TERNARY TRANSITION METAL ION COMPLEXES OF VARIOUS DRUGS WITH AMINO ACIDS AND THEIR ROLE IN BIOLOGICAL SYSTEMS

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ABSTRACT

Transition metals are chemical compounds characterized by having an incomplete d sub shell, examples of which include Mn (II), Fe (II), Fe (III), and others. Due to their inherent structural instability, these compounds can manifest various oxidation states and readily engage with diverse negatively charged molecules, thereby influencing the dynamic redox processes occurring within biological systems. The notable effectiveness of anticancer medications for example, cisplatin, carboplatin, and oxaliplatin has animated the investigation of metal-based pharmaceuticals, displaying significant potential in medical applications and presenting novel therapeutic prospects. While these metal-containing drugs have primarily undergone investigation for their efficacy against cancer, they have also displayed encouraging Many different illnesses and conditions, including diabetes, ulcers, rheumatoid arthritis, inflammatory disorders, cardiovascular disease, etc., have been targeted in their development. Curcumin is a phytoconstituent with the ability to undergo a ketoenol form change, and by taking use of this capability in the open chain design of the enolic structure, metal ions may bind to curcumin, creating a chelate structure. The chemical composition of the metal central cation allows for a wide range of possible syntheses of this chelate.

Keywords: cisplatin, carboplatin and oxaliplatin.

INTRODUCTION

In the realm of medicinal chemistry, metals have a prestigious position. The d block of the periodic table, which covers groups 3 through 12, is occupied by the transition metals. Filling of their respective shells is now in progress. Coordination compounds were first developed due to

this characteristic of transition metals. A metal complex, also known as a coordination compound, is a chemical in which a metal molecule is covalently bound to many other molecules or anions. In the middle of the 1870s, a Danish scientist named Sophus Jorgensen synthesised metal conjugates for the first time. In 1893, Alfred Werner made a significant discovery in this area by studying a sequence of chemicals that included cobalt, chlorine, and ammonia.

In 1913, he was given the Nobel Prize for his endeavors. Transition metals, such as Mn (II), Fe (II), and Fe (III) compounds, all have an incomplete d subshell and, as a result, exhibit variable oxidation numbers and electronic configurations, which in turn modulate the dynamic redox system within the body and display antioxidant and anticancer properties. By taking use of curcumin's keto-enol form transformation trademark in the open chain setup of enolic structure, metal ions may bind to the compound, creating a chelate structure in which curcumin functions as a ligand. The chemical composition of the metal central cation determines the optimal synthesis conditions for these chelates. The 1, 3-diketone segment of curcumin possesses the ability to undergo an automatic tautomerization process, resulting in the formation of a keto-enol tautomeric structure. This keto-enol tautomer is highly adaptable and can rapidly form complexes with metals, enabling it to effectively capture and neutralize the active free radicals responsible for the illness [1-7]. Transition metal complexes have a historical record dating back to at least the sixteenth century, where they were employed in the treatment of cancer and leukemia. Inorganic compound cis-diammine-dichloroplatinum (II) (cisplatin) was shown to have anti-tumor action in 1960. In recent years, cisplatin has emerged as a leading cytostatic medication for the treatment of solid carcinomas. Gallium, germanium, tin, bismuth, titanium, ruthenium, rhodium, iridium, molybdenum, copper, and gold are only few of the metals that have been found to be beneficial against tumors in humans and animals. In addition to their use as diagnostic agents, medications based on metals are being used to treat numerous conditions, including diabetes, rheumatoid joint aggravation, fiery ailments, and cardiovascular disease.[8-10] When compared to organic molecules, metal complexes haven't gotten a lot of love in the field of medical chemistry. In actuality, numerous organic compounds employed in the field of medicine rely on minute quantities of metal ions, whether through direct or indirect involvement, to activate or undergo biotransformation. Consequently, their mechanisms of action are not exclusively organic. The status of metal particles and their buildings with biomolecules inside

the body plays a crucial role in various aspects of health, aging, physiological processes, and disease development.

Approximately 30–40% of all identified proteins, which encompass metalloenzymes, necessitate metal cofactors (e.g., Fe, Cu, Zn, Ni, Mn) to achieve their proper three-dimensional structural configuration, underscoring the vital role of trace metals in biological functions. Coordination bonds can form between metal ions and ligands, provided that the ligand contains electron-donating atoms like N, O, S, P, and so forth. Chelation profoundly alters the biological properties of both the ligand and the metal component, often leading to a synergistic impact between the metal ion and the ligand.

Prominent examples of metal-based pharmaceuticals include lithium (Li), utilized in the treatment of manic depression via lithium carbonate; aluminum (Al) and zinc (Zn), employed as anti-ulcer agents in the forms of sucralfate and polaprezinc; and platinum (Pt), represented by anticancer medications such as cisplatin, carboplatin, and oxaliplatin.

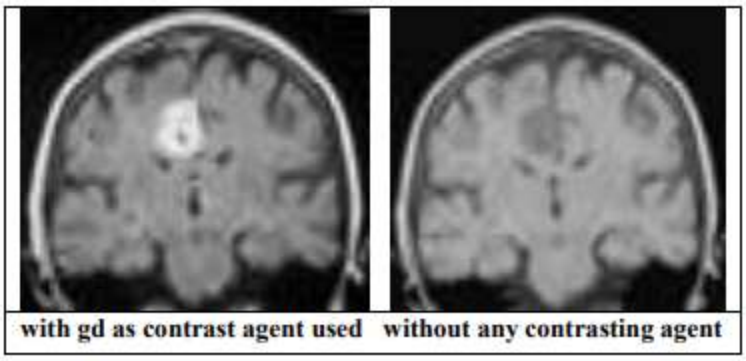

Fig: 1

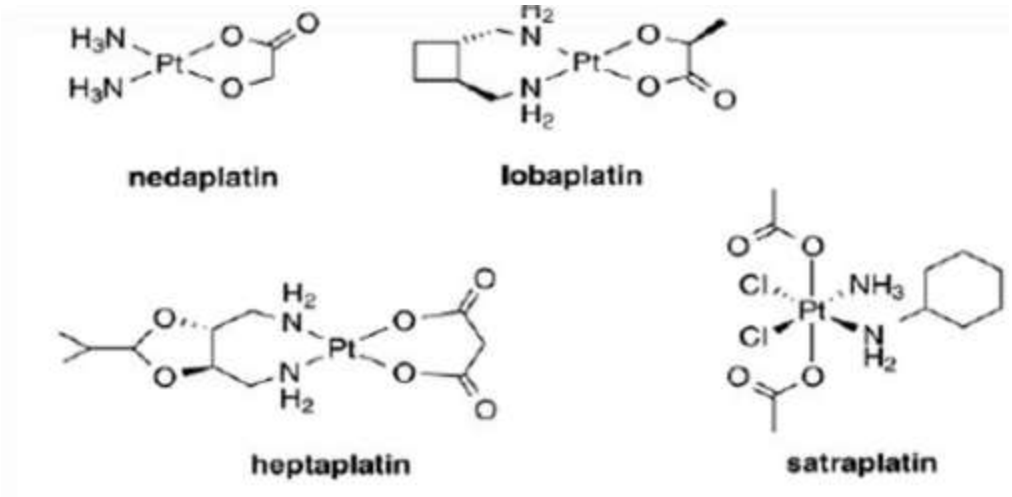

Fig: 2 various Cis structure

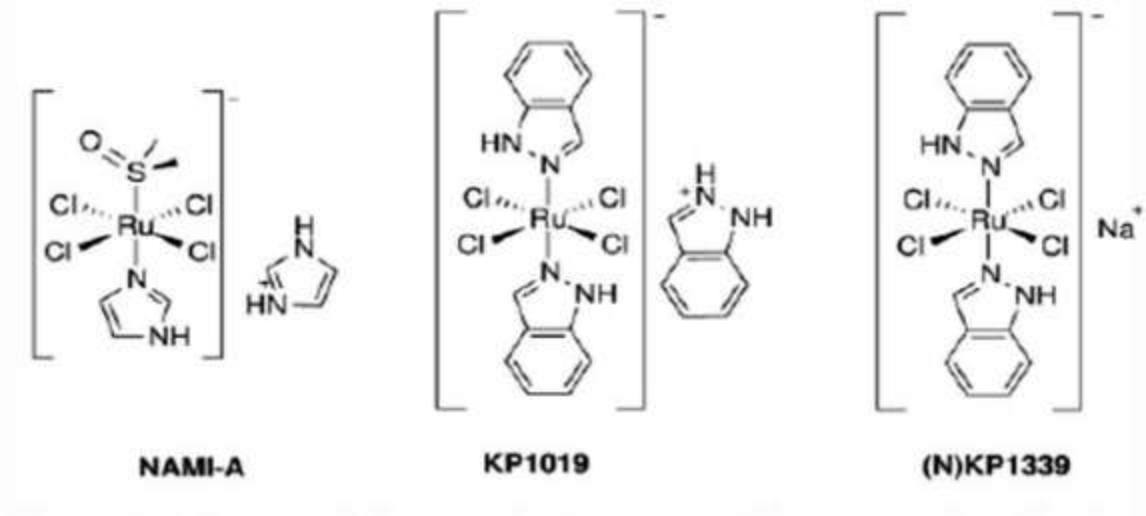

Fig:- 3 Anticancer Ru and Platinum Complexes

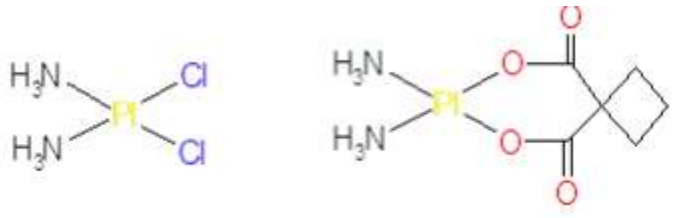

Fig:- 4 Transition Metals and Their Properties

The category of metallic elements situated at the central region of the periodic table is referred to as "transition metals."There are three distinct categories for these metals: those in the first row, those in the second row, and, you guessed it, those in the third row. Most metals employ s-orbitals for bonding, but the transition metals are the ones that eventually switch to d-orbitals, thus the name. This is why the d-block components have a name of their own. The melting and boiling points of these elements are quite high. The five d orbitals are increasingly occupied as one advances to one side along the intermittent table. The transition elements' high electrical conductivity and malleability are a result of the loose binding of their d electrons. Transition elements exhibit relatively low ionization energies, making them prone to losing electrons. Consequently, they display a diverse array of oxidation states, indicating varying degrees of positive charge. The abundance of these positive oxidation states enables transition elements to form a wide spectrum of ionic and somewhat ionic mixtures. Besides, the arrangement of these compounds results in the splitting of d orbitals into two distinct energy sublevels, rendering numerous complexes capable of absorbing specific wavelengths of light. Because of this, solutions and compounds containing complexes tend to take on distinctive hues. The comparatively poor solubility of certain chemicals may be improved by complexation processes.

Bioinorganic chemistry's fundamental subdomain involves the utilization of metal particles or metal particle restricting constituents integrated into natural frameworks to treat sicknesses. Contemporary bioinorganic chemistry researchers primarily emphasize the investigation of heterocyclic ligands and their relating metal edifices, looking to extend how they might interpret the pharmacological properties of these mixtures. Nitrogen-containing natural particles and their metal buildings show an expansive assortment of organic activities, including antibacterial, antifungal, anticancer, and antiviral properties. There are two major benefits to using transition metal complexes as DNA binders. Because of their well-defined coordination geometries, transition metal centers are especially appealing moiety for reversible acknowledgment of nucleic acids study. Additionally, they frequently show unique electrochemical or photophysical characteristics, which enhance the binding agent's efficacy. The remarkable attributes of these compounds have spurred their utilization in a diverse array of applications, ranging from serving as fluorescent markers and DNA foot printing specialists to working as electrochemical tests. Platinum and ruthenium ions (depicted in Figure 1) have garnered significant attention as central coordination entities in the development of potential anticancer medications. Nonetheless, there

is a growing fascination with the synthesis of cost-effective first-row coordination compounds that can effectively bind to DNA and potentially exhibit cytotoxic properties. Consequently, this article primarily delves into research exploring the pharmacological impacts of first-row transition metal coordination compounds, specifically V(IV), Co(II), Ni(II), Cu(II), and Zn(II). These metal ions are not only more economically viable but also more readily obtainable. Additionally, they happen to be the most abundant elements within the cells of living organisms. Most metalloproteins also include iron, making them the two most common trace metals in living systems. Several inorganic medications now use these metal ion additives.

Applications for transition metals extend beyond antibiotics and antimicrobials to include cancer treatment. The fact that these metal ions are already relatively non-toxic before they are coordinated with the ligands is another argument in their favour. Although there are an infinite number of ligands to choose from, the selected amino acids, N-heterocycles (1,10 phenanthroline, bipyridine), and pyrazolones all have special features that make them very useful for drug creation. Platinum and ruthenium ions are widely investigated because they are thought to be coordination centres of prospective anticancer drugs (Figure 1). There has been a growing interest in recent times regarding the creation of cost-effective first-row coordination compounds that can effectively bind to DNA and potentially exhibit cytotoxic properties. Consequently, this article predominantly centers on research endeavors that delve into the pharmacological impacts of first-row transition metal coordination compounds such as V(IV), Co(II), Ni(II), Cu(II), and Zn(II). These compounds are more affordable and readily obtainable, thus making them a focal point of investigation.. Furthermore, these metal ions are crucial components of the intracellular milieu of all living organisms. Most metalloproteins also include iron, making them the two most common trace metals in living systems. Inorganic medicines containing these metal ions are currently utilized to treat a wide range of illnesses; for example, they are employed as antibiotics, antifungals, and even cancer treatments. The fact that these metal ions are already relatively non-toxic before they are coordinated with the ligands is another argument in their favour. There are an infinite number of ligands that may be used in drug design, however the selected amino acids, N-heterocycles (1,10 phenanthroline, bipyridine), and pyrazolones all have advantageous features. There is a greater probability of success in constructing a less toxic and affordable medicine with high activity if the drug's environment is comparable to that of the tasks carried out within the body, since amino acids are the construction blocks of the human body. N-

heterocycles and pyrazolones as ligands also modify the complex environment to make the drug more lipophilic, which is an important considerationat every stage of developing a new medicine.

21	22	23	24	25	26	27	28	29	30
Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn
44.9559	47.867	50.9415	51.9961	54.938	55.845	58.9332	58.6934	63.546	65.4089
Scandium	Titanium	Vanadium	Chromium	Manganese	Iron	Cobalt	Nickel	Copper	Zinc
39	40	41	42	43	44	45	46	47	48
Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd
88.9058	91.224	92.9064	85.94	98	101.07	102.9055	106.42	107.8682	112.411
Yttrium	Zirconium	Niobium	Molybdenum	Technetium	Ruthenium	Rhodium	Palladium	Silver	Cadmium
71	72	73	74	75	76	77	78	79	80
Lu	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg
174.967	178.49	180.9497	183.84	186.207	190.23	192.217	195.084	196.9666	200.59
Lutetium	Hafnium	Tantalum	Tungsten	Rhenium	Osmium	Iridium	Platinum	Gold	Mercury

Fig :- 5 Transition Metal Ion Series

Evidence for the efficacy of metal-based treatments comes from their long history of usage in medicine, which extends back millennia. Physiologically relevant compounds employ active site models inspired by transition metal chelates. These models hold significant importance in the field of bio-inorganic chemistry and redox enzyme systems. They offer a foundation for the advancement of non-porphyrinic metal-based photodynamic treatment (PDT) specialists, equipped for DNA photocleavage under apparent light. This ability stems from their wide-ranging coordination geometry, adaptable redox properties, as well as their distinct spectral and magnetic features. Bioinorganic chemists, pathologists, pharmacologists, and oncologists all contribute to understanding the complex link between active metals and cancer. DNA cleavage may be induced by the reactive oxygen species (ROS) produced by redox-active metals. Use of metals and metal complexes in medicine was first documented in the sixteenth century. The primary use is in the treatment of cancer, since some heavy metals may kill malignant growth cells by restricting to DNA and triggering cell death via DNA distortion. The anticancer medicine cis-platin, for instance, is among the most effective and extensively used options available today. However, it only works for a narrow range of malignancies and has developed resistance over time. Metal-based medicines like oxaliplatin and carboplatin have been developed to overcome cis-platin's drawbacks.

INTERACTIONS IN DNA-METAL COMPLEXES

DNA stores and distributes essential information for life, and it is constantly accessible for this purpose. Therefore, it serves as the primary intracellular target for researchers who want to create a novel medicine to treat a wide assortment of issues, including malignant growth. This biological information may be accessed and manipulated to produce the desired effects by using tiny compounds that bind to and react with particular DNA locations. Covalent and non-covalent binding are only two of the numerous ways that tiny molecules may interact with DNA. Cisplatin prevents DNA from replicating by forming a covalent bond with the molecule. Intercalation is the most crucial non-covalent binding form because it causes cellular deterioration more often than groove binding or external electrostatic binding. Numerous laboratories are still actively studying the effects of V(IV), Ni(II), Co(II), Cu(II), and Zn(II) complexes on DNA, despite the abundance of published findings on such interactions. The majority of laboratories are focusing only on copper Schiff-base complexes. Copper holds a crucial position in the domains of redox science, development, and improvement, making it a minor component found inside every living creature. Different catalysts and proteins, for example, cytochrome oxidase, superoxide dismutase (Grass), ascorbate oxidase, and tyrosinase, rely upon copper to ensure their optimal performance. Copper, more so than any other divalent cation, has been discovered to bind DNA with great affinity, increasing the likelihood of DNA oxidation.

Two novel copper Schiff-base complexes were synthesized by Acquaye et al., and DNA interactions with CTDNA were performed. The resulting Kb values for the complexes are 1.52 105 M1 and 5.00 105 M1. Two new Schiff base copper(II) edifices including kaempferol and polyamines like ethylenediamine and diethylenetriamine have been synthesised and described by Yang and his coworkers. They analysed the DNA-DNA interactions with CT DNA and concluded that intercalation was the most likely method of contact. By synthesising two novel benzimidazole based copper complexes, Lin and his colleagues have performed extensive DNA-metal complex interaction. Researchers found evidence of incomplete intercalation of the compounds into DNA. Gup and Gokce's newly synthesised copper complexes efficiently cleave pBR322 DNA and show strong binding to calf thymus DNA through groove restricting and intercalation mechanisms. Enhanced intercalation into CT DNA was observed in three new copper(II) complexes synthesized by Xu et al.

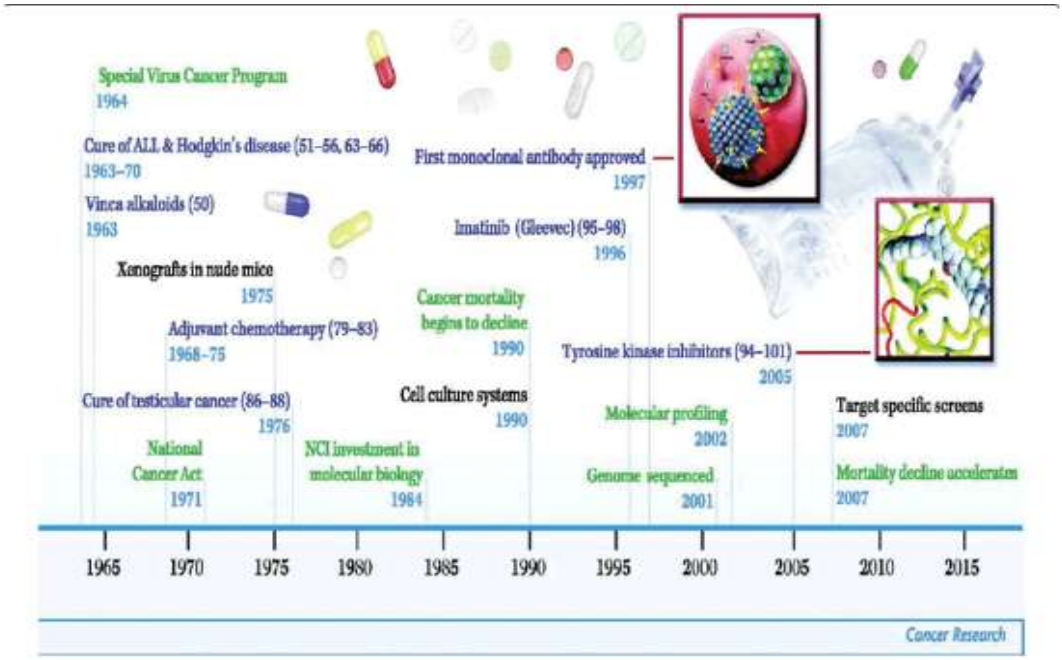

Fig :- 6 Yearly Metal complexes use in Chemotherapy of cancer.

When compared to organic substances, medicinal inorganic chemistry provides more options for the development of therapeutic medicines. The restorative scientist approaches a wide assortment of reactivities because of the extensive assortment of coordination numbers and estimations, open redox states, thermodynamic and engine characteristics, and innate features of the cationic metal molecule and ligand itself. As more and more microorganisms develop resistance to several drugs, it has become far more difficult to effectively treat infectious illnesses. The advent of both previously unknown and previously known antibiotic-resistant bacterial strains has resulted in an urgent need for the production of another class areas of strength for ofmedicines. This means that heterocyclic compounds are crucial in the development of new classes of structural entities with important therapeutic effects and novel mechanisms of action. Heterocyclic compounds offer a wide variety of pharmacological activities, including the more notable antimalarial, antibacterial, calming, hostile to disease, pain relieving, and anticonvulsant effects.

SUBSTANCES THAT KILL MICROBES

The problem of decreased quinolone medication absorption when taken with magnesium or aluminum antacids is the topic of a review by Turel. He discussed the antimicrobial properties and crystal structures of certain quinolonemetal compounds. The quinolone's chelate attaching to

the metal is postulated to be the cause of this phenomenon. The [Cu (cx)2] complex. Several bacteria were tested for susceptibility to 2H2O (where cx = cinoxacin), and the results showed that it had the same antibacterial activity as the free ligand [minimal inhibitory concentration (MIC) values].

Scozzafava and colleagues conducted an investigation into the antibacterial properties of complexes formed by ciprofloxacin with zinc and copper on a range of Gram-positive and Gram-negative bacterial strains. Recently, the Psomas research group evaluated the antimicrobial effectiveness of oxolinic acid (Hoxo) both with and without the presence of Lewis bases, such as 2,2′-bipyridine (bipy), 2,2′-bipyridylamine (bipyam), 1,10-phenanthroline (phen), pyridine (py), or 4-benzylpyridine (4bzpy). Their findings indicated that these complexes exhibited antimicrobial efficacy similar to that of free Hoxo.

Kumar et al. synthesized copper(II) complexes containing isoxazole Schiff bases, denoted as [Cu(L1)2], [Cu(L2)2], and [Cu(L3)2], where 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, C12H11BrN2O2]. Their results from antibacterial screening revealed that the Cu(II) complex with ligand L1 exhibited superior antimicrobial activity compared to the other ligands and the standard.

Devi et al. described a progression of blended ligand buildings of Co(II), Ni(II), Cu(II), and Zn(II) utilizing different strategies, including components investigation, conductometric studies, attractive helplessness estimations, and spectroscopic procedures. In vitro testing of various focuses (25, 50, 100, 200 g/mL) of ligands and their edifices against different pathogenic Gram-positive microscopic organisms, Gram-negative microbes, and parasites demonstrated that the copper(II) complex displayed the most potent antibacterial properties, surpassing the activity of the free ligands.

Dhanaraj et al. synthesized novel mixed ligand complexes of Co(II), Ni(II), Cu(II), and Zn(II) using N2, N3-bis(4-nitrophenyl) quinoxaline-2,3-diamine and 1,10-phenanthroline. These compounds were thoroughly characterized using a combination of techniques, including elemental analysis, attractive vulnerability estimations, molar conductance estimations, UV-Vis,

IR, 1H NMR, mass spectrometry, and ESR spectra. The antibacterial movement of these buildings was surveyed utilizing the plate dissemination strategy against different bacterial and parasitic strains, including E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Aspergillus niger, and Candida albicans, with the largest inhibition zone observed for the Cu(II) complex.

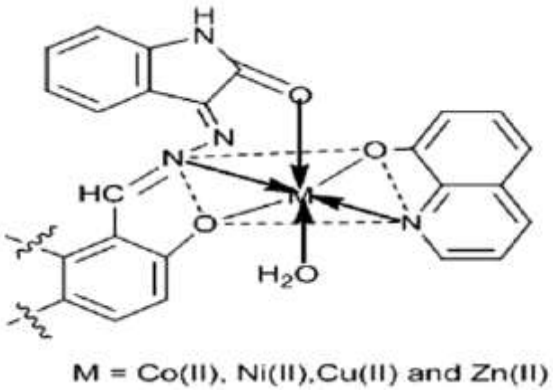

Fig :- 7

ANTI-TUMOR AGENTS

However, none of these studies delved into the purposeful synthesis of ternary copper(II) compounds. These compounds are created through the amalgamation of a bidentate N-donor heterocyclic ligand (such as phen, bpy, or their substituted versions) with various synthetic co-ligands (for instance, salicylic acid, tetracycline derivatives, terpyridine, or imidazolidine-2-thione).

Reedijk et al. have recently unearthed that their synthesized compound, [Cu(pyrimol)Cl], exhibited a remarkable ability to induce self-activated DNA breakage, resulting in lethal effects on both L1210 murine leukemia and A2780 human ovarian cancer cell lines. In a similar vein, scientists collaborating with Sadler have ascertained that mixed ligand bis(salicylato) copper(II) complexes, featuring diimines, demonstrate noteworthy cytotoxic and antiviral properties.

Palaniandavar and colleagues have described several ternary copper(II) complexes possessing potent DNA binding and cleavage capabilities, along with the ability to induce apoptosis in cancer cells. Furthermore, Kumbhar and fellow researchers have conducted studies on the cytotoxicity of various mixed ligand Cu(II) complexes against HeLa (cervical) cancer cell lines.

In the realm of anticancer therapeutics, success is often achieved through chemicals that directly damage DNA, hinder the production of nucleic acid precursors to indirectly impede DNA synthesis, or disrupt hormonal signals that stimulate cell growth. Sigman et al. have outlined the oxidation of DNA and RNA as a direct strategy for examining the connections between nucleic acids, oligonucleotides, and proteins. Burstyn and partners have uncovered that copper(II) buildings including macrocyclic triamines invigorate the hydrolytic cleavage of plasmid DNA..Because of their strong nucleobase affinity and biological accessibility, copper(II) complexes are being explored as possible reagents for both oxidative and hydrolytic breakage of DNA. Such metal complexes would allow for targeted delivery to particular DNA locations by mimicking the target's structure, symmetry, and functionality. Through investigations conducted both within living organisms (in vivo) and in controlled laboratory settings (in vitro), it has been observed that certain mixed chelate transition metal-based medications exhibit more potent anticancer effects compared to cisplatin. These studies have utilized human cancer cell lines as a valuable model for examining the impact of naturally occurring compounds and newly synthesized substances on the proliferation of tumor cells.

The Sinha research group has successfully synthesized a monoanionic tetradentate-N2O2 Schiff base, specifically 2-[[2-(dimethylamino) ethyl] imino] methyl. This compound, along with its analogues, [Co(LH)2 (NCS)]NO3 and [Co(LH)2(N3)]NO3, represents mononuclear Co(II) derivatives. Interestingly, the tetradentate ligand LH can coordinate with metal ions in either a bidentate-NO or terdentate-N2O manner.

To assess their anticancer potential in laboratory settings, these Co(II) derivatives have been tested on various human cell lines, including colorectal carcinoma cells (COLO 205 cells), hepatocellular carcinoma cells (PLC5 cells), lung carcinoma cells (A549 cells), and fibroblast cells (NIH 3T3). This in vitro analysis provides insights into the effectiveness of these compounds against different types of cancer cells. Both Co(II) derivatives have been shown to have negative biological effects on NIH 3T3 cell viability, suggesting that they promote cell death through apoptosis in human fibroblasts. Research using the chemical [Co(LH)2(N3)]NO3 on human fibroblasts cells (NIH 3T3) reveals the apoptotic capacities of the Co(II) complex and recommends that it initiates a mitochondria-intervened mechanism.

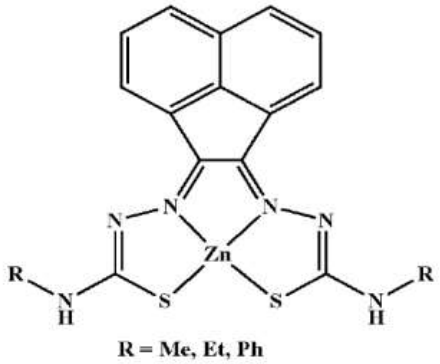

Fig :- 8

ANTIPARASITIC AGENTS

Some metal complexes, including those containing gold (Au), platinum (Pt), iridium (Ir), palladium (Pd), rhodium (Rh), and osmium (Os), have been shown to be effective against trypanosomatids. Parasites rely on cysteine proteases for a variety of functions during their life cycles, including feeding, invading hosts, digesting proteins, and avoiding the host immune system. There is evidence that arsenic and bismuth may be used to treat trypanosomiasis and leishmaniasis, respectively. Salversane and neosalversane have been studied extensively for its ability to treat syphilis. There has been a decline in the effectiveness of current antimalarial medications against the parasite Plasmodium. A rising number of intestinal sickness parasites have created protection from the antimalarial medication chloroquine, highlighting the critical need for alternative, highly effective treatments. Chloroquine and clotrimazole complexes with gold and ruthenium have also been created and tested against Plasmodium in the hopes of achieving more effective treatment outcomes. The ruthenium compound with chloroquine has been shown to be two to five times more effective than the standard chloroquine.

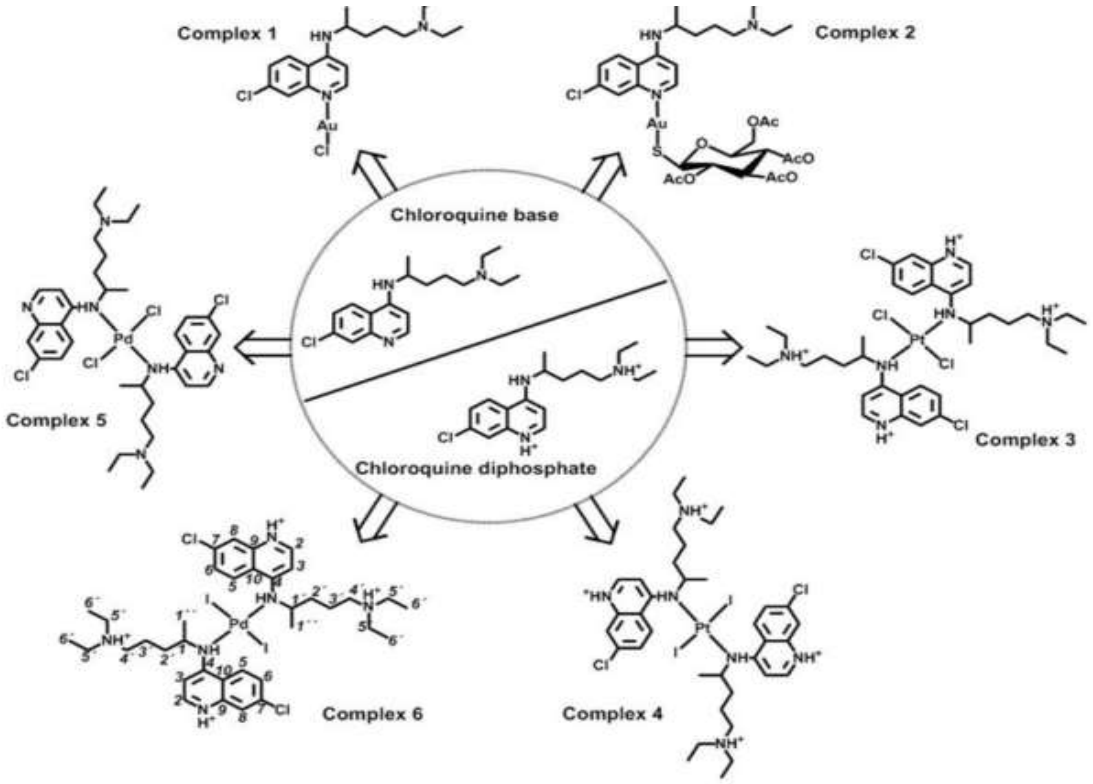

Figure :- 9

DRUGS BASED ON CHLOROQUINE AND ITS EFFECTS

Acute toxicity was not seen in an in vitro test against a chloroquine-safe kind of Plasmodium falciparum. The expansion of the metal increased chloroquine's effectiveness (101). Even in chloroquine-resistant instances, several of these complexes had better treatment outcomes. Antimony compounds used to treat leishmaniasis are another instance where metal complexes have proven effective.

CISPLATIN, AN ANTICANCER MEDICATION, AND ITS MODE OF ACTION.

Many compounds containing metals have a long history of use in medicine for the treatment of a broad range of diseases. Metal edifices have procured prevalence as indicative apparatuses and anticancer specialists in medicinal chemistry, a field formerly dominated by organic chemistry. In terms of global mortality rates, cancer ranks second. The cytotoxic effects of cisplatin, a metal complex, led to the identification of additional such compounds that may be used to treat cancer. The medical use of organo-metallic compounds dates back millennia. The pharmaceutical and

agricultural industries rely heavily on metal complexes. At the molecular level, the metallo-elements present in tiny amounts perform crucial functions. The activity of several enzymes depends on the presence of transition metal ions. Groups 3–12 of the periodic table are known as the D block, which contains the transition metals. Their d shells are now being filled. Transition metals with a partly filled d orbital provide useful electrical characteristics for use as probes in the development of cancer treatments. Coordination compounds were first developed due to this characteristic of transition metals. An inorganic compound called cisdiammine-dichloroplatinum (II) (cisplatin) was shown to have anti-tumor action in the year 1960. When it comes to treating solid carcinomas, cisplatin has quickly become one of the most popular and successful drugs available. In this article, we'll look at the progress made towards creating effective anticancer drugs including complexes of platinum, gold, copper, and ruthenium.

When it comes to creating novel therapeutic chemicals, metal-containing compounds have several benefits over their carbon-based counterparts. These benefits stem from the fact that these ligands can be coordinated in three dimensions, allowing for the functionalization of gatherings that can be controlled to tie to explicit atomic targets.Suitable probes for use in the development of anticancer drugs may be found in the partly filled d orbitals of transition metals. Due to its significance in determining the appropriate dosage and bioavailability of the delivered chemical, the oxidation state of a metal is similarly a fundamental figure the arrangement of coordination compounds. Furthermore, as shown by the commonly used medication cisplatin, metals' capacity to conduct ligand exchanging reactions provides a plethora of chances to interact and coordinate to biological molecules. In addition, one is not limited to the metals chosen by nature when constructing metal-based treatments; rather, one may take use of the special characteristics of other metals, such as those in the first and second rows of the periodic table, that can provide benefits beyond those found in nature.[6] Recent progress in the creation of platinum, ruthenium, copper, and gold anticancer drugs is the topic of this article.

PLATINUM-BASED ANTICANCER COMPLEX

For quite some time, platinum (II) complexes have been employed as anti-cancer medications, with cisplatin standing out as a particularly potent chemotherapeutic agent. This first-generation anticancer medication is still among the most powerful chemotherapeutics available today ([1]). Perhaps the most well-known example of a metal-containing medication with a tiny molecule is

cisplatin (cis-[PtCl2 (NH3)2], also known as cis-DDP) (Fig. 1).[2] New evidence suggests that the yeast and mammalian copper carrier Ctr1p is likewise engaged with the take-up of cisplatin into cells. Cisplatin's cytotoxicity results from the covalent cross-links it forms with DNA. When cisplatin binds to DNA, it significantly distorts the helical shape of the molecule, which in turn prevents DNA replication and transcription. Metals like Pt are removed from the cell through interacting with a variety of negatively charged biomolecules within the cell, including DNA, proteins, sulphur-containing substances like metallothioneins, and glutathione.Cisplatin and other DNA-binding anticancer medicines may exert their cytotoxicity primarily via DNA damage and the consequent activation of apoptosis, as discussed in [7].In addition to its usage for treating cervical, nasopharyngeal, esophageal, and head and neck diseases, cisplatin is also effective against small cell lung cancer, epithelial ovarian, and gestational trophoblastic tumours. Neuro-, hepato-, and nephrotoxicity significantly restrict the therapeutic use of cisplatin against this and other cancers despite its efficacy. Inborn or gained opposition is one more issue frequently connected with platinum-based meds, restricting their clinical use notwithstanding the huge foundational harmfulness.[4] Carboplatin and oxaliplatin, two platinum analogues of the second and third generations respectively (Fig. 1), were developed and tested in the clinic in an attempt to remedy these drawbacks.

Multiple structural properties are amenable to strategic modification while developing a novel platinum anticancer drug. A platinum anticancer complex typically consists of three distinct ligand types, as indicated in Figure 1. Nitrogen-donating ligands L are the norm. Because of their ability to make thermodynamically steady bonds with platinum and remain in the last platinum-DNA adduct, these ligands are suggested be "non-leaving pack" ligands. The accompanying platinum-DNA adducts and the cell fix components that answer them are very sensitive to the specific modifications of these ligands.

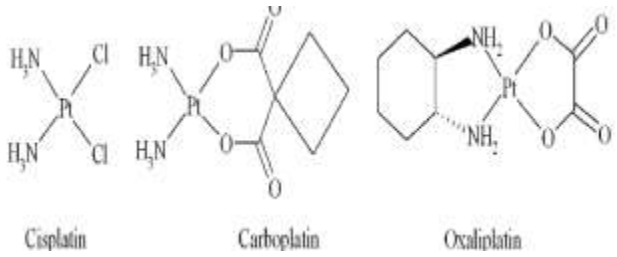

Figure:- 10 Chemical Structure of various Cis compounds

Solve the problem of the adducts. Compared to cisplatin, complexes featuring amine ligands structurally distinct from those found in cisplatin frequently show a more extensive range of action against malignant growth cell lines. Remarkably, these complexes tend to avoid developing resistance typically associated with cisplatin. Within this category lies oxaliplatin, distinguished by its chiral chelating 1,2-diaminocyclohexane (DACH) ligand, explicitly trans-1R,2R-DACH. Alterations in the leaving group ligands, referred to as X, can significantly impact the general response stoichiometry and aquation energy of a platinum-based anticancer complex. This is termed as such because these ligands are released during DNA binding.

Complexes with rapid reactivity, including those incorporating labile nitrate ligands, possess a greater potential for hazards due to their propensity to nonspecifically bind to biological nucleophiles. Conversely, carboplatin employs a CBDCA (CBDCA = 1,1-cyclobutane-dicarboxylato) ligand as its leaving group, known for its stability. Carboplatin boasts a reduced toxicity profile in comparison to cisplatin, enabling the administration of higher doses. Nevertheless, it's important to note that cross-resistance to cisplatin is observed with carboplatin due to the shared non-leaving bunch ammine ligands.

The third classification involves the axial ligands denoted as R, a feature just present in higher-valent platinum edifices like platinum(III) and platinum(IV). While natural decrease of the platinum complex may potentially lead to the dissociation of these axial ligands, there is no guarantee that this will occur.. They make it easy to attach nanoparticles or install tumor-targeting moieties. Changing one or more of the three ligand types may result in a platinum complex with different lipophilicity and water solubility. Both of these characteristics are crucial while developing a medicine. Both the stereochemistry and the total number of ligands may be changed.

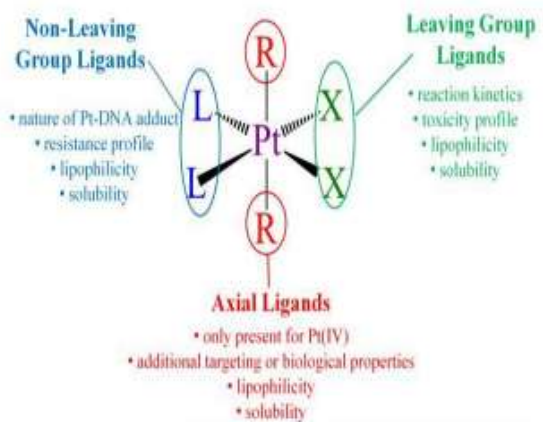

Fig :- 11 Different Cis Platin Structure

CONCLUSIONS

Catalysis, material production, photochemistry, treatment, and diagnostics are just few of the many areas where transition metal complexes are useful. Metal complexes of a number of pharmaceuticals have been examined for their chemical, optical, and magnetic characteristics. Numerous medicinal compounds, including pyrazinamide, nicotinamide, nicotinic acid, tolbutamide, theophylline, captopril, clonidine, and guanfacine, have been explored in the context of metal complexes. Valuable insights into these complexes and ligand structures have been derived from a spectrum of spectroscopic methods such as Fourier transform infrared spectroscopy, Raman spectroscopy, surface-enhanced Raman spectroscopy, X-ray spectroscopy, mass spectrometry, ultraviolet-visible spectrophotometry, electron paramagnetic resonance spectroscopy, and X-ray diffraction. Calculations of complexation ratios were conducted using methodologies distinct from elemental analysis, electrochemistry, and thermal analysis.

The examination of scanning electron microscope images has revealed whether the metal buildings have a glasslike or shapeless nature. As a result of their increasing clinical and economic importance, numerous research endeavors have been undertaken to synthesize and investigate metal buildings, in which the restorative mixtures satisfy the job of ligands.

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