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Various metal complexes and their biological implications

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Abstract
Transition metals with various oxidation states are proved to be very crucial biochemical components that perform several indispensable biochemical processes for living beings. They help to make a strong interaction with various numbers of high anionic chelating ligands. In the past, metal-based compounds were widely used in the treatment of disease conditions, but the lack of clear distinction between the therapeutic and toxic doses was a major challenge. This activity of transition metals in complex led to the current development of drugs molecules which are based on charge density of metals and are considered to be potent molecules for pharmacotherapy actions. It possesses preclinical pharmacological screenings like anti-microbial action, anti-inflammatory affect and anti-tumor power of newly synthetic various transition metal ligands complexes. Metal ligands complex possess antibacterial activity that help to get rid from antibiotic resistance is a growing threat in the treatment of bacterial diseases. Platinum drugs, such as cisplatin, carboplatin and oxaliplatin, are the mainstay of the metal-based compounds in the treatment of cancer. In line with this, many more metal-based compounds have been synthesized by redesigning the existing chemical structure through ligand substitution or building the entire new compound with enhanced safety and cytotoxic profile. However, because of increased emphasis on the clinical relevance of metal-based complexes, a few of these drugs are currently on clinical trial and many more are awaiting ethical approval to join the trial. The present article illustrates the role of metals and the recent progress in the field of medicinal bioinorganic chemistry regarding innovative metal-based drugs and their application.

Keywords: Metal ions, chelating agents, ligands, pharmacology, medicinal chemistry

Introduction
Metal ions with diverse charge density exhibits positive roles in biological systems concerned with the medical therapy or disease diagnosis in pharmaceutical world (Li *et al*., 2022) [19]. The introduction of diverse charge density metal ions with binding capabilities into a living world open a new era for the treatment of various diseases is one of the practical applications of bioinorganic chemistry (Muravev *et al*., 2022) [54]. A broad series of therapeutics actions such as antifungal, antibacterial, antioxidants anticancer and antiretroviral actions are exhibited by the nitrogen (N) atom containing ligands and their diverse charge density metal complexes (Mondal *et al*., 2022). They have a remarkable ability of DNA-binding agents. Predominantly, transition metal with diverse charge density centers is particularly attractive moieties for reversible identification of anionic nucleic acids (Lachowicz *et al*., 2022) [40]. Besides, they exhibit diverse electrochemical gradient or photophysical activities, thereby enhanced the binding capacity. These properties of metal complexes made it good fluorescent markers to DNA or nucleic acid foot printing molecules, to electrochemical gradient probes. Platinum drugs, such as carboplatin, cisplatin and oxaliplatin, are the mainstay of the metal-based compounds in the treatment of cancer (Zhang *et al*., 2022) [83]. Scientist's works to improve and develop diverse charge density metal-based compounds and platinum based complexes whose drugs mechanism of action is vary from known cisplatin drug (Ghosh *et al*., 2019) [25]. In order to achieve many more metal-based drug molecules synthesis by redesigning the existing molecular structure through substitution by different ligands or to build the whole new molecule with improved safety and cytotoxic potency (Yuan *et al*., 2022) [30]. However, because of increased emphasis on the clinical relevance of metal-based complexes, a few of these drugs molecules are currently on clinical trial and many more are awaiting ethical committee approval to join the trial. The synthesis of low cost first-row coordination complex compounds as efficient DNA motif binders with potent cytotoxic activity (Netalkar *et al*., 2022) [55].

The pharmacological actions of the first row transition with diverse density metal coordination compounds V(IV), Ni(II), Zn(II), Co(II) and Cu(II) complexes made it essential molecules present in the living cellular environment (Sheikh *et al*., 2013) [70]. These trace elements are a component of metalloproteins present in biological systems together with iron. Recently these metal ions with diverse charge density are used as drug molecules against a various diseases, ranging from antibacterial and antifungal to antitumor actions. These metal ions are known to be very potent molecules because of their less toxic nature which can be further reduced through coordinately binds with the ligands. The beneficial properties of these amino acids, N-heterocycles (1, 10 Phenanthroline, Bipyridine) and pyrazolones made it an ideal drug. The amino acids are the principal components of human body and the drug environment is similar to functions of amino acids in the body, provides a less toxic environment with high affectivity. In addition to that, the N containing heterocycles and pyrazolones molecules as donor or ligands alter the environment of the coordinated complex in such a way that their lipophilicity or non-polarity rises which play a major role in drug designing (Selvaganapathy and Natarajan, 2016) [67]. The chosen ligands and their characteristic are discussed in detail in the further sections. Thus, present review presents an overview on new approach to metal-based drug design and molecular target in various ailments.

Chelation and its association with diverse biological processes open a new path for designing novel/new therapeutic techniques meant for procurement of worldwide issue (Corce *et al*., 2016) [12]. These ligands are not only used in the expansion of coordination chemistry but also find applications in catalysis, optical and bioinorganic chemistry (Weberg *et al*., 2022) [78].

Bioactive chelating ligands

ONS donors: The Schiff bases, also called 'a privileged ligands' are the chemical compounds having azomethine functional group with general formula RHC=N–R', where R and R'=Alkyl, cyclo alkyl, aryl, or heterocyclic groups (Figure 1**)**. The C=N linkage is very crucial for the biological activity (Kumar *et al*., 2022) [9]. Their metal chelates possess synthetic flexibility, sensitivity and selectivity toward diverse metal ions (Liu *et al*., 2022) [19]. They have capability to stabilize different metals that too in various oxidation states. Sometimes, other donor atoms such as O and S are present in the backbones of the various ligands for coordinating to transition diverse charge density metal ions in the various modes to form the stable metal complexes (Rakhtshah *et al*., 2022) [61]. Aromatic Schiff bases exhibit more stablility as compare to Aliphatic Schiff bases because they possesses effective conjugation in condensation reactions, carbon of ketone contributes electron or charge density to the molecule azomethine carbon that makes the ketone less electrophilic to form very stable complexes with diverse charge density transition metal ions (Catanescu *et al*., 2001) [8].

Additional functional groups like –OH, $–NH_2$ or –SH serve as mixed-donor ligands that participate in bi-, tri-, tetra- and higher coordination modes (Ibrahim *et al*., 2021) [31]. These bases are classified into bidentate, tridentate, or polydentate ligands. The research findings demonstrate that the therapeutic and pharmacological actions depend on the type of metal ion, organic nature scaffold and specific DNA (anionic) binding motifs. Metal stabilization or chelation is an outstanding method to enhance the lipophilic (non-polar) nature of the organic moiety (Kim *et al*., 2017) [74]. Some ligands have become have become an important class that might improve the bioactivity profiles and causes structure-selective binding agents for nucleic acids. Schiff bases have a chelating structure and are in demand since they can be prepared directly and are moderate electron donors with easily tunable electronic and steric effects thus being versatile and one of the modest classes of biologically active agents. These have antimicrobial (Deswal *et al*., 2022) [16], anti-tuberculosis (Chandel *et al*., 2022) [9], antitumour activity (Chen *et al*., 2022; Sethi *et al*., 2019) [10, 68], anticonvulsant (Llanos *et al*., 2022) [45], anti-inflammatory (Braga *et al*., 2022) [6], anti-HIV (Murali *et al*., 2022) [53], antihelmintic (Larsen *et al*., 2015) [41] and cardiovascular (Makki *et al*., 2013) [48] activities and anti-carcinogenic properties (Fujiki *et al*., 2022). Currently a new copper(II) Schiff base complexes based SOD mimics with various nitrogen heteroatomic rings such as imidazole, pyrazole, 1,10-phenanthroline, 2,2'-bipyridine, pyridine etc. which possess remarkable DNA binding tendency (Marimuthu *et al*., 2022) [50]. These complexes have been evaluated for their DNA nuclease, antimicrobial and antitumor actions. They have a potency to develop an excellent chemotherapeutic potential. A Bis[N-(*p*-tolyl)imino] acenaphthene mixed coordinated ligand with Cu(II) state and also with novel cisplatin-based Cu(II) ion and Zn(II) ion complexes having Knoevenagel condensate Schiff base ligands are treated against Ehrlich ascites carcinoma (EAC) cells in Swiss albinic mice (Selvaganapathy *et al*., 2016) [67]. These compounds increased the life span, decreased tumors size of haematological components such as haemoglobin content, RBC and WBC counts towards normal (Milind *et al*., 2013) [52]. The macrophages are found to be developed in mice when treated with the compounds alone. Hence, these compounds can be considered as potent antitumor agents.

Amino acids: Amino acids derived Schiff bases are found to be very effective metal chelators (Ahmed *et al*., 2022) [1]. Their metal ligands complexes are models for a diversity of important biological systems (Abdel *et al*., 2022) [1]. They are the key intermediates in a number of metabolic reactions such as decarboxylation, transamination, racemization and C-C bond cleavage (Gupta *et al*., 2022) [28]. The reduced Schiff bases having a variety of amino acid based derivatives are potent multidentate ligands for creating attractive multidimensional framework leading to the establishment of surprising and remarkable structures (Zhu *et al*., 2022) [80]. Longer chains are preferred because long chain helps in inter/ intrastrand cross linking property with DNA while imparting lesser torsion strain making it a thermodynamically favored process. Amino acids can have a coordinating property through their amino (NH_2) and carboxylate (COO–) groups (Rottinghaus *et al*., 2022) [64]. For sulfur-containing amino acids, the SH group confers a more versatile coordination activity toward heavy metal ions. The –SH (sulfhydryl), $–NH_2$ (amino) and –COO– (carboxylate) groups are the possible coordination sites for the complexation processes. Sequestration of toxic heavy metal (Riyazuddin *et al*., 2021) [63].ions and obtaining safer drugs or antidotes for metal poisoning by complexation is a very promising field. As ligands, amino acids also act as ambidentate so that they can bind through (S, N), (N, O) or (S, O) donor atoms (Fabbrizzi *et al*., 2003) [21]. Due to the acidobasic behaviour, amino acids

are considered as ampholytes which means that with the negatively charged –COO- group or positively charged -NH_3^+ can behave outwardly as acids or as bases. These bound amino acids may be permanently or temporarily incorporated into the proteins or other possible biochemical functional structures (Kaura and Milind, 2015) [36]. Amino acids generated by modifying the known biogenic amino acids including dopamine neurotransmitter, histamine, noradrenaline hormone, ornithine, taurine amino acid, or growth factors spermine, sarcosine and spermidine (Su-Yeon *et al*., 2017) [74]. Several Schiff base metal coordinate complexes that are the derivatives of salicylaldehyde molecule, amino acid and reduced salicylidene amino acid, have been proven to be efficient DNA cleavers and as novel potent action of tumor chemotherapeutic & tumor radio-imaging agents. Recently, Singh *et al*., 2012 [71] have prepared Co (II), Ni (II) and Cu (II) complexes of 2-nitrobenzaldehyde–glycine and 2-nitrobenzaldehyde–methionine and evaluated their coordination properties. They evaluated the antimicrobial potential of these complexes against the growth of bacteria *in vitro*. They are found to be efficient antimicrobial agents (Sethi *et al*., 2014, Cucu *et al*., 2022) [68, 13].

Pyrazolones

Pyrazolones have been studied extensively due to their pharmaceutical properties (Ibrahim *et al*., 2022) [32] It is a 5-membered lactam ring which contains two nitrogen and a ketone in the same molecule and is an active moiety in pharmacological activity such as anti-inflammatory agents, analgesics and arthritis treatment (Dong *et al*., 2022) [19]. It is an active moiety as the pharmaceutical ingredient, especially in non-steroidal anti-inflammatory drugs (NSAID) and is used in the cure of arthritis and other musculoskeletal and joint disorders (Prabhakaran *et al*., 2021). Anticancer activity has also been reported. It is well known from the literature that 4-aminoantipyrine (pyrazolone derivative) is a potent reagent due to its variety of applications. Jayabalakrishnan and his associates have recently synthesized a Schiff base complex of copper(I) ion with 5-dimethyl-2-phenyl-4-[(pyridin-2-ylmethylene)- amino]-1, 2-dihydro-pyrazol-3-one and investigated its anionic DNA binding propensity, nuclease, radical-scavenging and cytotoxic activities which reveal that it can act as effective anti-cancer agent (Sathiyaraj *et al*., 2013) [66].

Nitrogen heterocycles: They have potential to readily fit in more than two donor atoms or two or more aromatic ring having N-containing heterocycles/alkaloids into one single molecule has afforded access to numerous stabilizing chelating and bridging ligands (Thansandote *et al*., 2009) [75]. These bridging ligands have high potency due to formation of multinuclear metallo-supramolecular assemblies, with various desirable structures and chemical properties. The stabilizing effect of ring formation or chelating to multiple metal atoms can be attained through the introduction of bidentate ligands that form either a 5- or 6 membered stable chelate ring with each coordinated metal centre (Zhao *et al*., 2022) [30].

1, 10-phenanthroline (phen) a classic nitrogen heterocycle/ chelating bidentate ligand for metal ions, has played a vital role in the progress of coordination chemistry. Phen is a rigid planar 2 dimensional, hydrophobic nature, low charge density heteroaromatic system, whose N atoms are so placed to act cooperatively in potive binding (Bencini *et al*., 2010) [5]. These structural features convey its coordination ability towards metal ions. Phen easily forms sp^3d^2 hybrid octahedral complexes with first-row transition metal cations in aqueous solution of the type $[M(phen)(H_2O)_4]^{2+}$, $[M(phen)_2(H_2O)_2]^{2+}$ and $[M(phen)_3]^{2+}$ (Qi *et al*., 2003) [60]. It is an appropriate ligand for DNA binding that are able to recognize specific base sequences or luminescent probes. Further, it has shown retardation of growth of a Sarcoma-37 tumor and it inhibits the cell proliferation of Ehrlich ascites. This chelating agent might exhibit better antitumor activity if the hydrophilic groups of the chelating agent are masked by metal ions to form neutral chelate compounds. This would be more permeable through the cell membrane and eventually behave as carriers of antitumor agents. This has been made possible by joining an element of specific recognition, 2, 9-dimethyl-1, 10-phenanthroline with Co (II) metallic center under a hydrothermal condition in the presence of Na_2MoO_4 catalyst. Raman and his coworkers recently synthesized a series of bio-active coordination compounds containing 1, 10-phenanthroline as co-ligand that exhibited the DNA binding properties and cleavage of transition metal (II) complexes. Antiproliferative activity has been carried out recently by his group targeting enzyme protein kinase & anionic DNA molecules by diimine-phthalate complexes. Thus, synthesized complexes have shown a good affinity in targeting the DNA and cyclin dependent kinase-2 molecules.

Bipyridine or 2, 2′-bipyridine is a chelating component. It forms a 5-membered chelate ring which is stable upon coordination of a metal. The 2, 2′-bipyridyl act as a chelating donor site within such bridging ligands providing robust redox stability & relative easiness of functionalization (Kaes *et al*., 2000) [35]. Related bridging ligands that comprise at least two di-2, 2′-pyridylmethyl or amino or N arms have been evaluated to studying metal–metal interactions to study anion–interactions as structural aspect and functional tertiary protein (enzyme) active site (Sumby *et al*., 2011) [73]. A series of Schiff base Cu (II) ion and Zn (II) ion metal complexes having polypyridyl ligands and explored their DNA interactions.

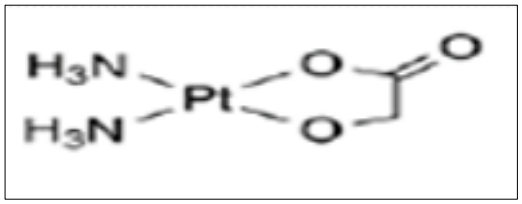
Biological implications

Transition metal chelates have varied coordination geometry, versatile redox, spectral and magnetic properties that play a key role in bio-inorganic chemistry as well as redox enzyme systems and serve as the basis of models for active sites in biologically important compounds (Marimuthu *et al*., 2022) [50]. Redox-active metals generally form reactive oxygen species (ROS) that can be used to induce DNA cleavage.

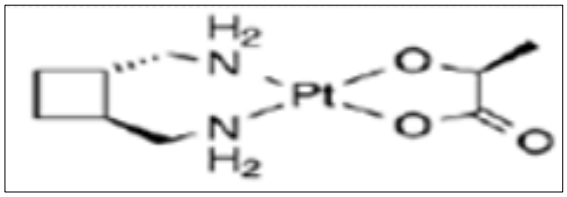
DNA-metal complex interactions

DNA acts as the main intracellular target to develop a new drug for innumerable diseases, especially cancer. The main application is the anti-tumour action of certain heavy metals which bind to DNA and distorting DNA causing cell death (Zhou *et al*., 2001) [85]. There are many binding modes by which the small molecules bind to the DNA which are covalent and non-covalent binding. Cisplatin binds covalently with the DNA thereby restricting its replication (Pil *et al*., 1992) [58]. Among the loosely non-covalent bonds, intercalation process, binding groove and external electrostatic interaction, is the most important. But Cisplatin cures only limited spectrum of cancer (Flrea *et al*., 2011) [22].

To overcome these limitations less toxicity and highly effective metallo drugs like carboplatin and oxaliplatin have been developed. Many research groups have reported the interactions of V (IV), Ni (II), Co (II), Zn (II) and Cu (II) complexes with DNA. Most of them are concentrating only copper Schiff-base complexes (Chen *et al*., 2022) [10] (Table 1).



Anti-cancer: Nedaplatin



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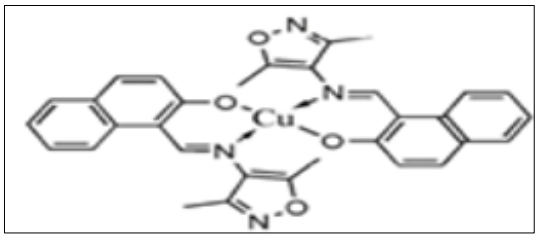
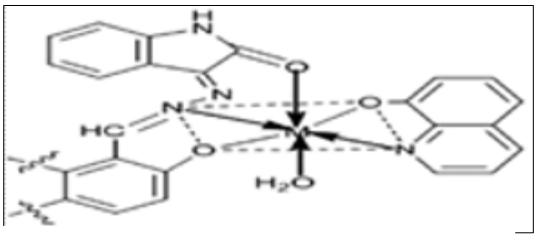
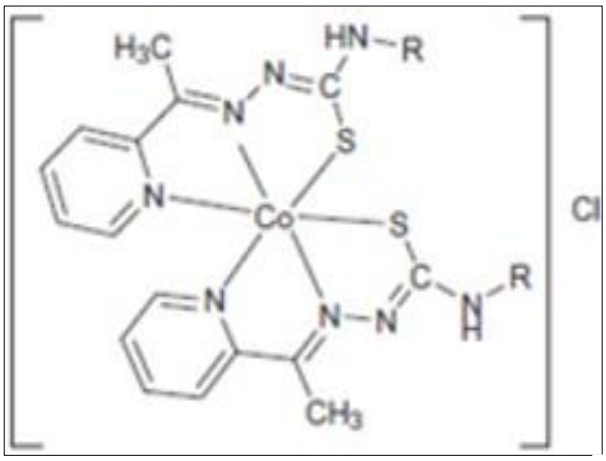


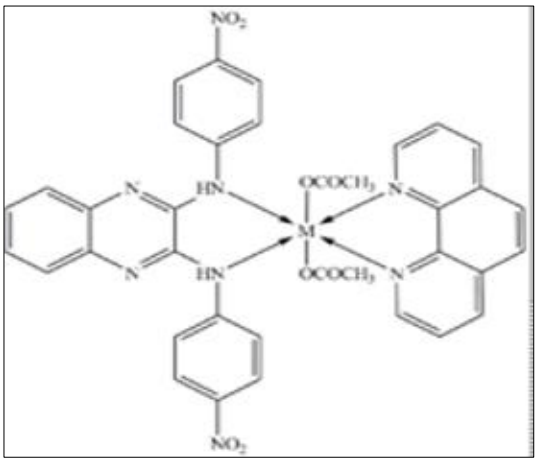
Antimicrobial agent: Copper (II) Complexes with Isoxazole Schiff base (1-((E)-(3.5- dimethylisoxazol-4-ylimino) methyl) naphthalen-2-ol



Antimicrobial agent: M= Co (II), Ni (II), Cu



Anti-inflammatory agent: Co (III) complex of 2-acetylpyrdine N-substituted rhiosemicarbazone



Anti-inflammatory agent: M= Co(II), Ni(II), Cu(II) and Zn(II), Structure of N2, N3-bis (4-nitrophenyl) quinoxaline- 2, 3-diamine based mixed lig and

Fig 1: Structures of some pharmacologically active transitional metal complexes

Cu is found in all biotic system that is a vital trace element in chemical combination, promoting growth and development. It is also significant for the action of several enzymes and proteins act as cofactor involved in $NADPH_2$ and $FADH_2$ production, respiration process and synthesis of DNA, particularly cytochrome oxidase activity, function of superoxide dismutase (SOD), ascorbate oxidase and tyrosinase (Abdou *et al*., 2019) [2]. Positive charge copper is found to bind negative charge DNA with high binding affinity other than any divalent cation, thus promoting oxidation of DNA (Theophanides and Anastassopulou, 2022) [76].

Table 1: Some examples Cu (II) complexes interacting with CT-DNA

S. No.	Complex	References
1.	New copper Schiff-base, derived Kaempferol and polyamines such as ethylenediamine (en) and ligand diethylenetriamine	Yang *et al*., 2012 [79]
2.	Novel copper complexes, found to bind significantly to calf thymus DNA and effectively cleave pBR322 DNA	Gup and Gokce, 2013 [27]
3.	Two new benzimidazole based copper complexes	Hu *et al*., 2022 [42]
4.	Three novel structurally associated copper(II) complexes	Parsekar *et al*., 2022 [56]
5.	Two new copper Schiff-base complexes	Ghasemi *et al*., 2022 [24]

Chemotherapeutic agents

The broad range of coordination numbers and geometries, available redox oxidation states, thermodynamic and kinetic characteristics and intrinsic properties of the cationic metal ion and ligand itself offer the medicinal chemist a large variety of reactivity's to be exploited (Santini *et al*., 2014) [65] (Table 2). Molecules that are approved for clinical could damage DNA, inhibit nucleic acid or anionic precursor biosynthesis thereby blocking DNA synthesis indirectly, or disrupt hormonal stimulation of cell growth as anticancer agents (Milind and Kaura, 2012) [51].

Table 2: Pharmacologically active chemotherapeutic agent

S. NO.	Complex	Action	Reference
1.	[Cu(pyrimol)Cl]	Efficient self-activated DNA, cleavage and cytotoxic effects toward L1210 murine leukemia and A2780 human ovarian carcinoma cell lines	Maheswari *et al*., 2006 [47]
2.	Mixed ligand bis (salicylato) Copper (II) complexes with diimines as co-ligands.	Cytotoxic and antiviral activities	Loganathan *et al*., 2014 [46]
3.	Ternary copper(II) complexes	Strong DNA binding and cleavage and induced apoptosis in cancer cells.	Ramakrishnan *et al*., 2009 [62]
4.	Cu(II) complexes	Cytotoxicity against HeLa (cervical) cancer cell lines	Parsekar *et al*., 2020 [57]
5.	Cu(II) complexes of macrocyclic triamines	Promote the hydrolytic cleavage of plasmid DNA	Itoh *et al*.,1997 [34]
6.	Mixed chelate transition metal-based drugs	Potent antitumor activity	Li *et al*., 2018[43]
7.	[Co(LH)2(NCS)]NO3 and [Co(LH)2(N3)]NO	Induce a decrease in cell-population of human fibroblast cells (NIH 3T3) with apoptosis.	Das *et al*., 2014 [15]
8.	Metal complexes having OO, ON, NS and ONS-donors	Anticancer activity against either Ehrlich ascites tumor cells (EACs) [	Kaya *et al*., 2021 [38]
9.	Co(II) complexes of 2-acetylpyridine N-substituted thiosemicarbazone with (PPh3)2	Exhibited excellent activity	Manikandan *et al*.,2014 [49]
10.	Zinc(II) complexes of 2-acetylpyridine1-(4-fluorophenyl)-piperazinylthiosemicarba zone	Highest selectivity is against K562 and MDA-MB-453 cancer cell lines	Stanojkovic *et al*., 2010 [72]
11.	Bis(η5-(3,4-dimethoxybenzyl) cyclopentadienyl)-vanadium(IV) dichloride complex	Significant anti-tumor properties	Gleeson *et al*., 2009 [26]

Anti-inflammatory agents Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli such as pathogens, damaged cells and irritants. Numerous complexes are developed for treating inflammation.

Table 3: Anti-inflammatory agents Inflammation

S. No.	Complex	Action	Reference
1.	N,NO-di(aminoethylene)-2, 6-pyridinedicarbonylamine (L1) and bis-(N, Ndimethylethyl)-2, 6- pyridinedicarboxamide (L2)	Non-steroidal anti-inflammatory drugs (NSAIDs)	Egza *et al*., 2020 [20]
2.	Aminopyridinylmethanols and aminopyridinamines niflumic acid and flunixin	Anti-inflammatory agents and for treating Alzheimer's disease	Brun *et al*., 2013 [7] Kaura *et al*., 2022) [17, 37]
3.	N-aryl substituted anthranilic acid (2-amino-3-pyridinecarboxylic acid)	Analgesic, anti-inflammatory and Anti-pyretic agents	Yang *et al*., 2016[80]
4.	1, 2-dihydroquinazolin-4(3H)-ones based metal complexes	Potent anti-inflammatory agents	Hoonur *et al*., 2010 [29]
5.	Schiff bases derived from 2-mercapto-3-formyl quinoline/2-hydroxy-3-formyl quinoline with 2, 6-diaminopyridine (DAP) and their corresponding Co(II), Ni(II), Cu(II) and Zn(II) complexes	Highest biological activities with least adverse effects	Dhumwad *et al*., 2013 [18]
6.	Enoxacin and their Cu(II) and Ni(II) complexes	Anti-inflammatory	Arayne *et al*., 2009 [4]
7.	Co(II) complexes of mefenamic acid ligand naproxen, diclofenac, diflunisal and flufenamic acid, Co(II) complexes of naproxen and tolfenamic acid, and Mn(II) complexes of tolfenamic acid	Potential anti-inflammatory agents	Arayne *et al*., 2009 [4]

Anti-microbial agent. The better activity of the metal complexes are due increased lipophilic nature of the complexes attributed to chelation and heteroatoms present in the ligand moiety.

Table 4: Anti-microbial agent

S. No.	Complex	Reference
	Quinolone-metal compounds	Turel 2002 [77]
	$[Cu(CX)_2].2H_2O$ (where CX = cinoxacin)	Turel 2002 [77]
	Zinc and copper ciprofloxacin complexes	Yu *et al*., 2022 [81]
4.	Quinolone cobalt(II) complexes	Psomas *et al*., 2013 [59]
5.	Copper(II) complexes with isoxazole Schiff bases, [Cu(L1)2], [Cu(L2)2] and [Cu(L3)2] L1= [(1-((E)-(3,5-dimethylisoxazol-4-ylimino)methyl)naphthalen-2-ol, C16H14N2O2), L2= [2-((E)-(3,5-dimethylisoxazol-4-ylimino) methyl)-4-methoxyphenol, C13H14N2O3 and L3 = (2-((E)-(3,5-dimethylisoxazol-4-ylimino) methyl)-4-bromophenol, $C_{12}H_{11}BrN_2O_2$]	Daravath *et al*., 2019 [14]

6.	Mixed ligand complexes of Co(II), Ni(II), Cu(II) and Zn(II) derived from isatin monohydrazone with 2-hydroxynapthaldehyde/substituted salicylaldehyde molecule and heterocyclic nitrogen base 8-hydroxyquinoline	Devi *et al*., 2015 [17]
7.	Cu(II), Ni(II), CoII) and Zn(II) mixed ligand complexes from N_2, N_3-bis(4-nitrophenyl)quinoxaline-2, 3-diamine and 1, 10-phenanthroline	Irfan *et al*., 2017 [33]

Conclusion

The current research focused primarily on coordinated transition metal compounds chiefly V(IV), Cu(II), Ni(II), Zn(II) and Ni(II) complexes. They are easily available, less toxic, cheaper, indispensable elements of biological intracellular environment and are employed against assortment of diseases, ranging from antibacterial and antifungal to anticancer applications. Aforementioned properties could be improved by coordinating them with ligands such as amino acids, N-heterocycles, pyrazolones etc. We evaluate the relevance of bioinorganic chemistry to medicine is a hastily developing field. Novel restorative and analytical metal complexes are at this moment having an impact on medical platform. Progress in bioinorganic chemistry is vital for improving the blueprint of compounds to trim down lethal side-effects and recognize their mechanisms of action. Hence, chelation for stabilization and its potent activity in various biological processes open a new significant path for designing new therapeutic approaches used for procurement of worldwide issues (Corce *et al*., 2016) [12]. These ligands are not only utilized in the development of coordination chemistry but also find applications in catalysis, optical and bioinorganic chemistry (Weberg *et al*., 2022) [78].

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