yusuf [1*], Joshua A. Obaleye[2], Zulkiflu A. Abdullahi [3] & Aminu G. Abdullahi PTDF[4]
[1]Department of Chemistry, Federal University Dutsin-Ma, PMB 5001, Katsina State, Nigeria
[2]Department of Chemistry, University of Ilorin, PMB 1515, Ilorin, Kwara State, Nigeria
[3]Department of Chemistry, Gombe State, PMB 127, Gombe, Gombe State, Nigeria
Corresponding Email: myusuf15@fudutsinma.edu.ng, Tel: +2348105057703,

ABSTRACT
Metal complexes drew the attention of scientists searching for more potent antibiotics than those currently in use. This is conceivable because many drugs possess modified pharmacological and toxicological properties when they appear in the form of metal complexes. The study of biological materials containing metal atoms has also progressed rapidly. The field of bioinorganic chemistry which deal with study of metal complexes in biological system has open a new horizon for scientific research in coordination chemistry, some metal complexes of mixed ligands drugs were synthesized by reacting the metals with the ligands in a 1:1:1 ratio the structures of the complexes were investigated by testing their melting point, conductivity, elemental analysis, FTIR, electronic absorption and some other spectroscopic analytical techniques. The sharp melting point of the complexes signified the purity and chelation in the complexes, and the low conductivity values showed the complexes are non-electrolytes. The FTIR result of the complexes shows new peaks at the fingerprint region (700 – 400 cm-1) signifying new bonding to the metal ion with a different point of chelation. The UV-Visible spectra of the complexes revealed various absorption bands for the different types of electronic transitions that exist in the ultraviolet-visible region for the complexes. The metal complexes were screened for different applications/activity using different bacteria and fungi isolate including, klebsiella oxytoca, salmonella enterica, staphylococcus aureus and pseudomonas aeruginosa for antibacterial studies while candida albacore and aspergillus niger were used for antifungal test, some other applications include; anticancer agent, anti-inflammatory, antidiabetic, anti-hypertensive and covid-19 drugs, the complexes showed high efficacy when compared with the free ligands.

Keywords:
Metal complex,
Biological Application,
Ligands and Characterization

INTRODUCTION

Scientists looking for drugs with greater potency than those currently on the market were interested in metal complexes of antibiotics (Fazary *et al.,* 2016). This makes sense because many medications that exist as metal complexes have altered pharmacological and toxicological characteristics (Eugene-O et al., 2020). According to Lee et al. (2003), research on biological materials containing metal atoms has also advanced quickly. The study of metal complexes in biological systems, or bioinorganic chemistry, has expanded the field of coordination chemistry research (Fred Basolo, 2003). One effective tactic to stop the spread of antibiotic-resistant strains of bacteria is to combine antibiotics (Eugene-O. et al., 2020). In medicine, antibiotic-metal ion complexes have exciting prospects. Fundamentally, because of chelation, which lessens the polarity of the metal atom, metal complexes are more effective than free ligands (Ii Of, & Vitamins, 2015); (Hutchings et al., 2020). The use of metal drugs allows for low-dose intake into the body, enhancement of bioavailability, and benefit from the pharmaceutical effects of both ligand antibiotics and metal ions (Eugene, 2020). The development of anti-infective drugs and the underlying concept of chemotherapy, to a great extent, is accredited to Paul Ehrlich, who developed the synthetic

arsenic-based pro-drugs salvarsan (salvation arsenic) (Hutchings *et al.,* 2020).

Metal Complex

A metal complex is made up of a metal atom that is linked to many ligands, which are ions or molecules that contain one more pair of electrons that can be shared to form complexes through a coordinate covalent bond. Metal complexes are commonly found in various fields, including chemistry, biology, and material science. They have diverse applications, such as catalysis, medicine, for example, in chemotherapy, and even in the design of new materials with specific properties. The study of metal complexes is a crucial area in inorganic chemistry that explores the interactions between metal ions and ligand and their impact on the properties and behavior of these compounds. Metal complexes are paramount in catalysis, material science, photochemistry, and biological systems. They showcase many chemical, optical and magnetic properties (Pindiga & Zulqiflu, 2018).

Roles of Metal Complexes

Essential metal complexes containing a metal or ion (particularly of the 3D transition metals) are involved in many biological mechanisms among which are photosynthesis and oxygen transport in blood (oxy-hemoglobin).

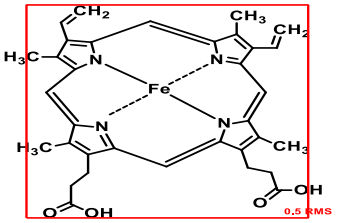


Figure 1: Structure of Hemoglobin

Coordination of some metabolic processes, pathological states, and enzymatic reactions, life processes in plants and animals involve metallic ions, which represent about 5% of the body composition. Many biomolecules (amino acids, peptides, carboxylic acid etc.) can form metal complexes with different stabilities, having biomedical potential. Some drugs have a certain therapeutic effect (e.g., antimicrobial, diuretic, antidepressant) due to the complexation of the metallic ion (Cu^{2+}, Fe^{2+}, Zn^{2+}, Mg^{2+}, etc) paramount for a certain biochemical pathway (Fazary *et al.,* 2016). All salts of the alkali metal ions are soluble in water, and the ions are spectators in most aqueou s reactions (except for those involving the alkali metals in their elemental form. However, these ions play an important role in human physiology. Sodium and potassium ions, for example, are major components of blood plasma and intracellular fluid, respectively, with average concentrations of 0.1 *M*. These electrolytes serve as vital charge carriers in normal cellular function. In disparity, the lithium ion has no known function in human physiology. Since it discovery in 1817(Theodore L. Brown, 2011).

Metal Complexes as Therapeutic Agents

In the last decades, metal complexes have been widely used for applications in the chemical and physical sciences due to their unique electronic and stereochemical character (Duncan & White, 2012). Metals are integral to many physiological processes in the human body. Biologically active metals are referred to as trace metals. Metal complexes have been widely used for applications in the chemical and physical sciences due to their unique electronic and stereochemical properties. For decades the use of metal complexes for medicinal applications has been postulated and demonstrated. The distinct characteristics of metal complexes, including their molecular geometries (that are not readily accessed by organic molecules), as well as their ligand exchange, redox, catalytic, and photophysical reactions, give these compounds the potential to interact and react with biomolecules in unique ways and by distinct mechanisms of action (Johannes *et al.,* 2021). In this, the latent of metal complexes to act as components of bioactive therapeutic compounds is discussed. Recent medicinal chemistry and chemical biology are based on the identification of compounds with well-defined biological effects, so metals have esteem place in medicinal chemistry (Rafique *et al.,* 2010). While typically the realm of organic molecules, metal complexes can offer distinctive properties and can make use of alternative modes of action. While this might be surprising for some readers, metal ions and their coordination complexes have been used since ancient times for medical applications. Although mixtures of compounds have been employed for centuries, the use of the arsenic-containing organometallic complex Arsphenamine, also referred to as Salvarsan, or Compound 606, was the earliest example of a structurally defined metal complex to be isolated and biologically evaluated near the beginning of the 20th century. Metal ions play many essential functions in humans. Deficiency of some metal ions can lead to disease like pernicious anaemia resulting from iron deficiency, growth retardation arising from insufficient dietary zinc, and heart disease in infants owing to copper deficiency. The ability to understand the molecular level and to treat diseases caused by inadequate metal-ion function constitutes an important aspect of medicinal bioinorganic chemistry. Metal ions are required in biology for their role as pharmaceuticals as well as diagnostic agents. Metals are endowed with unique

characteristics that include redox activity, variable coordination modes, and reactivity towards organic substrates. Due to their reactivity, metals are tightly regulated under normal conditions and aberrant metal ion concentrations are associated with various pathological disorders, including cancer. For these reasons, coordination complexes, either as drugs or pro-drugs, become very attractive probes in medicinal chemistry (Sodhi, 2019). In nature, many biological systems make extensive use of metal ions, such as zinc and copper, which play critical roles in the normal functioning of organisms. Transition metals such as copper, iron, and manganese, among others, are involved in multiple biological processes, from electron transfer to catalysis to structural roles, and are frequently associated with active sites of proteins and enzymes. However, deregulations of some of these essential metals during normal biochemical processing have been implicated in the development of various pathological disorders, such as cancer. These cellular functions only require the "trace metals" in miniscule but tightly regulated amounts. Research has shown substantial advancement in utilization of transition metal complexes as drugs to treat several human diseases (Sodhi, 2019).

Metal Complexes as Antimicrobial Agent

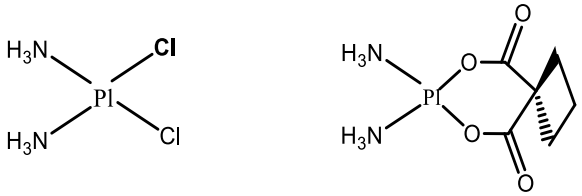
Metals have been used as antimicrobial agents since antiquity, but throughout most of history their modes of action have remained unclear. Recent studies indicate that different metals cause discrete and distinct types of injuries to microbial cells as a result of oxidative stress, protein dysfunction or membrane damage. Here, we describe the chemical and toxicological principles that underlie the antimicrobial activity of metals and discuss the preferences of metal atoms for specific microbial targets. Interdisciplinary research is advancing not only our understanding of metal toxicity but also the design of metal-based compounds for use as antimicrobial agents and alternatives to antibiotics (Obaleye *et al.,* 2011). Many metal complexes have powerful antifungal activities and are already in common day to day use such as silver derma (Silver complex of sulfadiazine) and Flammazine (Zinc complex of silver diazine). Navarro *et al,* (2001) synthesized and characterized complexes of Copper (II) and Gold (I) with Clotrimazole and ketoconazole. It was found out that the ligands coordinated to Gold through imidazole N (1) atom of each ligand with linear structure. The clotrimazole and ketoconazole coordinated to copper (II) through N (3) of the ligand atom with square planar structure. The new compounds were tested for *in vitro* activity against cultures of *epimastigotes* of *trypanosomacruzi*. At concentration equivalent to 10.6M of total clotrimazole and ketoconazole in dimethyl sulfoxide. All the complexes exhibited higher inhibitory activity than their respective parental compounds. Bankole *et al., (*1979) reported the synthesis of organosilicon derivatives of p-aminosalicylic, salicylic and benzoic acids. It was discovered that the presence of silicon in the p-aminosalicyclic acid- silicon complex- prolonged and increased the antitubercular activity of p-amino salicyclic acid in the body (Obaleye *et al.,* 2011). The metal complexes of antibiotics play a significant role in medicinal chemistry and the related bioprocesses in the human physiological system. The pharmacological behavior of antibiotics depends upon metal coordination/complexation (Khurana *et al.,* 2021).

Metal Complexes as Anticancer Agent

About 10 million fatalities were recorded worldwide in 2020 due to cancer and statistical projections estimate the number to increase by 60% in 2040. With such a substantial rise in the global cancer burden, the disease will continue to impose a huge socio-economic burden on society. Currently, the most widely used clinical treatment modality is cytotoxic chemotherapy using platinum drugs which is used to treat variety of cancers. Despite its clinical success, critical challenges like resistance, off-target side effects and cancer variability often reduce its overall therapeutic efficiency. These challenges require faster diagnosis, simultaneous therapy and a more personalized approach toward cancer management. To this end, small-molecule 'theranostic' agents have presented a viable solution combining diagnosis and therapy into a single platform. Cancer is a noncommunicable disease which is characterized by the development of abnormal cells that divide uncontrollably and have the ability to spread throughout the human body. Despite significant advances in the understanding of cancer cell biology and anticancer drug development, cancer remains as one of the leading causes of morbidity and mortality worldwide. With 10 million worldwide deaths in 2020, it became the second leading cause of death after cardiovascular diseases. As per the prediction, the number of people diagnosed with cancer will increase by 60% within next two decades. With the rapid rise in global cancer burden, the disease continues to impose a huge socio-economic burden on society.(Obaleye *et al.,* 2012) However, chemotherapy with cytotoxic small-molecule drugs remains the mainstay of cancer treatment. Chemotherapeutic drugs are effective against a variety of cancers and can also be employed for the treatment of metastatic cancers. Small-molecule based chemotherapeutics also tend to be affordable as compared to some of the other treatment modalities. Doxorubicin, Gemcitabine and Bleomycin are some examples of small-molecule based chemotherapeutic drugs which are used clinically. Platinum (Pt) drugs cisplatin, carboplatin and oxaliplatin are used as frontline chemotherapeutics for treatment of many different types of cancers. Approximately 50% of cancer patients who

are receiving chemotherapy are being treated with Pt drugs. Resistance is often encountered during the treatment cycle which renders the drug ineffective and finally leads to treatment failure.

Some of the Discovered Anticancer Drugs



Cisplatin Carboplatin

Figure 2: Structures of cisplatin and carboplatin

REVIEW

(Eugene *et al.,* 2020) reported the synthesis of Cu (II), Co (II), Mn (II), Ni (II), and Zn (II) of ofloxacin and metronidazole metal complexes. The complexes gave varying shade of colored complexes in low to moderate yield. The complexes are reported to have low value of conductivity. The complexes;$[Cu(OFL)(MET)(H_2O)_2]$ $[Ni(OFL)(MET)(H_2O)_2]$ $[Co(OFL)(MET)(H2O)_2]$ $[Mn(OFL)(MET)(H_2O)_2]$ and $[Zn(OFL)(MET)(H2O)_2]$ were characterized using IR Spectroscopy, UV-Visible spectroscopy and magnetic moment, From the analytical and spectral data, the ligands coordinated in bidentate form to the metal ions; ofloxacin through the carboxy group oxygen and the pyridine carbonyl oxygen and metronidazole via the imidazole nitrogen atom and the hydroxyl oxygen atom of the terminal ethanol group to give octahedral geometries. Antimicrobial screening showed that coordination of the mixed antibiotic ligands to the metals leads to enhancement of their antimicrobial activities with the cobalt complex $[Co(OFL)(MET)(H_2O)_2]$ showing the best activity at the concentration of 100 µg/ml.

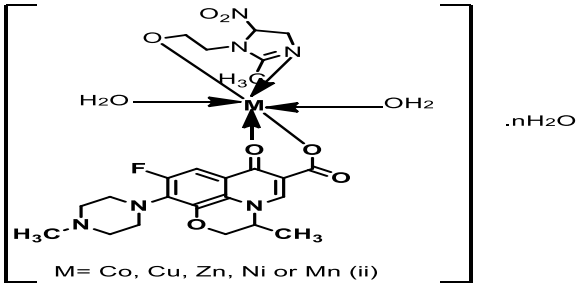


Figure 3: Proposed structure by Eugene *et al.,* 2020

Lekaa and Al-Noor, 2020 reported a synthesis of Schiff base of HL synthesized from amoxicillin drug and 4-Chlorobenzophenone, subsequently Cr (III), Fe (III), Co (II), Ni (II), Cu (II), Cd (II) and Hg (II) mixed ligands complexes of Schiff base and Nicotinamide, the synthesized ligand and its complexes are characterized by 1HNMR, 13CNMR and thermal analysis for HL ligand, FTIR, UV-visible, molar conductance, CHN analysis, magnetic susceptivity and atomic absorption. Octahedral geometries have been suggested for all complexes. All compounds under study were subjected to antimicrobial activity test against four type of bacteria such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Bacilli subtilis* in nutrient agar. The results show the linked of HL format with metal ions through the nitrogen of Schiff base group and oxygen β- lactam and carboxylate ion groups while Nicotinamide coordinates through nitrogen atom of pyridine ring. Electronic spectra and magnetic susceptibility of prepared complexes show that the shape of complexes is octahedral geometry, The biological test of complexes has been shown a various activity against different type of bacteria.

Ahmed E. Fazary *et al.,* (2016) reported the bioactivities of novel metal complexes involving B vitamins and glycine. The complexes were formed between a metal ion of (Cu(II), Cd(II), Mn(II), Fe(III), Ni(II), Pb(II)) and vitamins (B 3 and B 9) as primary ligands, and glycine as secondary ligand. Melting points, conductivities, and magnetic susceptibilities of the synthesized complexes were determined and the complexes were subjected to elemental analyses. The presence of coordination water molecules in the complex was also supported by TG/DTG thermal analysis. Full elucidation of the molecular structures for the synthesized mixed ligand complexes were confirmed using detailed spectroscopic IR, 1H-NMR, 13C-NMR, and XRD techniques. In addition, cytotoxic and antioxidant activities of the synthesized solid complexes were tested to evaluate their bioactivities, most of the synthesized metal complexes showed moderate cytotoxic and antioxidant activities.

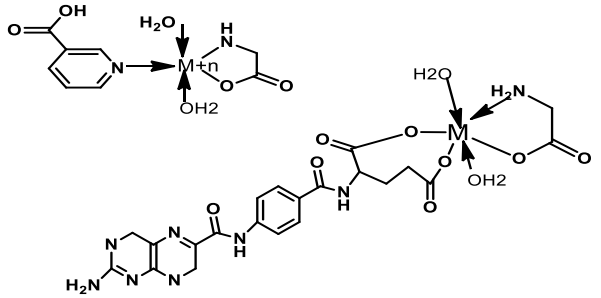


Figure 4: Proposed structure by Fazary *et al.,* 2016

Sharfaddin *et al.,* (2021) reported the synthesized transition metal complexes of sulfaclozine (SCZ) with Cu (II), Co (II), Ni (II), Zn (II), and Fe (II). The chemical

structure of each complex was characterized using elemental analysis (CHN), IR spectroscopy, UV–Visible spectroscopy, thermogravimetric analysis (TGA), and electronic paramagnetic resonance (EPR) spectroscopy. IR spectra indicated that the donor atoms were one sulfonyl oxygen atom and one pyrazine nitrogen atom, which associated with the metal ions to form a stable hexagonal coordination ring. The metal–ligand stability constant (Kf) revealed that Cu (II) and Ni (II) have good coordination stability among the metal compounds. Theoretical studies using DFT/B3LYP were performed to further validate the proposed structures. The obtained results indicated that Cu (II) has a trigonal bipyramidal geometry, whereas Fe (II), Co (II), and Ni (II) have an octahedral structure, while Zn (II) has a tetrahedral arrangement. The bio-activities of the characterized complexes were evaluated using DNA binding titration and molecular docking. The binding constant values for the metal complexes were promising, with a maximum value for the copper metal ion complex, which was 9 × 105 M-1. Molecular docking simulations were also carried out to evaluate the interaction strength and properties of the synthesized metal complexes with both DNA and selected cancer-relevant proteins. These results were supported by in vitro cytotoxicity assays showing that the Cu (II) and Ni (II) complexes display promising antitumor activity against colon and breast cancer cell lines, The experimental cytotoxicity results presented a moderated anticancer strength of the Cu–SCZ compound. Finally, we suggest as a future perspective to study the activity of these complexes or other metal complexes by external inducements such as light or oxidizing materials.

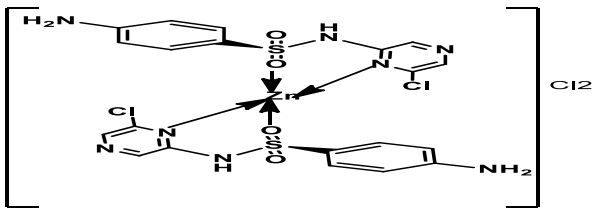


Figure 5: Proposed Structure by Sharfalddin *et al.*, 2021

Obaleye *et al.,* (2021) reported the synthesis characterization, Invitro Anti-inflammatory and antimicrobial screening of metal (II) complexes OF Mn (II), Co (II), Ni (II), Cu (II) and Zn (II), after establishing the *identity* of the complexes, the anti-inflammatory activity reveal the [Cu-B] complex to be the best with a 45.17% inhibition of a concentration of 200ppm, thus suggesting it as a promising antidote in metal chemotherapy.

Obaleye *et al.,* (2012) latter reported a remarkable work carried out by Biot and co-workers which they inserted ferrocene (organometallic compound) in to the molecular structure of some antimalaria drugs. Since the parasite need iron for it development inside the red blood cells. (Biot *et al.,* 1999) made attempt to insert a ferrocenyl group in to the side chain of chloroquine, thus producing a hybrid compound called ferroquine(Obaleye *et al.,* 2012)

Ferroquine synthesized by them is found to be more potent in mice than chloroquine. Test have shown that ferroquine is active against both chloroquine sensitive and chloroquine resistance strains of plasmodium and that its safe and effective in mice as well as being non mutanogenic.(Obaleye *et al.,* 2012)

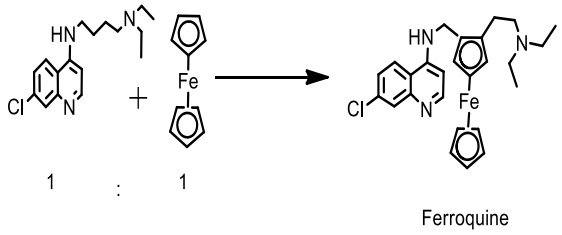


Figure 6: Reported Structure by (Obaleye *et al.*, 2012)

Nedeljkovic *et al.,* (2021) reported the interaction of bio-essential metal with quinolone antibiotic, structural features of copper (II), zinc (II) and cobalt (II)-quinolone complexes were presented. Antimicrobial and antitumor activity as well as the binding affinity of selected coordination compounds to calf-thymus DNA, bovine and human serum albumins are also investigated. Further perspectives related to the choice of the metal ion, quinolone ligand and various co-ligands are also discussed to clarify and predict the main factors that contribute to biological activity of the bio essential metal complexes. The usage of the novel quinolone members such as fourth-generation quinolones as ligands may lead to the complexes with enhanced biological activity (Nedeljković et al., 2021).

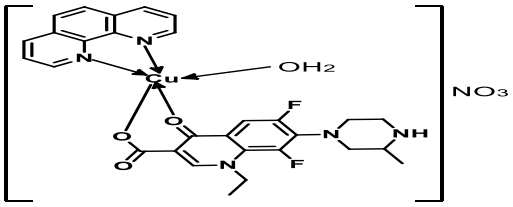


Figure 7: Proposed structure by Nedelkovic *et al.*, 2021

Lewis *et al.,* 2023 reported the interaction of bio essential metal with quinolone antibiotic of novel Ga (III) polypyridyl catecholate complexes Ga(III) polypyridyl catecholate complexes of type $[Ga(bipy)_2(O,O)](NO_3)$ or $[Ga(phen)_2(O,O)](NO3)$ respectively were readily

synthesized on reaction of $Ga(NO_3)_3$ in methanol with 1 equivalent of catecholate ligand (CafA) and then 2 equivalents of either bipyridine or phenanthrene. The complexes were characterized in full including by X-ray crystallography, which established that the catecholate ligands coordinate the Ga(III) centers in a bidentate manner via the two deprotonated hydroxy groups. All Ga(III) complexes exhibited good in vitro antibacterial activity against the Gram-negative pathogenic bacteria *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The complexes were inactive against the Gram-positive pathogenic bacteria *Staphylococcus aureus* including against a methicillin resistant *Staphylococcus aureus strain* (MRSA). $[Ga(bipy)2(2,3\text{-}DHBA\text{-}2H)](NO_3)\cdot 1.5H_2O$ was shown to be non-toxic in vivo in larvae of Galleria mellonella at doses up to 2000 µg mL−1 and to offer protection at doses of 100 and 250 µg mL−1 at 48 and 96 h to larvae infected with P. aeruginosa. All Ga(III) complexes exhibited good in vitro antibacterial activity against the Gram-negative pathogenic bacteria *E. coli, K. pneumoniae* and *P. aeruginosa*. This study builds on previous reports, which associated Ga-based compounds with good antibacterial activity against *P. aeruginosa*. Specifically lead Ga(III) polypyridyl catecholate complexes, $[Ga(bipy)2(2,3\text{-}DHBA\text{-}2H)](NO_3)$ (1), was shown to be non-toxic in vivo in larvae of G. mellonella at doses up to 2000 µg mL−1 and to offer protection at doses of 100 and 250 µg mL−1 at 48 and 96 h to larvae infected with P. aeruginosa. P. aeruginosa is a major cause of lung infections in people living with cystic fibrosis (CF).(O'Ferrall, *et al.,* 2023).

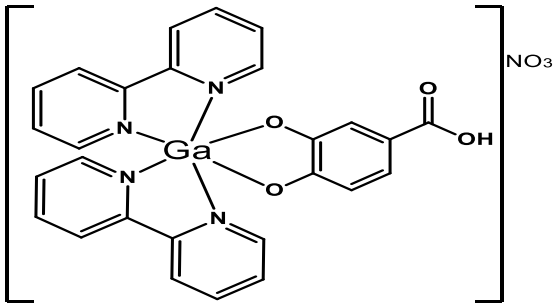


Figure 8: Proposed structure by O'Ferrall *et al.*, 2023

(Tella et al., 2016) reported the Synthesis characterization, ctystal structure and antimicrobial studies of a novel Cu (II) complex base itanomic acid and nicotinamide A novel complex was synthesized from Cu (II), nicotinamide and itaconic acid and is formulated as $[Cu(C_5H_4O_4)_2(C_6H_6N_2O)_2(H_2O)_2 \quad 2(H_2O)]$. The compound was characterized by elemental analysis, FTIR spectroscopy, UV-Vis and single crystal X-ray diffraction. The complex crystallizes in the triclinic P-1 space group, The octahedral geometry around the copper (II) ion is of the form CuN_2O4 consisting of two molecules of nicotinamide acting as monodentate ligand through the nitrogen atoms, two molecules itaconate ligand and two coordinated water molecules each coordinating through the oxygen atoms. The antimicrobial study of the synthesized complex was investigated and showed higher antibacterial activity against all the organisms comparing with Copper (II) nicotinamide and Copper (II) itaconate. These studies may lead to the discovery of new chemotherapeutic agents that are metal-based.

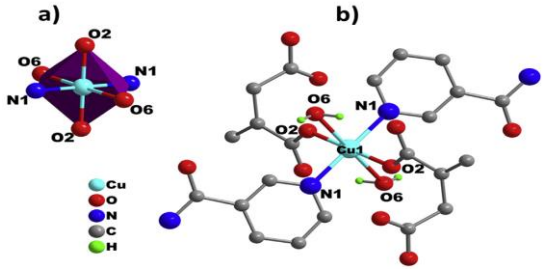


Figure 9: Crystal structure by Tella *et al.*, 2016

Hassani *et al.,* (2016) reported synthesis, characterization, theoretical studies and bioactivity of Co(ii), Ni(ii), Cu(ii), Pd(ii), Pt(iv) and Cd(ii) complexes with bidentate 3-{[(z)-1h-pyrrol-3-ylmethylidene]amino}-2-thioxoimidazolidin-4-one, the complexes of Co(II), Ni(II), Cu(II), Pd(II), Pt(IV) and Cd(II) were synthesized with new heterocyclic ligand [3-{[(Z)-1H-pyrrol-3-ylmethylidene]amino}-2-thioxoimidazolidin-4-one]. This ligand was characterized by C.H.N.S analysis, FTIR, UV-Vis, 1H NMR, 13C NMR and mass spectral analysis, the synthesized complexes were identified and their geometrical were suggested in solid state by using (FTIR) and (UV-Vis) spectroscopy, elemental analysis (C.H.N.S), flame atomic absorption technique, in addition to magnetic susceptibility and conductivity measurements, The free ligand (L) and its metal complexes show significant antimicrobial activity, all the complexes are found to be effective than the free ligand. The free ligand (L) and its metal complexes show significant antimicrobial activity.

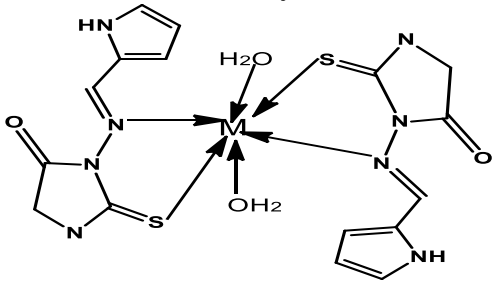
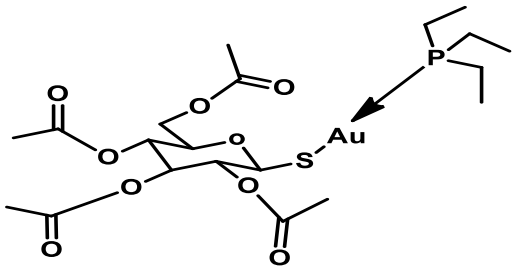


Figure 10: Proposed structure by Hassani *et al.*, 2016

(Ashiq *et al.,* 2021) reported metallodrugs, such as a gold drug called auranofin seems a potential candidate for COVID-19, yet few other approved metal complexes are also creditable. He further highlighted that; chemically diverse libraries of inorganic compounds can be monitored to identify molecules with efficient activity against COVID-19. Though there is no specific treatment available for the COVID-19, and in this regard, exploration of the metal complexes can be proved fruitful. It is suggested that the activity of the metal complexes should be appraised by using appropriate in vitro and in vivo models.



Auranofin

Figure 11: Reported structure of Auranofin as covid-19 drug

CONCLUSION

Metal complexes' distinct chemical and biological characteristics have made them attractive therapeutic candidates. In ways that conventional organic molecules cannot, they can interact with biological targets thanks to their capacity to coordinate with a variety of ligands. This adaptability has been used in many different biomedical applications. A number of metal complexes are noteworthy for their strong antibacterial properties, which provide fresh approaches to the problem of growing antibiotic resistance. Their capacity to imitate or affect insulin action and glucose metabolism is associated with their antidiabetic qualities. Metal complexes have the potential to be anti-inflammatory drugs because they reduce inflammation by altering oxidative stress and inflammatory signalling pathways.

Additionally, their ability to disrupt enzymes or receptors involved in blood pressure regulation is what makes them antihypertensive agents. Perhaps most remarkably, a number of studies conducted in the wake of the COVID-19 pandemic have suggested that some metal-based medications may have antiviral activity against SARS-CoV-2, either by preventing viral replication or altering host immune responses. Given these many uses, metal complexes provide a platform for focused, effective, and possibly less harmful treatments in addition to being essential in the development of next-generation therapies. Further investigation and advancement in this area may result in innovations to address some of the most important health issues of our day.

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