RESEARCH PAPER

Biological Role of Metal Complexes and Applications

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ABSTRACT
In this scientific research paper has described theoretical investigation of different metal complexes biological applications. It have been revealed that transition metals have shown many applications, such as anticancer, antimicrobial, anti-inflammatory properties. Depending on the structure of ligands transition metal complexes have shown antitumor properties. It have also been accomplished that not all iron containing complexes have shown anticancer properties, there is also iron containing complexes which increases cancer diseases or no anticancer effect. Here discussed that if ligands show anticancer property, adding metals in the structure of complex improves property.We have improved that many anticancer complexes in vivo level exposed hydrolyses decrease effect. It have discussed the reason of different metal complexes different properties ability forming complex with different ligands. We have concluded our thoughts most anticancer complexes are Pt, Fe, and Zn containing compounds. Cobalt containing complexes have shown moderate or no cancer property. Investigation of Nickel containing complexes is started recently.There are ligands containing nickel complexes shown anticancer property.

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INTRODUCTION

The metals are essential components of human cells chosen by nature[1]. They are frequently found in the enzymes structure and participated in many biological processes, from the exchange of electrons to catalysis and structural roles. In living systems three metals plays much more important role than others. They are iron, zinc and copper. Iron participated in transport, storage, energy production, DNA synthesis and enzyme activity[2]. Containing all enzymes structure zinc plays crucial role in catalytic activity, cell division. Copper contain structure of many enzymes has shown antioxidant properties of human body and significance role of metal in our living systems[3]. On the basis of these properties have opened new ways to scientists in the research field of inorganic biochemistry[4]. The advances in inorganic chemistry provide better opportunities to use metal complexes as therapeutic agents. The investigation has shown significant progress in utilization of transition metal complexes as drugs to treat several human diseases[5].

Medicinal inorganic chemistry can exploit the unique properties of metal ions for the design of new drugs[6]. The use of transition metal complexes as therapeutic compounds has become more and more pronounced. The complexes offer a great diversity in their action, they do not only have anticancer properties but have also been used as anti-inflammatory, antimicrobial, anti-infective and anti-diabetic compounds [7]. Metal complexes have been widely used for applications in the chemical and physical sciences due to their unique electronic and sterochemical properties . For decades the use of metal complexes for medicinal applications have been postulated and demonstrated. The distinct characteristics of metal complexes, including their molecular geometrics as well as their ligand exchange.[8]

For statistics in 2022 20 million people injected cancer and 9.7 million people have been dead. By 2040 year expected to rise 29.9 million and the number of cancer-related deaths will be reach to 15.3 million[9]. The aim of anticancer treatment is to

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induce apoptosis, it means to preserve healthy cell unaffected. Nowadays metal containing compounds used treatment of different disorder such as cancer one of the well-known drug Cisplatin is used treatment of different types of cancer disease. Cisplatin was firstly discovered by M.Peyrone and anticancer properties was discovered accidentaly by B.Rosenberg. But Cisplatin have analogous carboplatin and oxaliplatin. Approximately 50 % of chemotherapeutic procedure is used cisplatin and its derivatives. In the treatment of cancer disease DNA is main target. Cisplatin with DNA form two types of adducts GG dinucleotide sequences (60-65 %), and AG sequences (20-25%) which treat the DNA damages [10]. Platinium (II) and Platinium (IV) molecules classified three parts: classical nonclassical and nanodelivery molecules. Classical Platinium (II) molecules are normally designed to follow the SARs of cisplatin and its analogues, non-classical compounds are designed to focus on different mechanisms of action, e.g., trans-compounds or monofunctional complexes, as well as platinum (II) molecules which do not bind covalently to the DNA, for example metallointercalators, which are able to intercalate in the DNA[11] Because of drawbacks of cisplatin scientists explored alternative transition metal complexes. Satraplatin (JM216) is a platinum (IV) complex that was the first orally active platinum agent to be reported. JM216 showed less cytotoxic effects on the liver and gastrointestinal system than cisplatin and carboplatin effects in vivo studies. Picoplatin was primarily designed to overcome one of the known mechanisms of platinum resistance detoxifcation by intracellular thiols. In the end iproplatin is one of the most clinically studied platium compounds to have not been yet approved for marketing, with several trials ranging from phase.[12].

Among the transition metals Ru attracted interest nonplatinum cancer drugs [13]. Nowadays ruthenium anticancer drugs passed first and second clinical trials [14]. Palladium is among the metal which investigated anticancer drug design [15]. When they change metal with palladium kinetic parameters changed fastly [16]. Therefore when palladium complexes injected they hydrolyses and couldn't reach DNA [17]. Scientist accepted that palladium complexes which are anologue of cisplatin and carbo- platin show no antitumor properties [18]. But then when they changed ligand complexes have shown antitumor properties [19].It means antitumor properties not only depending on metals, here also crucial role plays ligands [20]. Metals 8, 9, and 10 groups show high anticancer properties, because they are heavier without changing they can reach to DNA [21].

Iron containing compounds

Iron is first element which participated life important processes in our living systems.Here we are going to show you review of different iron containing compounds. Iron containing anticancer compounds classified, iron photocytotoxic compounds, iron multinuclear compounds, ferrocenyl compounds, salen compounds, iron cyclopentadienyl, iron polypyridyl complexes. Among then ferrocene derivatives plays important role in therapeutic procedure. Cancer cell can accumulate and use iron more than normal cell, due to profileration and DNA synthesis. Iron alsp participate cell cycle. In this paper scientist investigated anticancer properties of half sandwich compounds. Scientist firstly investigated the antiprofelative properties cationic and neutral iron complexes. This work is first in vivo study in CpFe-NHC complexes in anticancer drug. Both complexes anticancer properties have been investigated and compared with cisplatin. The investigation revealed that first complex is less toxic, most active in vivo and highest cytotoxic potential [22].

The next work cover the synthesis of iron cyclopentadienyl complexes bearing different phosphine and phosphite ligands. All complexes were investigated anticancer properties. Scientists concluded that all complexes show high anticancer properties, and they dont participated inducing of DNA [23].

In the next work scientist have shown action of iron ions in cancer human body. Here scientist explain that iron plays important role growth of cancer cell. If ligand is standalone it can be restrict the growth of cancer cell. Therefore scientist proved that if stability constant is high the complex will show high anticancer properties, but if stability constant is low both ligand and ferric ions will separately act on the cell. In this paper scientist successfully investigated in complex stability implies the action of ferric ions and ligand. When ligand pose standalone cytotoxic effects on the cancer, combination of ferric ions can be beneficial. However when ligands stimulate cancer cell, combination with ferric ions can be promote cancer cell. In that way anticancer iron ion can be easy transported and release from the body. Last part of the paper summarizes the results of clinical trials and in vitro studies of novel iron chelates such as: PRLX 93,936, Ferumoxytol,

Talactoferrin, DPC, Triapine, VLX600, Tachypyridine, Ciclopiroxamine, Thiosemicarbazone, Deferoxamine and Deferasirox. Among the iron chelators triaphine suggested potential prostate, breast and pancrease cancer drug [24].

In this work covers green synthesis of iron nanoparticles from the Rhazya stricta .In modern time nanotechnology is primarily concerned with synthesizing, manipulating, and applying materials with dimensions ranging from less than a micron to distinct atom. It means synthesis of nanoparticles in the cancer treatment by the cytotoxical side, less amount drug, less toxity. Metals Al, Ti, Zn, Pd, Pb, Cd, Fe, Co, Ag, Au is used as a nanoparticles. Scientist collected Rhazya Stricta , dried it, then boiled in water, then reaction with iron chloride, formed iron nanoparticles. Scientists studied in vitro anticancer properties and the nanoparticles has shown anticancer properties [25].

It is evidently known that cancer cell demonstrate requirement for iron than normal tissue cells. Nowadays iron chelating agent is used for its anticancer properties. In iron chelators lipophilicity and membrane permeability is a key role in the synthesis of anticancer drug. Scientist designed new iron chelator 6-methyl-3-{(2 E)-2-[1-(2-pyridynl) ethylidene] hydrazine}-5H-[1,2,4]-triazino[5,6-b] indole (VLX-600) . Complex affinity of ligand were studied. This ligand anticancer properties in vitro level investigated and revealed that metal chelator show high anticancer properties [26].

The next work cover synthesis of iron oxide nanoparticles and chitosan coated iron oxide nanoparticles and anticancer properties of HCC. By the analytical methods confirmed successful synthesis of nanoparticles. Our findings advocate for the further exploration of Fe3O4-CS nanoparticles in the development of anticancer drugs, emphasizing their capability to trigger oxidative stress and enhance antioxidant defense mechanisms [27].

Nickel containing metal complexes

Nickel is metal which can form metalorganic compounds, but not as well studied as Pt, Pd, Cu compounds for cytotoxic activity. Scientist were studied cytotoxic activity of nickel comparing with Cu, Pd, and Pt the result is acceptable but is not outstanding. But nickel may still have some pharmacological properties which are useful in the design of anticancer drug, because metalloproteins exhibit nickel ions. 17 different complexes with _-hydroxydithiocinnamic acid esters as O,S bidendate ligands for Pt, Pd and Ni were synthesized. Anticancer properties were investigated and revealed that in vitro level they have shown high antitumor cativity [28].

Schiff bases are compounds which form many metal complexes and show high antimicrobial properties. This work cover synthesis and anticancer study of Ni(II), Mn(II), Co(II) Schiff bases complexes.Ligand was synthesized by the condensation of salicyclic aldehyde and 4-chlorobenzyhydrazide. Synthesized compounds structures were studied different spectral methods. Anticancer properties of complexes were studied and revealed that nickel complex have shown super anticancer activity of both breath and colon cancer. Manganese complex has shown moderate anticancer activity both breast and colon cancer, but cobalt has shown super anticancer properties in breast cancer , weak anticancer properties in colon cancer [29].

After synthesis and successful antitumor investigation of iron (III) N, N^1 bis-(salicyclidene)-1,2(phenylidenediamine (SAP) scientist decided to continue next triad elements Co(II) and Ni(II) SAP complexes. They have been succesfully synthesized cobalt and nickel complexes with SAP. They have investigated antprofilerative , antimetabolic and cell death inducing properties against leukemia (HL-60 and ovarian carsinoma tumor cell. Result of research have shown that Nickel complexes were basicly inactive because limited uptake into cancer cells, but cobalt complexes were accumulated in the cancer cells and showed redox pairs similar to iron complexes. The cytotoxity of cobalt complexes depend on length of the alkyl chain in the ester substructure . The compounds of propyl and butyl ester complexes completely inhibited profileration of A 2780 cis cells [30]

Aminoacid Schiff bases is usually formed condensation of aminoacids and carbonyl groups. In fact Schiff bases and its metal complexes are outstanding in the field of metal base drug. Nickel is essential trace elements which have been consistuent of many enzymes. Schiff bases complexes were synthesized and studied antimicrobial, anti inflammatory and anticancer properties. To take this into account scientist synthesized Schiff bases Nickel complexes and studied its anticancer properties. A series of tryptophan Schiff bases Ni (II) complexes have been synthesized. These complexes showed moderate cytotoxity toward Eca-109 cell and one of the complexes was selected for further investigation [31].

Aminoacids is very important for complexformation, because it consist both amine and carboxylic groups. When it combine with carbonyl compounds forms Schiff bases.These ligand existed high biological applications. They have shown high anti-cancer, anti-tumor, anti-microbial, anti-flammatory agents. In this work scientist have shown synthesis of ligand by the condensation of 2-amino-3-methylbutanoic acid with acetylacetonate .They have prepared Cu, Co, Ni, and Mn complexes of this ligand. They have studied antibacterial properties of ligand and metal complexes. All complexes has shown high antimicrobial properties< but Cu is best antibacterial agent [32].

Breast cancer is cancer type which spreading effects it is stand in the second. Scientist was found three types of breast cancer:estrogene/progestrogene dependent (ER/PR+), epidermal growth 2 factor(HER2+), triple negative breast cancer (TNBC). Most dangerous type of breast cancer is TNBC. Because it has multidrug resistant ability and it is frequently resulting in a likelihood brain and lung cancer.. In this scientific work scientist were synthesized Nickel and palladium complexes and studied anticancer activity against TNBC . Cancer metastasis is a process which primary cancer cell spreaded secondary cell. Palladium complexes is which complexes manifested promising antitumor activity against various breast cancer cell lines and showed lower activity on healthy cells , they were chosen further investigation.[33]

Chemical, physical and biological process is used to generate nanoparticles. Au, Ag, Pd, Ni, Pt, Se nanoparticles were synthesized.Among the nanoparticles ZnO inexpensive synthesize methods and ecofriendly nature plays important biological role. Mentha longifolia L.(M:ML) is a Lamiceae family member also called wild mint.The goal of this research was to assess the cytotoxic activities of ML-ZnONPs derived from *M. longifolia* aqueous leaf extract in an ecologically friendly way. Wild mint leaves collected< then dried, after grinding process, it is disolved in distillated water and boiled 4 hours. After boiling process solution filtered out and then coolled. Synthesis of nanoparticles carried out 4 hours at temperature 65. After reaction solution centrifuged at 30 minutes (6000rpm). Dried compounds washed out several times with water. In this document, the cytotoxic effects of zinc oxide nanoparticles (ZnONPs) derived from the leaves of *Mentha longifolia* L. (ML) on the deadly cancer cells OVCAR-3 (ovarian adenocarcinoma) anand time on the viability of both cancer cell lines was negative. In future studies, minimizing the d HCT-116 (colorectal carcinoma) were assessed [34]

ZnO nanoparticles with its unique compatibility , high selectivity and cytotoxity may be a promising anticancer agent. Zn is one of major elements of the human body co factor more than 300 mammalian enzymes, it is important DNT replication, DNT repair, cell cycle progression and apoptosis. Size is one of the key properties of nanoparticles. A size range of 10-100 nm is considered good for biological application. The lower scale this size range is based on the measurement of the sieving coefficient for the glomerular capillary wall, as the threshold for first pass elimination by the kidneys is estimated to be 10 nm in diameter. In some researchs particles size equal less than 10 nm and in this case smaller nanoparticles can penetrate tumor cell and repair it. The tumor suppressor p53 gene and caspase enzyme help to check cells regularly and prevent them from becoming cancerous. If a cell shows any kind of malignancy, a DNA repair mechanism activated.to repair the altered DNA . If this mechanism fail to repair the DNA then the cell undergoes programmed cell death [35]

Nutmeg in indian medicine is having antidiabetic, antianalgesic, antioxidant, antimicrobial and antiflammatory properties. Oleoresin is natural mixture of resin and essential oil derived from the leaves of olea europaea tree. Oleoresins are organic solvent extracted mixture of essential oils, and resins extracted from spics. Oleoresins contain both volatile and nonvolatile elements. For large anticancer properties of zinc researchers synthesized from nutmeg oleoresins with ZnO nanoparticles. The natural combination of ZnO nanoparticles utilizing plant extract gives an ecological well disposed, straightforward and proficient course for amalgamation of nanoparticles. ZnO nanoparticles were synthesized in a chemical and green approach using Zerumbone as a reducing and capping agent. Green Zno nanoparticles shows enhancing anticancer axctivity than chemical ZnO nanoparticles [36].

Artemizia annua (Qinghaosu), artemisinin is used treatment of malaria, it is also used for anticancer activity, much lower potency.Iron and heme have been proposed activator of artemisinin. In this paper scientist have shown zinc protoporphyrin-9 a heme homolog and natural metabolite dihydroartemisinin in multiple cell lines. Here authors have shown both synergestic mechanism inhibiting anticancel cells in vitro and in vivo level [37].

Biological trace metals such as iron, copper, zinc, manganese are essential to our life. After discovery platinium drugs in chemoteraphy, has rapidly growth interest synthesis of metal complexes. Here scientists have shown different zinc complexes application treatment of diabetic mellitus [38].

It is evidently known that silver can be apply as antimicrobial agents in an compound form. Because silver as a metal doesn't existed antimicrobial properties. When silver form ionic compounds, it haven't shown toxicity. Therefore scientist in this days have been working in the synthesis of silver containing metal complexes. When silver atom bind with carboxylate acide, for complex compound which have shown high antimicrobial properties. In this scientific research cover synthesis of silver citrate complex. Scientist have been synthesized citrate complexes in several ways. They have also been studied antimicrobial properties. They have revealed that citrate complexes has shown high bactericidial properties [39].

Complex of VO(IV), Cr(III), Fe(III), MO_2(VI), WO_2(VI), UO_2(VI), with pyrazinecarbohydrazine ligand (N-(1-(5-chloro-2-hydroxoyphenyl)etylidene)pyrazine-2-carbohydrazide) were synthesized. The antimicrobial activity of ligand and metal complexes weremeasured. All compound have shown high antimicrobial properties. All synthesized were measured in the in the temperature range of 313-373K conductivity of compound increases increasing temperature, decreases cooling. The conductivity of compounds described H_2L<UO_2<WO_2<Fe<CR<MoO_2<VO increased [40].

New coordination compounds of Mn(II), Fe(III), Co(II) and Ni(II) and the biologically active ligand [(N-benzylidenepiperazine-2-carbohydrazonoamide) were synthesized and characterized by appropriate analytical technigues.The complex were screened for antibacterial and antifungal activities by the microdilution broth method using Mueller-Hinton broth with 2% glucose for growth of fungi.The synthesis of the complex was aimed at increasing the likelihood of crossing the blood-brain barrier. In silica research confirmed the assumption about the anticancer effect. The glioblastoma lines were selected because the tested compounds showed a crossing of the blood-brain barrier and a high probability of being active against these tumor ceels.The complex Co(L)Cl_2 and Ni(L)Cl_2 C_2H_5OH showed significant activity against U87M9 tumor cells (IC_{50}=7,69++2,17 and 42,82+_4,27 mg\ml respectively) It is also important to highlight that in all cases, complexation decreased cytotoxicity against normal cells. The free ligand exhibited moderate bioactivity against the referencee gram-positive cocci((Saureus, S epidermides, M lutesus, E faccalis) and Gram positive, spore forming lacille (15 subtiles and B cereiss). Even though the tested complexes did not exhibited significantly higher bioactivity.Fe(L)Cl_3,CH_3OH showed very strong selective, bacteriostatic activity against stophylocci(Saureus, S epidermides) and the Co(L)Cl_2 complex was less active but had good bioactivity against Gram positive cocuM(L)CL, showed moderate activity against yeast (126-500mg}l). The improvement in the biological activity resulting from the complexation highlights the great possibilities of coordination chemistry in ferms of possible applications in medicine [41].

The Fe(III), Ru(III), Co(II), Ni(II),Cu(II), Pd(II),Zn(II),Cd(II) and Hg(II) complexes of A Schiff base derived from Pyrazine-2-carboxamide and 2-hydroxybenzaldehyde (HBPCA) have been synthesized and structurally characterized by various physico-chemical data. Ligand metal complexes have been screened for their antimicrobial activities against two grain positive bacterial strains. Both the antibacterial and antifungal activities of the synthesized metal complexes were found to be more as compared to that of the ligand [42].

Four novel monodentate 2-(3^1-(4^{11}-sub-aryl)-1^1-phenyl-1H-pyrazole-4-yl)-1H-benzo[d] imidazole pyrazole aldehydes by adding oxidizing agent urea ammonium-nitrate as catalyst in presence of hydrogen peroxide in alcoholic media. The non chelated Cu(II) and Ni(II) complexes of newly synthesized monodentate 2-substituted benzimidazole (1a-d) ligands were prepared in 1:2 metal ligand stoichiometry. The monodentate behavior of the ligand was confirmed on the bases of spectral studies. A suggestion of the metal probable stereochemistry of the synthesized Cu(II) and NI(II) complexes is given by its magnetic moment TGA graphs of complexes shows four weight loss steps in the range 30-1000^0 C [43].

A new polynuclear cationic complex of copper (II) with pyrazine as a ligand and perchlorate acting as a counter ion was obtained x ray diffraction results accounted for 2 D polymer array of cations in which the metal ions were located on an ideal square pyramidal coordination environment defined by four nitrogen atoms of pyrazines and one chloride.A solution of pyrazine in MeOH was carefully layered

on top of an aquous solutions of Cu(II) chloride and sodium perchlorate[44].

A new series of metal complexes with 1-(2-methylphenyl)-4,4,6-trimethyl pyrimidine-2-thione(2-HL1) and 1-(4-methylphenyl-4,4,6-trimethyl pyrimidine-2thione ligands [$M(mppt)_2(H_2O)_n$] (M(II))=Cu, Mn, Co, n=2 and M=(II)=Ni, Zn, n=0) On comparing the experimental data discovered that the 4 HL1 and its metal complexes are more active than the 2-HL-1 and its metal complexes against all bacteria. The data confirmed that this activity increases considerably on coordination/ chelation All of these compounds were evaluated for their DNA photo cleavage ability and as antibacterial agents. In future some structural alternations in the ligand may lead to formation of better DNA binding agents [45]

A new 4-(4-bromophenol)-6-methyl-2-thioxo 1,2,3,4 tetrahydropyrimidine-5-carbohydrazide ligand; Its Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) have been synthesized and characterized via elemental analysis XRD, Uv-vis, İR, TGA, DTA, NMR and TEM. The ligand acts as neü trial bidentate and is coordinate via the oxygen atom of the carbonyl group and the terminal nitrogen atom of hydrazide moiety. The conductivity measurement showed that all the complexes are nonelectrolytes. The magnetic susceptibility of Cr(III), Mn(II), Fe(III) 3,75 5,60, 5,80, 3,50, 2,80 and 1,52 B.M. Cd(II) complex showed the the highest antimicrobial against Staphyloccus aureus, Escherichia coli and Candida albicans. All compounds didn't show any activity against Aspergillus flavus except Cd(II) complex gave a high activity [46].

The many of metal complexes of Co(III), Ni(II),Cu(II), Zn(II), Cd(II), Hg(II), and Au(III) have been preparation and characterization using novel azo Schiff base ligand derived from azo compound namely (1,5 dimetyl-4-(4-methyl-1H- imidazole-2-yl)-2-benzyl-1,2-dihydro-3H-pyrazol-3-one) with 2amino pyrimidine. The structure of the new ligand azo Schiff base and their transition metal complexes are characterization using several techniques. Thhe antimicrobial properties of synthesized compounds were investigated and revealed high antimicrobial properties [47].

Interaction of Biavelent ions Co(II), Ni(II), Cu(II) and Zn(II) reacts with 4,6-dihydroxy-2-mercapto-pyrimidine (DHMP) in presence oxalic (OX), malonic acid (Mal), 0-phenylene diamine (OPDA) 2,2-bipyridyl(Bipy), 1, 10 phenanthroline (phen) and ethylene diamine (En) has been investigated by potentiometric studies [48].

Schiff bases derived from amino acids and their corresponding metal complexes have been widely studied in different ways and have increased intention of chemistry in biological, pharmaceutical fields due to their easy synthesis and broad spectrum of applications. In this review, we have focused on the synthesis and biological evaluation involving antifungal , antibacterial, anticancer antioxidant and antidiabetic activities of some amino acid derived Schiff bases and their respective metal complexes. Organic compound having an azomethine group (-CH=N-) known as Schiff base. Schiff product was innovated by German chemist Hugo Schiff. Schiff base ligands are very important in branch of coordination chemistry, since Schiff base formed potentially stable when coordinate to metal ions. Schiff bases are generally easy to synthesize, derivate and have good ligation power. Schiff bases usually with different donor sites i.e. N,O or S responsible for formation of stable complexes with different transition metals. Amino acid Schiff base complexes have received important from the inorganic and biochemistry aspects and due to their pharmacological and physiological activities [49].

Metal coordination compounds derived from several closely related yet different multidentate reduced Schiff base ligands are discussed in term of their mode of binding and coordination to supramolecular network structures. These multidentate ligands have flexccole backborn with hydrogen bond donors and acceptors and readily form metal complexes and coordination polymers with metal ions such as Cu(II), Zn(II) and Ni(II) various solid-state metal as supramolecular network structure are delinated ranging from hydrogen bonded linear polymer and helical coordination polymers 2D sheets to 3 D network architectenes constructed N-H….O, C=O….H-O solvent, O-H…..O, N-H….O=C hydrogen bond and C=O…pi C-H…pi and pi…pi stacking interactions. The review gives an account of the observed structural diversity in relation to the role of different donors and acceptors, aqua ligand and solvents, nature of the ligands and metal ions, coordination geometry around the metal ions and counter ions besides the experimental conditions such as temperature, Ph etc in directing the formation of supramolecular structure in the solid state [50].

A Schiff base of Nicotinic acide hydrazide was designed with the aim to develop novel antimicrobial agent of synthetic origin having broad spectrum of

activity and high potency. The Schiff base nicotine hydrazide formed by the condensation of nicotinic acide hydrazide and thiophene-2 carboxaldehyde, was treated with metal chlorides[M(II), Co(II), and Zn(II) to prepare the complexes. The metal complexes and ligand were investigated antimicrobial properties and revealed high antimicrobial properties [51].

The synthesis and structural characterization of Co(II) complexes of amino acid Schiff Base was prepared from Salicylicaldehyde and three aminoacid (Valine, Leucine and Isoleucine) in basic medium. The metal complexes was synthesized by treating an ethanolic solution the ligand with appropriate solution of the ligand with appropriate amount of metal salts [1;] [M;L] ration. The synthesized Schiff bases and their metal complexes have been investigated on the bases of elemental chemical analysis, FTIR, electronic spectral, 1HNMR, 13CNMR, MS, molar conductance and magnetic susceptibility measurements.The electronic spectra of the metal complexes and their magnetic suspectibility measurement suggest octahedral structure are ther probable coordination geometries for the isolated complexes The Schiff bases and their complexes were preliminary scanned against various strains of microbes to study their biological effect [52].

İn this research novel complexes of Zn(II) were produced using amino acid Schiff bases 3-metoxy-2-hydroxybenzaldehyde(o-vanillin) and amino acid metyl esters (isoleucine, phenylalanine, methionine). In this study Zn complexes based on Schiff base ligands have been prepared.The results of the analyses were found to be in agreement with the literature findings. Choliesterase inhibitorsare the first –line medications in the clinical treatment of AD, although they cannot stop the desease progression and have been shown to significantly improve cognitive functioning [53].

We explore the synthesis of metal complexes of a renowned antitberculosis drug, pyrazineamide (PZ) with copper, ferrous, ferric, cobalt and manganese a detailed characterization of the resulting complexes was performed for establishing their structures by using spectroscopic techniques. These compounds were also explored for anticancer activityon SNB-19, HCT-15, COLO-205 and KB-3-1 cell lines and were found to be non-or-low toxicity as most of the tested compounds IC_{50}>100muM [54].

The catalytic activity of Schiff bases their corrosion inhibition behavior as well as the action as photosensitizers and fluorescent chemosensors tools for the detection of Cu^{2+} and Fe^{3+} metal ions have been reported [55].

A number of coordination compounds containing ligands able to participate in easy and reversible one-electron redox processes are known. Nitroxyl radicals, spatially hindered o-quinones, quinoneimines, and phenoxazinone systems are examunique structural, magnetic, and electronic properties and are of considerable interest because the oxidation state of the ligands in these systems, leading to paramagnetism, mimics biochemical processes such as respiration and photosynthesis. Other fields ples of such ligands.Compounds of this type, obtained for all transition metals, have intriguing and of application include their use as medicinal chemotherapeutic (antitumor) and organ-imaging agents, in biological intercalation studies, and as solid-state materials [56].

The acidity constants of citric acid and the stability constant of the citrate complexes of copper (II), iron(II) and iron (II) have been measured at 25 ^{0} C in 0,1 M KNO_3 backround. The measurement were based on mass balances on hydrogen ions, supplemented in the case of Cu(II and Fe(III) complexes by measurement of free metal concentration with a solid state copper ion sensitive electrode and redox electrode respectively. The data reuired the assumption of binuclear copper complex, but all complex characterized were of 1.1 stochiometry. Most investigation published in the past twenty years have shown 1.1 stochiometry in the reaction of copper . Most investigation in the past twenty years have shown 1;1 stochiometry in the reactions of copper (II) and iron (II) with citric acid, and this has been confirmed by the resultrs in this study . Also in agreement with several previous studies , it was observed that up to four protons were displaced through complex formation per ,metal ion or per molecule of citric acid reacting [57].

The complexes were characterized by melting point / decomposition temperature, solubility, conductivity measurement, elemental analyses, UV-Vis and IR spectroscopies, mass spectrometry. In all the complexes, the ligand is bidentate , sulphadimidine coordinates with metal ions either through pyrimidine N and sulfonyl N atom orthrough NH2 group and oxygen atom of the sulphoxide. The complexes are powderyand attempt to obtain single crystals suitable for X-ray crystallographtetrahedral geometry. The free ligand and its respective metal chelates were screened ic analysis failed. All the

complexes have octahedral geometry except Cd(II) sulphadimidine which has against bacteria to assess their potential as antimicrobial agent. The complexes showed greater activity against the three micro-organisms when compared to parent compound. The stability constant data revealed the possibility of using the ligand as antidote orchelating agent for medical treatment of metals overload or poisoning [58].

The reaction of copper chloride salt with a series of p-substituted salicylaldimine Schiff bases yielded both the prevalent inner metal chelates were non-electloytes while the Schiff base adducts were either 1;1 or 2;1 electrolytes electrolytes in dimethylformamide. The Cu(II) complexes exhibited significant antifungal activity against Candida albicans [59].

Our research group studies were carried out with the intention of obtaining new complex combinations of Cu^{2+} with N-substituted sulfonamide liqgands with antitumor and antibacterial activities with possible medical applications. For this purpose , we synthesized new Cu(II) complexes with N-sulfonamide ligands, ligands with antitumor and antibacterial activities with possible medical applications. For this purpose we synthesized two new Cu(II). The x-ray crystal structure of the complexes were determined and the compounds were characterized wia FTIR and UV –vis spectroscopy. The antibacterial and cytotoxic activities [60].

Zinc is one of the important trace element in human body. It plays vital role bone formation, cell mediated immunity, brain function and tissue growth, among others. Zinc has ability to accept certain proteins domains to form zinc finger proteins (ZNFS) this can interact with DNA , RNA and proteins such as PAR and are involved in the regulation of several cellular processes.Scientist investigations concersns bis(aminoacedate) zinc (II) complexes as potentially safe and effective antibacterial components for dermotological treatment.The combination of zinc, one of the most important trace elements, with proteinogenetic aminoacids afforded compounds expected to be non toxicwell tolerable and effective agents for skin deseases involving inflammation and irritation of the skin such asulars and acne vulgaris The synthesis was designed in such a way that the final complexes did not contain any counter ions, such as Cl^-, NO_3-, or SO_4^{2-} that could cause skin irritations. The simplicity of the complexes composition is their advantage, they contain only zinc and aminoacidates ligands. The antimicrobial analysis found two compounds, [61].

Schiff bases are versatile compounds with a series of applications, from synthetic to biological to technological spheres. There was a lots of development took place in recent years in the field of Schiff bases due to their broad spectrum of aplications. The presence of reactive C=N function in Schiff bases makes them as more versatile scaffolds for the synthesizes of varied classes of biologically active heterocycles, complex compounds with transition metal ions.Discovery of carbonic anhydrase inhibitors is crucial for their clinical use as antiepileptic, diurectic and antiglaucoma agents. The sets of benzenesulfonamides incorporated with hydrophobic tails by hydrazido or hydrazine linkers have inhibit inhibitory activity towards four human carbonic anhydrase isoformds with the K_1 ranges; 76,8-357,4The discussion on the physical properties, like electronic, optical and positive solvatochromism, solute-solvent interaction, anti corrosion properties, exploration of chemical reactivity of Schiff base derivatives in this review might be useful for the researchers working in this area all over [62].

Zinc(II), Pd(II) comple with N^1,N^1-dimethyl-N^2-(thiophen-2-ylmethylene) ethane-1,2-diamine(L_{TK}) ligand are synthesized and structuraly characterized. Density functional theory (DFT) electronic structure calculations and variable temperature NMR support the presence of two conformers and a dynamic interconversion process of the minor conformer to thids major one in solution.In this study Zn(II), Pd(II) and Cd(II) complexes, namely with the iminomethylthiophene derived ligand (L_{TK}) were synthesized and characterized. X-ray crystallography revealed diverse coordination geometries of the result and M(II) complexes DFT calculations showed that the rotation of the thiophene moiety of the ligand(L_{TK}) can be observed for Zn(II) and Cd(II) centers, confirmed by VTNMR, but no such rotation is evident for Pd(II) [63]

The advances in inorganic chemistry offer enhanced opportunities to use metal complexes as therapeutic agents Metal have been used in the treatment of deseases of human since ancient times The empirical formula and geometry of the complexes are confirmed by elemental analyses (CHNS)ş TH metal to ligand ratio of ethylenediamine zinc (II) complex is 1;3 with empirical formula $ZnN_6C_6H_{24}SO_4$. But $[ZN(meen)_2]^{2+}$ complex and $[Zn(prin)_2]^{2+}$ complex with thre percentage of C,H,N, and S exhibit 1;2 ratio with the empirical formula $ZnN_4C_6H_{20}SO_4$ and

$ZnN_4C_{10}H_{28}SO_4$ respectively. The binding of the ligand to the metal, confirms through the infrared spectroscopy. On comparing thr antidiabetic activity of Zn(en), Zn(meen) and Zn(pren) complex Zn(pren) complex shows greater actively than others. It might be increase in the carbon chain of the ligand. Zinc is natural component of insulin a substance crucial to the regulation of carbohydrate metabolism [64].

Schiff bases are a well-documented class of ligands that are capable of bonding to almost all metals of the periodic table. They are generally formed through a condensation reaction of carbonyl compounds with primary amines, in which mono-, di- or tri functional amines lead to bi, tri, tetra- or polydentate Schiff bases.New Schiff baes and their Fe, Cu and Zn complexes were synthesized and characterized by various spectroscopic methods. The structure of the compounds were determined by DFT calculations and X-ray diffraction measurements. The crystalllographically determined geometry of the ligands, as well as the measured vibrational spectra of are good agreement with the theoretical results. The antimicrobial properties of Schiff bases and their metal complexes well evaluated [65].

This study has demonstrated that at pH 9–10 under sulfate-reducing conditions bacteria can ferment citrate, a widely used decontaminant in the nuclear industry. The citrate fermentation products can then support sulfidation in low Ni systems to partially precipitate nickel sulfides and bioreduce U(VI) to form poorly soluble non-crystalline U(IV)–phosphates. Removal of citrate by biodegradation in wastes at high pH will eliminate the potential for radionuclide-citrate complexation, and the implied elevated solubility of radionuclides, notably Ni^{2+}, in radioactive waste disposal scenarios where citrate is present. [66].

Schiff bases are formed by the condensation of a primary amine with a carbonyl compound [67]. We have been synthesized different Schiff bases and their metal complexes. We have studied antimicrobial, antioxidant, anticorrosion properties of synthesis metal complexes [68]. We have observed that many Schiff bases and their complexes even a very low concentration shown antimicrobial properties [69] . Schiff bases and complexes bio-stability have been investigated and revealed that complexes were durable even 8 weeks [70]. We have synthesized Schiff bases and hydrogenated Schiff bases metal complexes. Result of this investigation we have observed high results. When Schiff base hydrogenated, hydrogen atom enters azomethine groups and double bond break down, complex formation ability of ligand getting easeier, in this case antimicrobial properties increase [71].

Metals plays crucial biological roles, serving as catalysts, structural components and electron carriers, among other functions [72-73]. When they bind with organic compounds, they plays lifely important biological roles in our living systems. Taking into account in this natural processes, scientists have been synthesizing different organic substituted metal complexes. In our body synthetic metal complexes may participate and replace different metal ions functions[73-81].

CONCLUSION

In this review paper we have discussed different metal complexes with different ligands. We have investigated many application of complexes. This complexes apply in different sides of our life. Nowadays metal complexes used in clinical applications. Transition metal complexes have shown less side effects. But heavy metal complexes have shown toxic properties. Metal complexes also used treatment of water, biocides, antimicrobial agent, pesticides. In future application of metal complexes will develop as rechargable batteries, semiconductors and superconductors

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