



Review Article

Metal Complexes as Potential Antimicrobial Agent: A Review

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Abstract: Metal ions play many critical functions in humans. Deficiency of some metal ions can lead to disease like pernicious anemia resulting from iron deficiency, growth retardation arising from insufficient dietary zinc, and heart disease in infants owing to copper deficiency. Antibiotic resistance has been growing at an alarming rate and consequently the activity of antibiotics against Gram-negative and Gram-positive bacteria has dropped dramatically day by day. In this sense there is a strong need to synthesis new substances that not only have good spectrum of activity, but having new mechanisms of action. Inorganic compounds particularly metal complexes have played an important role in the development of new metal based drugs. A significantly rising interest in the design of metal complexes as drugs and diagnostic agents is currently observed in the area of scientific inquiry, specifically termed medicinal inorganic chemistry. In this review our main focused on research undertaken over the past few decades which has sought to possess preclinical pharmacological screenings like anti-bacterial, anti-fungal, anti-inflammatory, anti-cancer, DNA- interaction and anti-tumor action of synthetic metal complexes.

Keywords: Metal Based Drugs, Antibacterial, Antifungal, Anti-inflammatory, Anti-Cancer, DNA-Interaction and Anti-tumor Activity

1. Introduction

Metal ions play important roles in biological processes and the field of knowledge concerned with the application of inorganic chemistry to therapy or diagnosis of disease is medicinal inorganic chemistry [1]. The introduction of metal ions or metal ion binding components into a biological system for the treatment of diseases is one of the main subdivisions in the field of bioinorganic chemistry [2-5]. A characteristic of metals is that they easily lose electrons to form positively charged ions which tend to be soluble in biological fluids. It is in this cationic form that metals play their role in biology. Metal ions are electron deficient, whereas most biological molecules such as proteins and DNA are electron rich. The attraction of these opposing charges leads to a general tendency for metal ions to bind and interact with biological molecules [6-7]. This same principle applies to the affinity of metal ions for many small molecules and ions

crucial to life, such as oxygen. Given this wide scope for the interaction of metals in biology, it is not surprising that natural evolution has incorporated many metals into essential biological functions. Metals perform a wide variety of tasks such as carrying oxygen throughout the body and shuttling electrons. Hemoglobin, an iron-containing protein that binds to oxygen by which it carries this vital molecule to body tissues. Similarly, calcium-containing minerals are the basis of bones, the structural framework of the human body. Metals such as copper, zinc, iron and manganese are incorporated into catalytic proteins, the metalloenzymes, which facilitate a multitude of chemical reactions needed for life. Metal complexes are already in clinical use, and encourage further studies for new metallo drugs such as metal mediated antibiotics, antibacterials, antivirals, antiparasitics, anti-HIV [8], anti-diabetes, radio-sensitizing agents and anticancer compounds [9-23]. Transition metal complexes offer two distinct advantages as DNA-binding agents [24-29]. Hence,

herein the attention is focused primarily on the research concerning with a few pharmacological activities of the cheaper and easily available first-row transition metal coordination compounds V(IV), V(II), Cr(III), Mn(II), Fe(II) and Co(II) complexes. Moreover, these metal ions are the essential elements present in the biological intracellular environment of living organisms. They are most abundantly found trace elements present in biological systems together with iron and most of the metalloproteins have these elements [30-33]. These metal ions are nowadays present in several inorganic pharmaceuticals used as drugs against a variety of diseases, ranging from antibacterial and antifungal to anticancer applications [34-41]. In addition to that, the N-heterocycles, pyrazolones and quinazolinone derivatives as ligands affect the environment of the complex in such a way that their lipophilicity increases which is a major factor in designing a drug [42-53]. The literature survey reveals that numerous review articles and books have been published on medicinal inorganic chemistry in the field of metallodrugs [54-64] and especially on anticancer and anti-tumor treatments [65-72]. In this paper we have explored the overview of important application of metal complexes in medicine and drugs.

2. Metal Complexes as Biologically Active

2.1. Antimicrobial Activity of Some Metal Complexes

Antibiotics are substances which, even at low concentrations, inhibit the growth and reproduction of bacteria and fungi. The treatment of infectious diseases would be inconceivable today without antibiotics (Koolman and Roehm, 2005). Hakan Arslan *et al.* [73] synthesized five thiourea derivatives ligand and their Ni²⁺ and Cu²⁺ complexes. Those compounds were screened for their *in vitro* anti-bacterial activity using Gram-positive bacteria (two different standard strains of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Streptococcus pyogenes*, *Bacillus cereus*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Proteus vulgaris*, *Enterobacter aerogenes*). Sohail Saeed *et al.* prepared nickel(II) and copper(II) complexes of *N* - (alkyl (aryl) carbamothioyl) - 4 - nitrobenzamide and those complexes were screened for antibacterial activity against *S. aureus*, *S. epidermidis*, *E. faecalis*, *E. coli*, *E. cloacae* and *P. vulgaris* by the broth microdilution procedure [74]. Yu-Ye Yu *et al.* synthesized Mn(II), Co(II), Ni(II), Cu(II) and Cd(II) complexes with Schiff base ligand 2-[(4-methylphenylimino) methyl]-6-methoxyphenol, obtained by condensation of *o*-vanillin (2-hydroxy-3-methoxybenzaldehyde) with *p*-toluidine. The Schiff base ligand and its complexes have been tested *in vitro* to evaluate their antibacterial activity against bacteria, viz., *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis* [75]. Yu-Ye Yu *et al.* [76] synthesized two Zinc(II) Complexes with a Schiff base derived from

o-vanillin and *p*-toluidine and investigated their *in vitro* antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Proteus vulgaris*, *Enterobacter aerogenes*. Co(II), Ni(II) and Cu(II) complexes were synthesized with 2,5-diamino-1,3,4-thiadiazole ligand. The ligand and metal complexes were tested against bacteria viz *Salmonella typhi*, *Shigella species*, *Escherichia coli*, *Klebsiella species*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Nisseria gonorrhoe* [77]. Obaleye, J. A *et al.* Ni(II) Complex of Mefloquine Hydrochloride and investigated their antimicrobial activity [78]. Abdullah M. Asiri and Salman A. Khan prepared Pd(II) metal complexes with Steroidal Thiosemicarbazones and investigated their *in vitro* antibacterial activity against bacterial species. The results showed that steroidal complexes are better inhibitors of both types of the bacteria (Gram-positive and Gram-negative) as compared to steroidal thiosemicarbazones [79]. A. Budakoti, synthesized new Pd(II) complexes with 1-*N*-substituted thiocarbamoyl-3,5-diphenyl-2-pyrazoline derivatives and investigated their *in vitro* biological activity [80]. 3-Aminocoumarin has been synthesized and used as a ligand for the formation of Cr(III), Ni(II), and Cu(II) complexes by Abdul Amir H *et al.* [81]. The ligand and metal complexes (figure 1) were screened against both Gram positive and Gram negative bacteria.

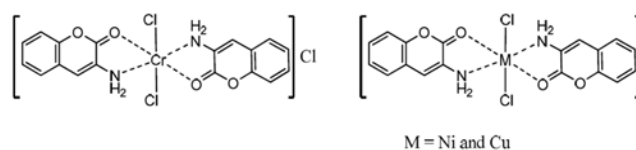


Figure 1. The proposed structure for the complexes.

Palladium complexes of pyrazoline thiocarbamoyl derivatives were investigated for antiamoebic activity. In general, their effects on *Entamoeba histolytica* were more pronounced than those of the corresponding ligands. The IC₅₀ value of complex (figure 2) was significantly less than that of metronidazole.

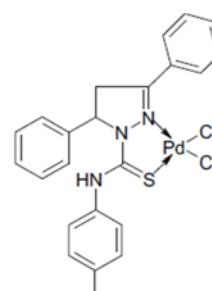


Figure 2. Structure of Pd(II) complex.

Coordination compounds of other thiocarbamoyl dihydropyrazoles with copper and nickel showed good inhibitory activity against several *Candida* strains. The activity decreased in the order CuL > NiL > L for the separate compounds. Co-administration of the coordination compounds (figure 3) and amphotericin B or fluconazole gave the reverse order L > NiL > CuL.

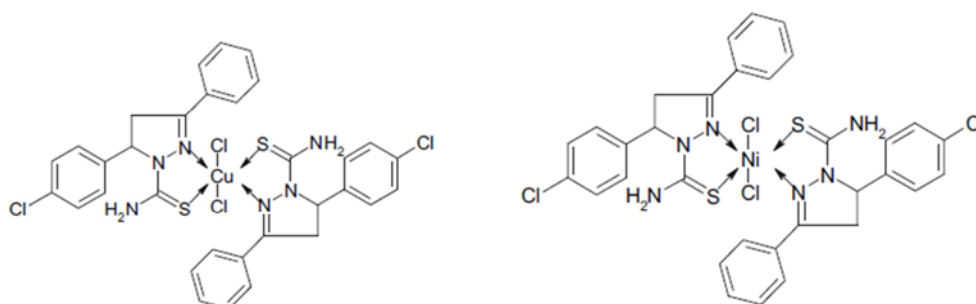


Figure 3. Proposed structure of Cu(II) and Ni(II) complexes.

The Schiff base hydrazone ligand was prepared by the condensation reaction of 7-chloro-4-quinoline with *o*-hydroxyacetophenone. The ligand behaves either as monobasic bidentate or dibasic tridentate and contain ONN coordination sites. This was accounted for the presence in the ligand of a phenolic azomethine and imine groups. It reacts with Cu(II), Ni(II), Co(II), Mn(II), UO₂(VI) and Fe(II) to form

either mono- or binuclear complexes (figure 4). The ligand HL and metal complexes were tested against a strain of Gram positive bacteria (*Staphylococcus aureus*), Gram negative bacteria (*Escherichia coli*), and fungi (*Candida albicans*). The tested compounds exhibited high antibacterial activities, investigated by Nora H. Al-Shaalan [82].

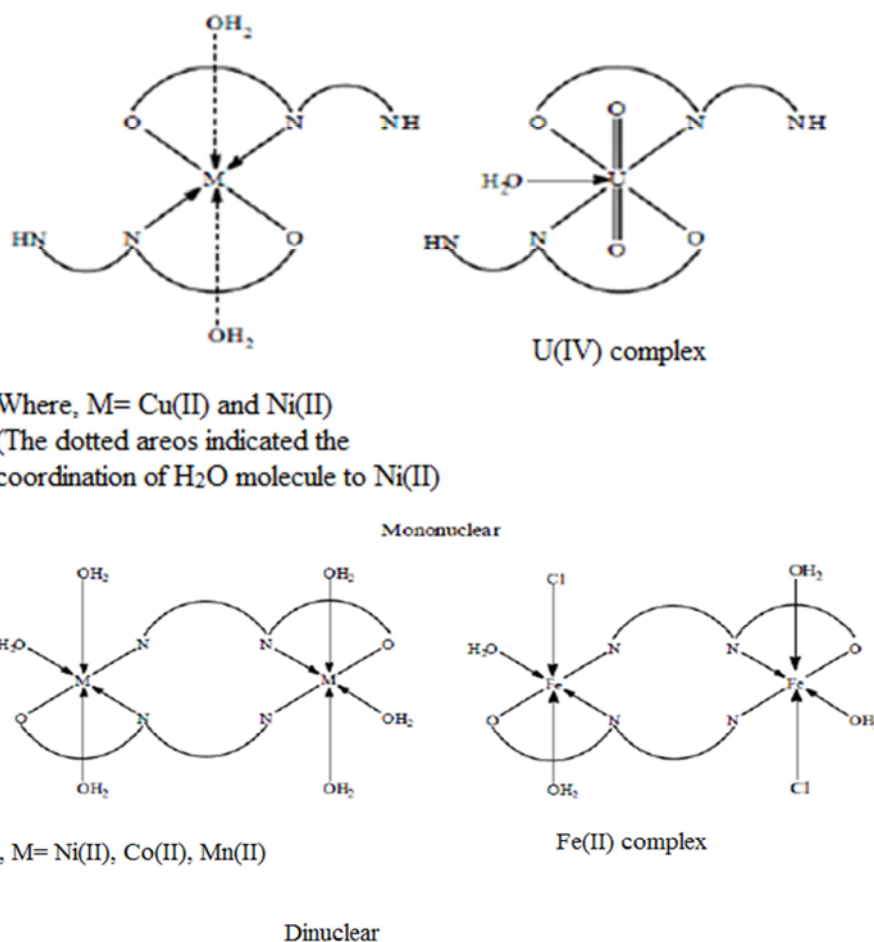


Figure 4. Structure of Cu(II), Ni(II), Co(II), Mn(II), UO₂ (VI) and Fe(II).

A series of Schiff bases derived from 2-acetylpyridine and their metal complexes were synthesized by Nura Suleiman Gwaram [83]. The complexes were screened for anti-bacterial activity against Methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii* (AC), *Klebsiella pneumoniae* (KB) and *Pseudomonas aeruginosa* (PA) using the

disc diffusion and micro broth dilution assays. Based on the overall results, the complexes showed the highest activities against MRSA while a weak antibacterial activity was observed against *A. baumannii* and *P. aeruginosa*. The reaction pathway of the coordinated complexes was shown in (Figure 5).

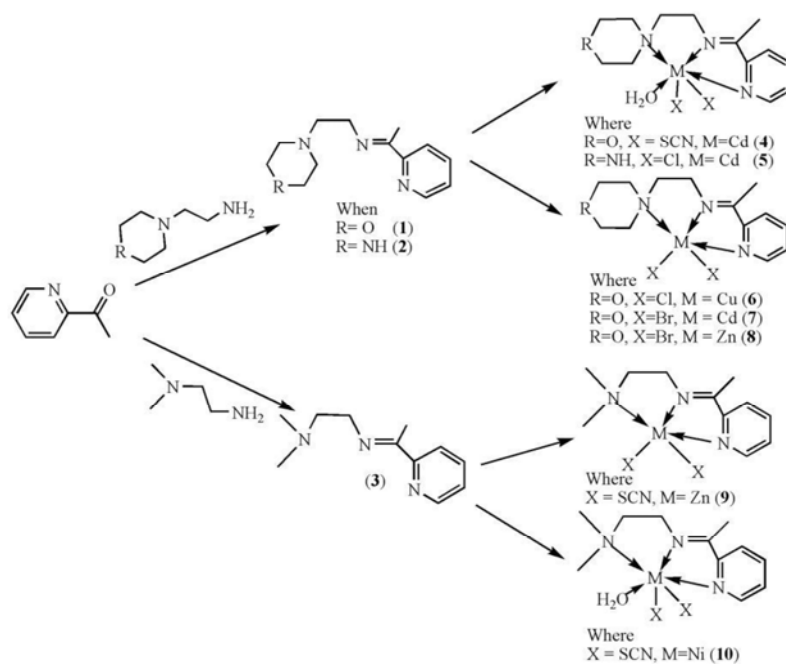


Figure 5. Reaction pathway of the Schiff base and their metal complexes.

Three azo group-containing Schiff base ligands, namely 1- $\{3-[(3\text{-hydroxypropylimino})\text{ methyl}]\text{ -4 hydroxyphenylazo}\}$ -4-nitrobenzene (2a), 1- $\{3-[(3\text{-hydroxypropylimino})\text{ methyl}]\text{ -4 hydroxyphenylazo}\}$ -2-chloro-4-nitrobenzene (2b) and 1- $\{3-[(3\text{-hydroxypropylimino})\text{ methyl}]\text{ -4 hydroxyphenylazo}\}$ -4-chloro-3-nitrobenzene (2c) and their Cu(II) and Co(II) were prepared (Figure 6) respectively by Raziye Arab Ahmadi and Saeid Amani [84].

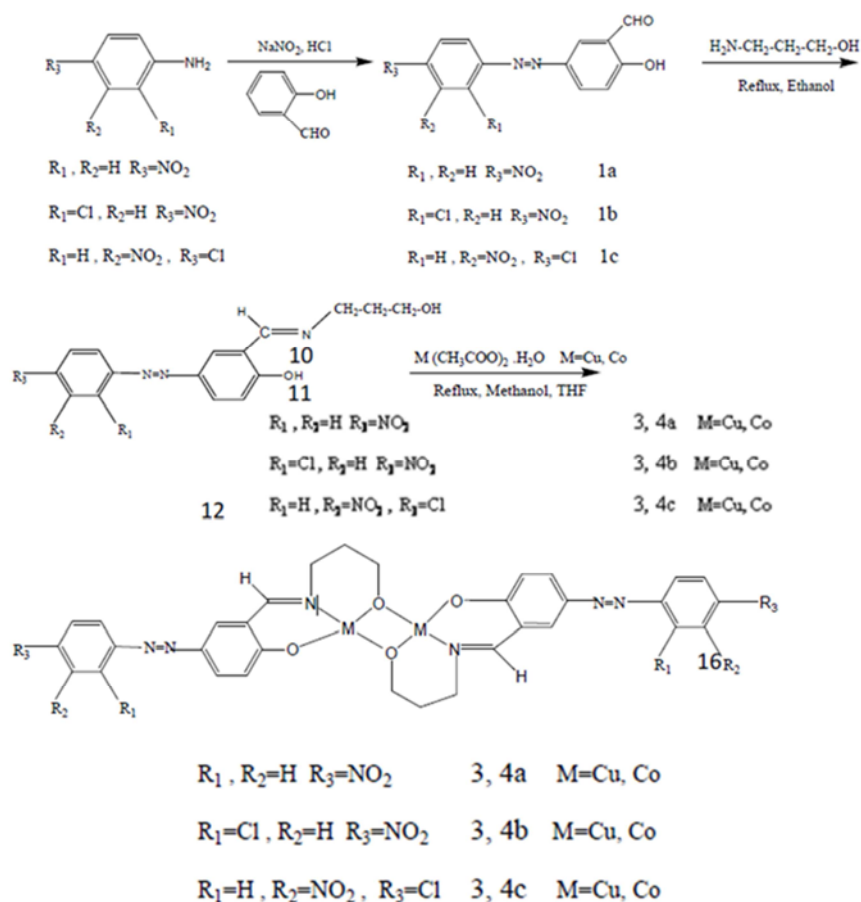


Figure 6. Preparation pathway of ligand and metal complexes.

Two novel organoantimony (V) and two organobismuth (V) complexes were synthesized with benzoic acid derivatives by Arshad Islam and *et al.* [85]. The metal complexes, their metal salts and ligands (Figure 7) were evaluated *in vitro* for their activities against *Leishmania infantum* and *amazonensis* promastigotes and *Staphylococcus aureus* and *Pseudomonas*

aeruginosa bacteria. Both the metal complexes showed antileishmanial and antibacterial activities but the bismuth complexes were the most active. Intriguingly, complexation of organobismuth (V) salt reduced its activity against *Leishmania*, but increased it against bacteria.

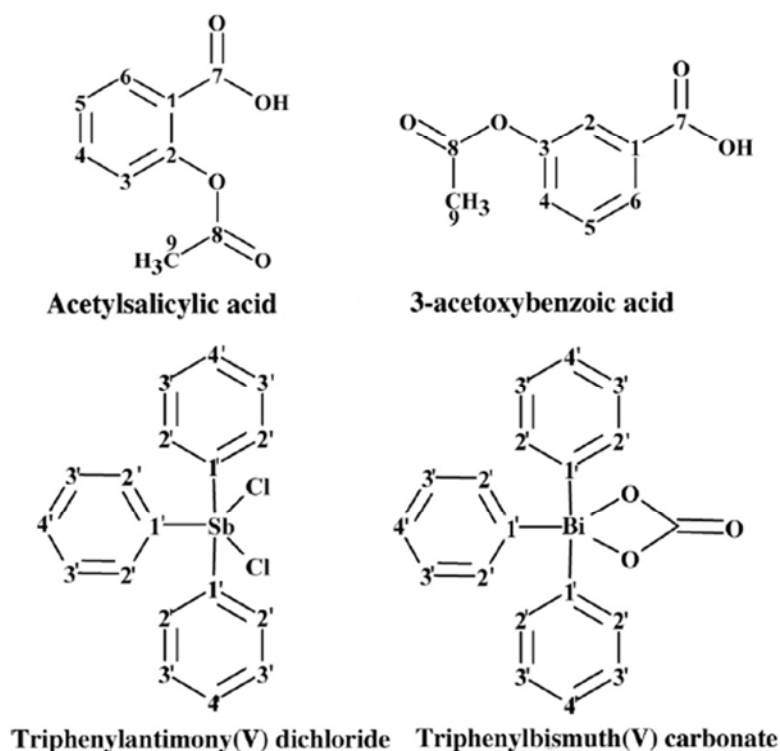


Figure 7. Structure of ligand and metal complexes.

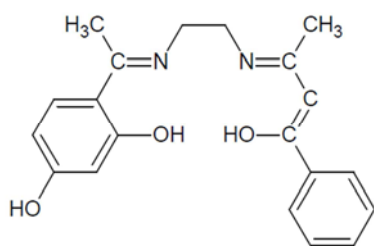


Figure 8. Structure of Schiff base (DEPH₂).

Some new Zn(II) and Cu(II) complexes with novel cyclohexane-1,3-dione ligands were synthesized by Nevin Turan *et al.* [86]. The synthesized ligands and their complexes were tested for antibacterial activity against *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 25923, and *Salmonella typhimurium* CCM 583. Some of complexes showed medium-level antibacterial activity against the tested bacteria compared with ampicillin. Ikechukwu P. Ejidike and Peter A. were synthesized Co(II), Ni(II), Zn(II) and Cu(II) complexes of (3*E*)-3-[(2-{(E)-[1-(2,4-dihydroxyphenyl)ethylidene]amino}ethyl)imino]-1-phenylbutan-1-one (DEPH₂) derived from ethylenediamine, 2',4'-dihydroxyacetophenone and

1-phenylbutane-1,3-dione. The ligand (Figure 8) and their metal complexes (Figure 9) were screened for antibacterial activity against Gram positive and Gram negative bacteria by the agar well diffusion method [87].

Antibacterial activity of a series of six nitrate silver (I) complexes with pyridine and (benz)imidazole derivatives were investigated by Urszula Kalinowska-Lis *et al.* against three Gram-negative strains: *Pseudomonas aeruginosa* ATCC 15442, *Escherichia coli* ATCC 25922 and *Proteus hauseri* ATCC 13315. The results were compared with those of silver nitrate, a silver sulfadiazine drug and appropriate ligands. The most significant antibacterial properties were exerted by silver (I) complexes containing benzimidazole derivatives [88]. New Cu(II), Pd(II) and Pt(II) complexes were synthesized from 8-ethyl-2-hydroxytricyclo (7.3.1.0^{2,7})tridecan-13-one thiosemicarbazone by Elena Pahont *et al.* [89]. The free ligand and the metal complexes (Figure 10) have been tested for their antimicrobial activity against *E. coli*, *S. enteritidis*, *S. aureus*, *E. faecalis*, *C. albicans* and cytotoxicity against the NCI-H1573 lung adenocarcinoma, SKBR-3 human breast, MCF-7 human breast, A375 human melanoma and HL-60 human promyelocytic leukemia cell lines. Copper complex 2 exhibited the best antiproliferative activities against MCF-7 human breast cancer cells.

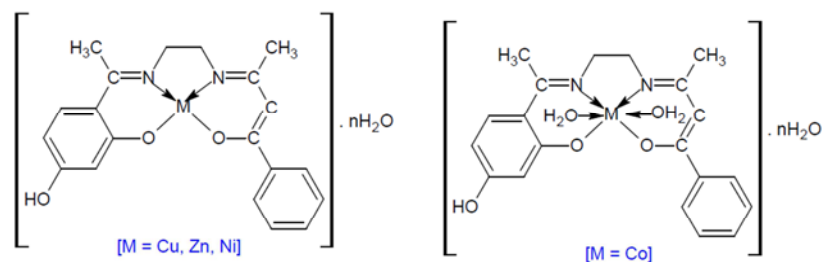


Figure 9. Structure of Schiff base metal complexes.

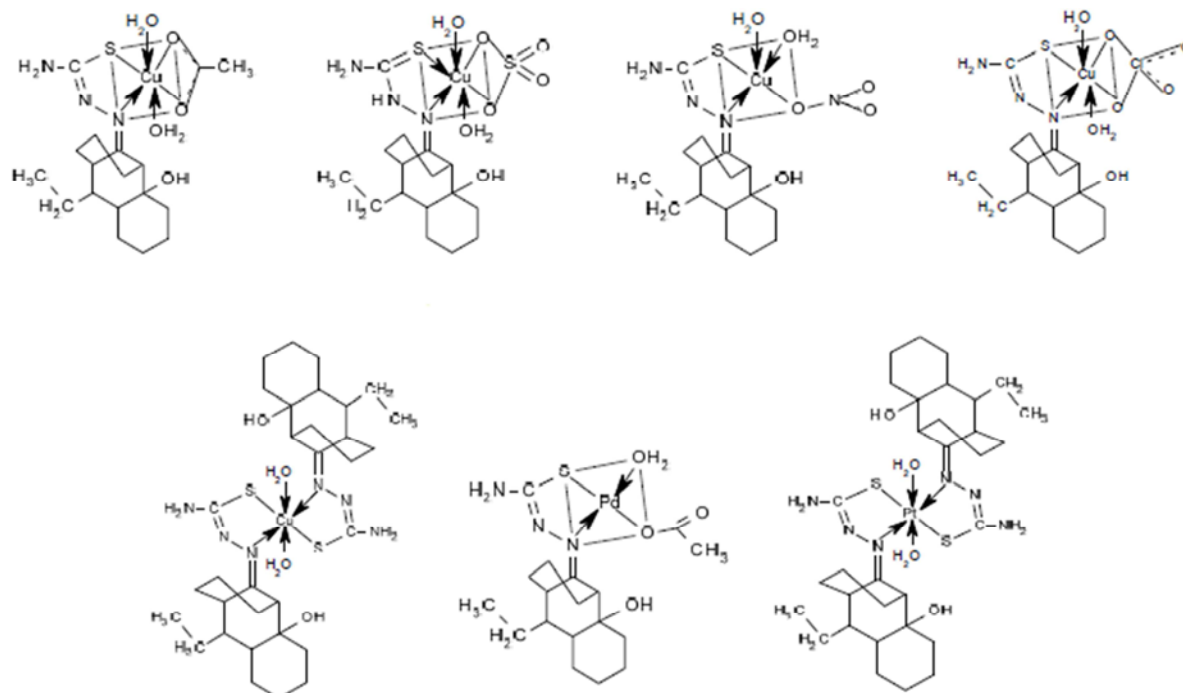


Figure 10. Proposed structure of Cu(II), Pd(II) and Pt(II) metal complexes.

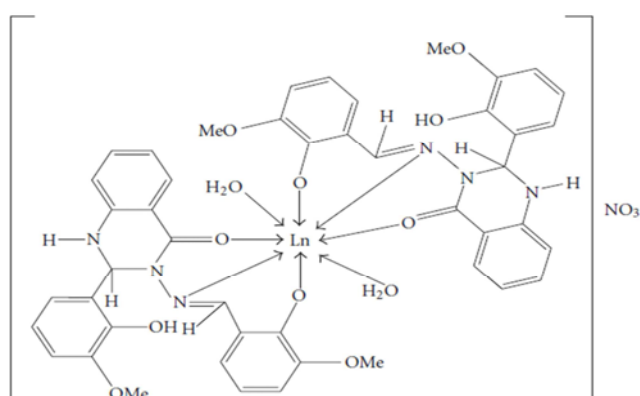


Figure 11. Proposed structure of lanthanide (III) metal complexes.

Four copper(II) complexes with a series of differently substituted fluorine-containing Schiff bases starting from the drug isoniazid (isonicotinylhydrazide) were prepared by Ladislav Habala and *et al.* The prepared compounds were evaluated for their antimicrobial activity and urease inhibition.

Two of the Schiff bases exerted activity against *C. albicans*. All copper(II) complexes showed excellent inhibitory properties against jack bean urease, considerably better than that of the standard inhibitor acetohydroxamic acid [90]. Omoruyi G. Idemudia *et al.* were synthesized Mn(II), Ni(II), Co(II), and Cu(II) complexes with new bioactive pyrazolone phenylhydrazones. Synthesized compounds were screened against Gram-positive *Staphylococcus aureus*, *Bacillus pumilus*, and Gram-negative *Proteus vulgaris*, *Aeromonas hydrophila* bacterial species [91]. Peter A. Ajibade and Nonkululeko H. Zulu were prepared Co(II), Cu(II), Zn(II) and Fe(III) complexes of diisopropylthiourea. The complexes were screened for their antibacterial activities against six bacteria: *Escherichia coli*, *Pseudomonas auriginosa*, *Klebsiella pneumoniae*, *Bacillus cereus*, *Staphylococcus aureus* and *Bacillus pumilus* [92]. A Barbara *et al.* were synthesized metal complexes of α -N-heterocyclic carboxaldehyde thiosemicarbazones. The synthesized metal complexes were investigated against *Shewanella oneidensis* [93]. New lanthanide(III) complexes (Figure 11) such as La(III), Pr(III), Nd(III), Sm(III), Eu(III), Gd(III), Th(III), Dy(III),

and Y(III) were synthesized and characterized by B. Kalagouda and et al. [94]. The metal complexes were screened against both Gram positive and Gram negative bacterial species.

Zahid H. Chohan and *et al.* were prepared and characterized Co(II) and Ni(II) complexes of N-(2-furanylmethylene)-2-aminothiadiazole and role of SO_4^{2-} , NO_3^- , $\text{C}_2\text{O}_4^{2-}$ and CH_3COO^- anions. The complexes were screened against *in vitro* antibacterial activities [95]. New bidentate or tridentate Schiff bases and their VO(II) and Co(II) complexes formed by the condensation of methyl isobutyl ketone with nicotinamide (mna)/2-amino-4-chlorophenol (map) and 2-hydroxyacetophenone with nicotinamide (han)/isoniazide (hai). Some of the complexes have been screened for their antimicrobial activity by the well diffusion technique using DMSO as solvent on different species of pathogenic bacteria/fungi, that is, *E. coli*, *S. aureus*, *S. fecalis*, *A. niger*, *T. polysporum* [96]. Some antifertility inhibitors of 18 to 24-membered tetraazamacrocyclic complexes of iron(II) and manganese(II) have been synthesised by the template condensation using 1,3-phenylenediamine with malonic acid, succinic acid, glutaric acid and adipic acid by Ashu Chaudhary *et al* [97].

The complexes have been screened *in vitro* against a number of fungi and bacteria to assess their growth inhibiting potential. Thirty two new Cu(II), Ni(II) and Zn(II) complexes (1–32) with salicylidene thiosemicarbazones (H_2L^1 – H_2L^{10}) were synthesized (Figure 12). Salicylidene thiosemicarbazones, of general formula (X)N-NH-C(S)-NH(Y), were prepared through the condensation reaction of 2-hydroxybenzaldehyde and its derivatives (X) with thiosemicarbazide or 4-phenylthiosemicarbazide (Y = H, C_6H_5). All the ligand and metal complexes have also been tested for their *in vitro* antibacterial activity against *Staphylococcus aureus* (Wood-46, Smith, 209-P), *Staphylococcus saprophyticus*, *Streptococcus* (group A), *Enterococcus faecalis* (Gram-positive), *Escherichia coli* (O-111), *Salmonella typhimurium*, *Salmonella enteritidis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Proteus mirabilis* (Gram-negative) and antifungal activity against *Aspergillus niger*, *Aspergillus fumigatus*, *Candida albicans* and *Penicillium* strains [98]. The general structure of metal complexes were shown in (Figure 13)

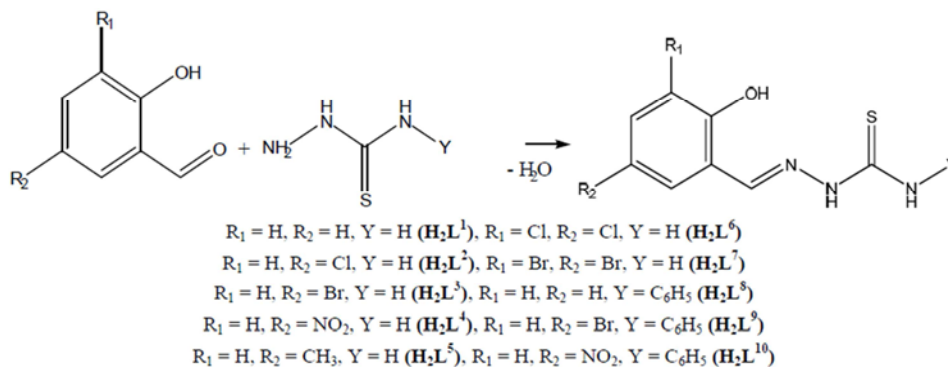


Figure 12. General synthesis of ligand $\text{H}_2\text{L}^{1-10}$.

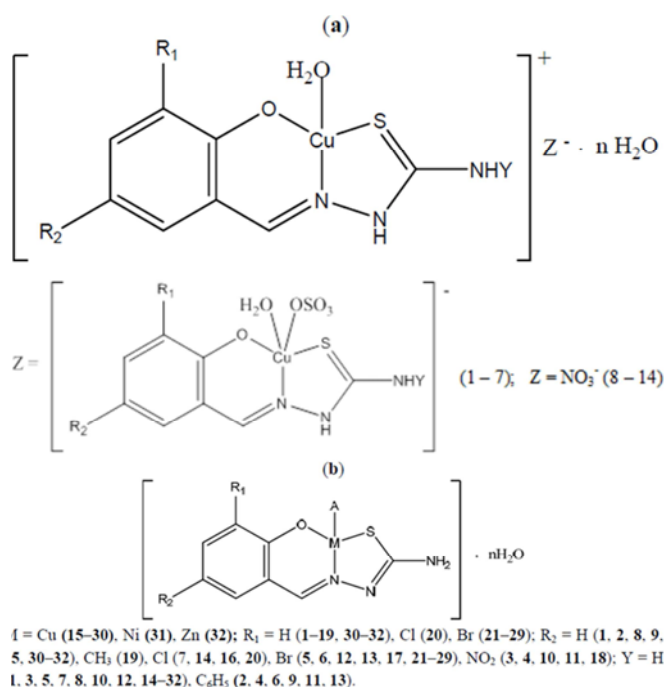


Figure 13. (a) General Structure of complexes (1-14), (b) general structure of complexes(15-32).

Sulekh Chandra *et al.* [99] were synthesized transition metal complexes of Co(II), Ni(II) and Cu(II) metal ions with pentadentate Schiff base derivative of 4-Aminoantipyrine. The ligand (Figure 14) and its complexes have been screened

for their antifungal and antibacterial activities against three fungi, i.e. *Alternaria brassicae*, *Aspergillus niger* and *Fusarium oxysporum* and two bacteria, i.e. *Xanthomonas compestris* and *Pseudomonas aeruginosa*.

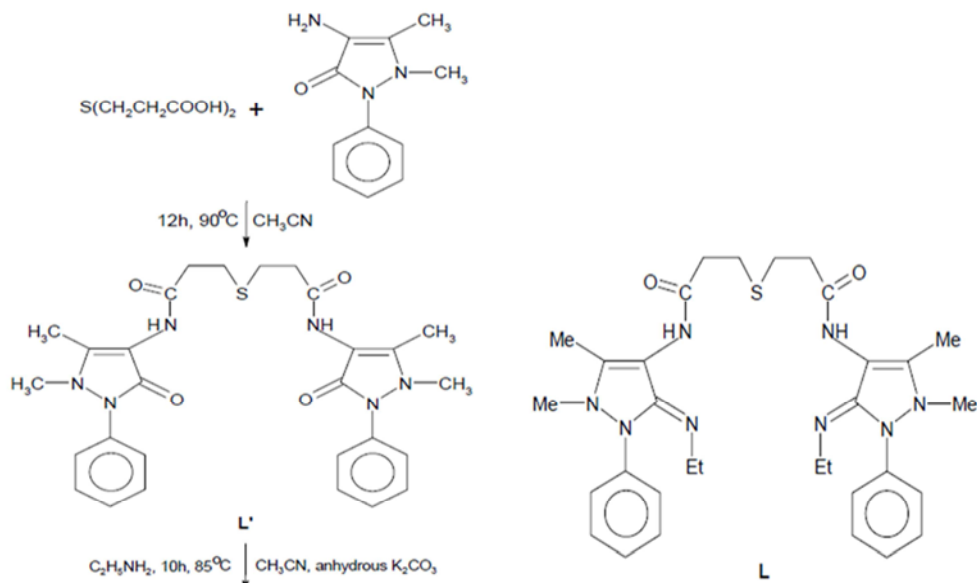


Figure 14. Structure of Schiff base ligand.

Manganese(II) and iron(II) macrocyclic complexes of polyamide groups have been synthesized by the template condensation of diamines (2, 6 diaminopyridine, 1, 2 phenylenediamine and 1,3 phenylenediamine) and triamine

(diethylenetriamine) with phthalic acid in 1:2:2 molar ratios by Ashu Chaudhary [100]. The complexes (Figure 15) have been screened in vitro against a number of fungi and bacteria to assess their growth inhibiting potential.

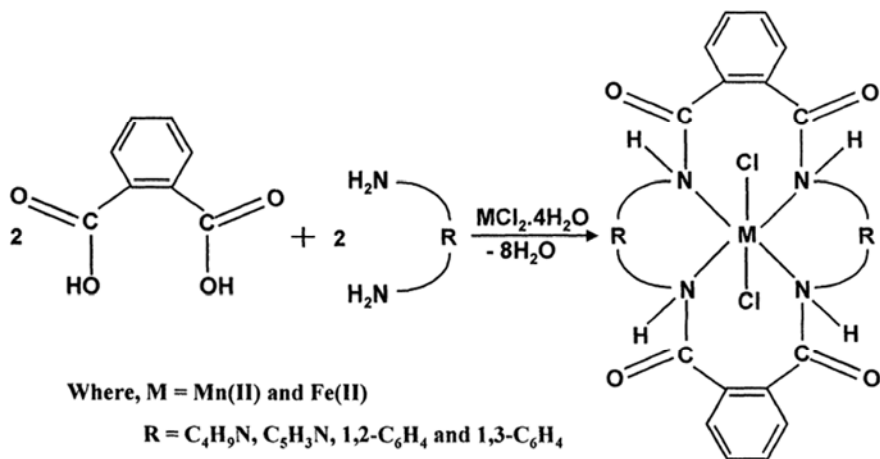


Figure 15. Synthesis of Metal complexes.

Six diorganotin(IV) carboxylates prepared by reacting diorganotin(IV) dichlorides with the respective silver carboxylate have been tested for antifungal activity against *Aspergillus niger*, *Aspergillus flavus* and *Penicillium citrinum* in Sabourand dextrose broth. The compounds generally exhibit greater fungitoxicity than the diorganotin(IV) dichlorides and the carboxylic acids from which they were synthesized [101]. Metal complexes of dichloro-tetramorpholino-cyclophosphazatriene containing divalent cations such as Ni(II), Co(II), and Mn(II) have been

prepared and characterised by standard physico-chemical procedures. The newly synthesized compounds possessed antifungal activity against *Aspergillus* and *Candida* spp., some of them showing effects comparable to ketoconazole (with minimum inhibitory concentrations in the range of 2- 30 $\mu\text{g/mL}$) but being generally less active as compared to the azole. Best activity was detected against *C. albicans*, and worst activity against *A. niger*. The mechanism of action of these compounds probably involves inhibition of ergosterol biosynthesis, and interaction with

lanosterol-14- α -demethylase (CYP51A 1), since reduced amounts of ergosterol were evidenced by means of HPLC in cultures of the sensitive strain *A. niger* treated with some of these inhibitors [102].

2.2. DNA Binding and Cleavage Properties of Metal Complexes

Mixed ligand copper(II) complexes containing derivatives of salicylic acid and heterocyclic ligands with nitrogen donor atoms have been prepared by Lenka Kuckova and et al. The derivatives of salicylic acids in the coordination environment of copper(II) complexes are responsible for radicals scavenging activity (predominantly towards superoxide radical anion), incorporation of chelating ligand 2,9-dimethyl-1,10-phenanthroline into the copper(II) complexes significantly enhances their capability of binding to DNA via intercalation [103]. The metal complexes investigated so far, Cu(II) complexes of 1,10-phenanthroline (phen) and their derivatives have attracted much attention as they function as chemical nucleases. Sigman *et al.* demonstrated that $[\text{Cu}(\text{phen})_2]^+$ complex inhibits DNA or

RNA polymerase activities and induces strand scission of DNA in the presence of H_2O_2 or thiol [104] by catalyzing the formation of reactive oxygen species (ROS), which involves Cu(II)/Cu(I) redox cycle [105]. The coordination geometry of a Cu(II) complex bound to DNA affects the Cu(II)/Cu(I) redox behavior and a change in the coordination geometry has been found to primarily determine the properties of Cu(II) rather than Cu(I) complex species [106]. The Cu^{2+} , Ni^{2+} , and Zn^{2+} complexes were prepared from two bidentate NS ligands. The ligands (Figure 16) were synthesized by the condensation reaction of S-2-methylbenzylthiocarbamate (S2MBDTC) with 2-methoxybenzaldehyde (2MB) and 3-methoxybenzaldehyde (3MB). The Schiff bases and their metal complexes were evaluated for their biological activities against estrogen receptor-positive (MCF-7) and estrogen receptor-negative (MDA-MB-231) breast cancer cell lines. Only the Cu(II) complexes showed marked cytotoxicity against the cancer cell lines. Both Schiff bases and other metal complexes were found to be inactive. In concordance with the cytotoxicity studies, the DNA binding studies indicated that Cu(II) complexes have a strong DNA binding affinity [107].

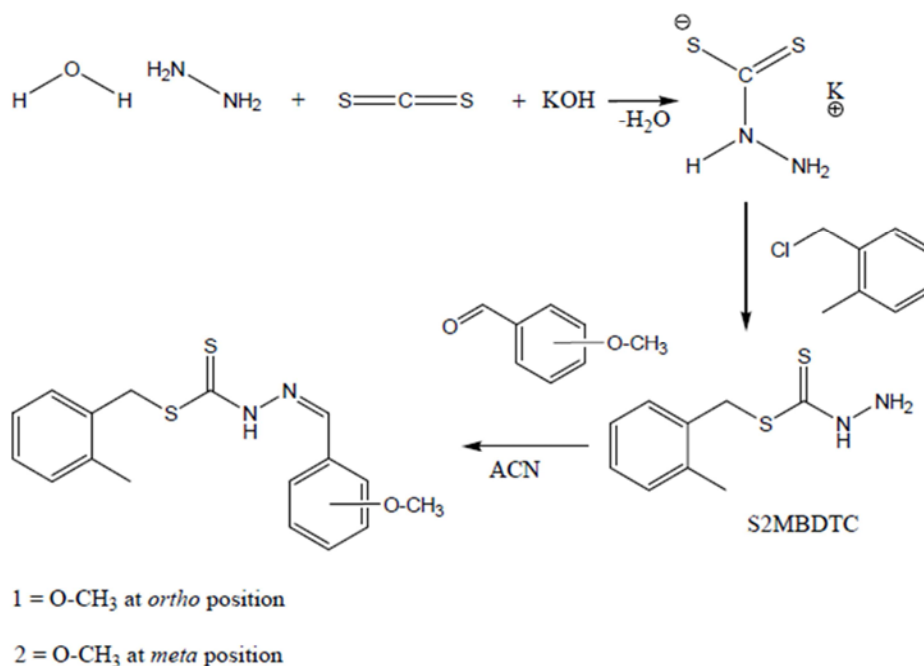


Figure 16. Synthesis of Schiff base ligand (S2MBDTC).

The interaction of $[\text{Co}(\text{H}_2\text{O})_4 (\text{p-NO}_2\text{C}_6\text{H}_4\text{COO})_2] \cdot 2\text{H}_2\text{O}$ with sheep genomic DNA has been investigated by spectroscopic studies and electrophoresis measurements. The interaction between cobalt(II) *p*-nitrobenzoate and DNA has been followed by gel electrophoresis while the concentration of the complex. The spectroscopic study and electrophoretic experiments support the fact that the complex binds to DNA by intercalation via *p*-nitrobenzoate into the base pairs of DNA. The mobility of the bands decreased as the concentration of complex was increased, indicating that there was increase in interaction between the metal ion and DNA [108]. Interaction between cobalt(II) *p*-nitrobenzoate and genomic DNA was shown in (Figure 17)

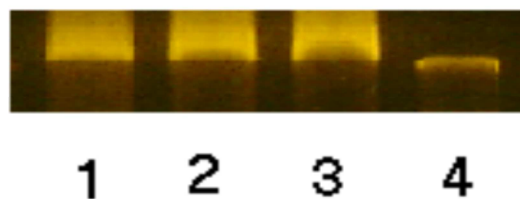


Figure 17. Interaction between cobalt(II) *p*-nitrobenzoate and genomic DNA in presence of TAE buffer at pH 7.3 in air, and 24 h incubation. Lane 1-3: DNA + cobalt(II) *p*-nitrobenzoate with 0.14, 1.4 to 14 mM, respectively; lane 4: untreated genomic DNA in in TAE buffer at pH 7.3 in air, and incubation for 24 h.

Two novel cobalt(III) pyridine complexes (1) $[\text{Co}(\text{en})_2(\text{py})_2]^{3+}$ and (2) $[\text{Co}(\text{en})_2(\text{mepy})_2]^{3+}$ (en=ethylenediamine, py=pyridine, and mepy = methylpyridine) have been synthesized and characterized. The interaction of these complexes with calf thymus DNA was investigated by absorption, emission spectroscopy, viscosity measurements, DNA melting, and DNA photocleavage. Results suggest that the two complexes bind to DNA via groove mode and complex 2 binds more strongly to CT DNA than complex 1. Moreover, these Co(III) complexes have been found to promote the photo cleavage of plasmid DNA pBR322 under irradiation at 365 nm, cytotoxicity results of complexes are also showing anticancer activity [109]. A novel transition metal coordination polymer $[\text{Co}_3(\text{C}_{14}\text{H}_8\text{NO}_4\text{Cl})_4(\text{CH}_3\text{OH})_4 4\text{CH}_3\text{OH}]_n$ with Schiff base $(\text{C}_{14}\text{H}_8\text{NO}_4\text{Cl}: 4\text{-chloroanthranilic acid-2,4 dihydroxybenzaldehyde})$ was synthesized using 4-chloroanthranilic acid, 2, 4-dihydroxybenzaldehyde and cobalt(II) acetate as source, and its structure was characterized by IR spectroscopy, elemental analysis, ^1H NMR and single crystal X-ray diffraction. The interaction of the Co(II) complex with calf-thymus DNA (CT-DNA) was investigated by UV absorption spectroscopy, fluorescence emission spectroscopy, viscosity and cyclic

voltammetry. All measurements revealed that the Co(II) complex binds to DNA *via* an intercalative mode [110]. DNA binding properties of the ligand and its metal complexes have been investigated by electronic absorption spectroscopy, fluorescence spectra, ethidium bromide displacement experiments, iodide quenching experiments, salt effect and viscosity measurements. Results suggest that all the compounds bind to DNA *via* an intercalation binding mode. J. Joseph & K. Nagashri were synthesized copper(II) complexes of hydroxyflavone Schiff bases and investigated their antimicrobial and DNA interaction properties [111]. Abijit Pal and *et al.* [112] synthesized Fe(II) compound $[\text{Fe}(\text{L})](\text{ClO}_4)_2$ (1) $[\text{L} = \text{N}-(1\text{-pyridin-2-yl-phenylidene})[2-((1\text{-pyridin-2-ylphenylidene})\text{amino})\text{ethyl}]\text{amino})\text{ethyl}]\text{ethane-1,2-diamine}$ (1) is reported. 1 crystallizes in P-1 space group with $a = 11.9241(3) \text{ \AA}$, $b = 12.1994(3) \text{ \AA}$ and $c = 13.0622(4) \text{ \AA}$. The binding property of the complex with DNA (Figure 18) has been investigated using absorption and emission studies, thermal melting, viscosity experiments and circular dichroism studies. The binding constant (K_b) and the linear Stern–Volmer quenching constant (K_{sv}) of the complex have been determined as $3.5 \times 10^{-3} \text{ M}$ and $2.73 \times 10^{-4} \text{ M}$, respectively.

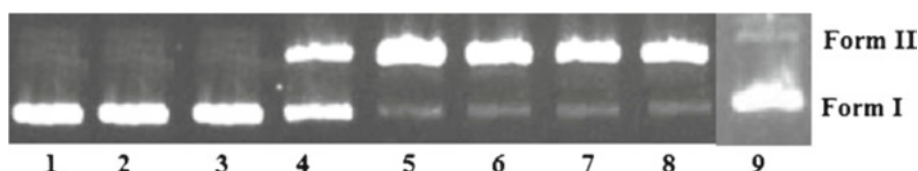


Figure 18. Concentration dependant cleavage of SC pUC 18 DNA upon addition of 1 in the presence of H_2O_2 . DNA (400 ng) was incubated with the complex of various concentrations for 12 h in Tris buffer (pH 7.2) Lane 1, DNA control; lane 2, DNA + complex; lane 3, DNA + peroxide (1 μM) alone; lane 4, DNA + complex (20 μM) + H_2O_2 (1 μM); lane 5, DNA + complex (40 μM) + H_2O_2 (1 μM); lane 6, DNA + complex (60 μM) + H_2O_2 (1 μM); lane 7, DNA + complex (80 μM) + H_2O_2 (1 μM); lane 8, DNA + complex (100 μM) + H_2O_2 (1 μM); lane 9, DNA + complex (20 μM) + H_2O_2 (1 μM) + DMSO.

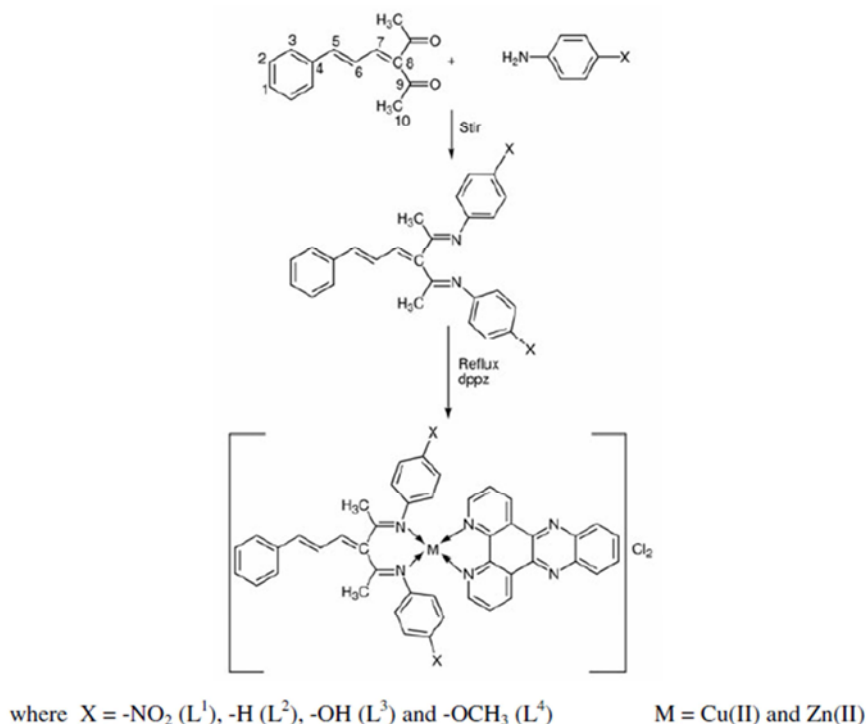


Figure 19. The outline of the synthesis of metal complexes.

The neutral mononuclear Ln(III) complexes (Ln = La, Sm) with 7-methoxychrom-one-3- carbaldehyde-isonicotinoyl hydrazone ligand (L) have been synthesized, characterized and investigated their interactions with calf-thymus DNA by Qian Wang E *et al* [113]. Novel copper(II) and zinc(II) complexes (Figure 19) of the type [ML(dppz)]Cl₂, [L = Schiff base derived from the condensation of 3- (3-phenyl-allylidene) -pentane-2,4-dione and para-substituted aniline; X = -NO₂ (L¹), -H (L²), -OH (L³) and -OCH₃ (L⁴); dppz = dipyrdo phenazine] were synthesized and characterized by various analytical and spectral techniques by N. Ramana and *et al*. [114]. The hydrolytic cleavage of DNA by the zinc complexes was supported by the evidence from free radical quenching and T4 ligase ligation.

Table 1. Structures and abbreviation of the Schiff base ligands and abbreviation of their corresponding complexes.

Acronym Ligand bsal	Complex baslc	R CH ₃
bsphal	bsphalc	
bsas	basc	CH ₂ COOH
bsh	bshc	
bsar	basarc	

The copper(II) complexes of N, O- donor ligand and ciprofloxacin have been synthesized and were characterized by physicochemical parameters like elemental analysis, electronic, FT-IR and LC-MS spectra. The complexes were screened for their antimicrobial activity against Gram positive i.e. *Staphylococcus aureus*, *Bacillus subtilis*, and Gram negative, i.e. *Serratia marcescens*, *Pseudomonas aeruginosa* and *Escherichia coli*, microorganisms in terms of minimum inhibitory concentration and colony-forming unit. To determine the binding mode of complexes with Herring Sperm DNA, absorption titration and viscosity measurement were employed. DNA cleavage activity was carried out by gel electrophoresis experiment using supercoiled form of pUC19 DNA [115]. The DNA interaction efficacies of mixedligand complexes [ML(phen)₂]Cl [L = a Schiff base derived from p-substituted benzaldehyde (L1 = NO₂/ L2 = -OCH₃) and methionine; phen = 1,10-phenanthroline, the co-ligand] have been explored by absorption, electrochemistry, viscosity measurements, and agarose gel electrophoresis. The results indicate that these complexes can bind to calf thymus DNA via an intercalative mode and show efficient cleavage activity in the presence of H₂O₂ [116]. Ahmed M. Abu-Dief and *et al*. [117] synthesized five novel Cu(II) complexes derived from the condensation between 5-bromosalicylaldehyde (bs) and α-amino acids (L-alanine, l-phenylalanine, L-aspartic acid, L-histidine and L-arginine) and characterized by their elemental analyses, thermogravimetric analysis, IR, mass and electronic spectra, conductance and magnetic measurements. The interaction of the base amino acid Cu(II) complexes with calf thymus DNA has been investigated by absorption spectra, viscosity and gel electrophoresis measurement and the mode of CTDNA binding to the complexes has been explored. The investigated complexes exhibit cooperative binding and presumably intercalate into DNA and follow the trend: bsarc>bshc>bsalc>bsphalc>bsasc (Table-1).

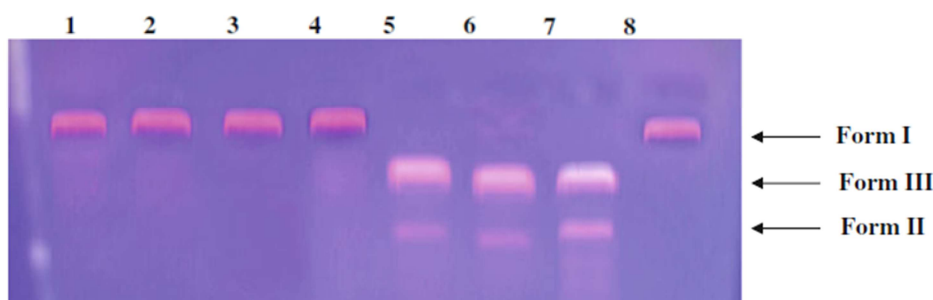


Figure 20. Changes in the agarose gel electrophoretic pattern of pUC19 DNA induced by ascorbic acid and Cu(II), Ni(II), Co(II), and Zn(II) complexes: lane 1, DNA alone; lane 2, DNA, ascorbic acid; lane 3, DNA ligand ascorbic acid; lane 4, DNA[CuL(phen)₂]Cl; lane 5, DNA [CuL(phen)₂]Cl ascorbic acid; lane 6, DNA [NiL(phen)₂]Cl ascorbic acid; lane 7, DNA [CoL(phen)₂]Cl ascorbic acid; lane 8, DNA [ZnL(phen)₂]Cl ascorbic acid. Complexes of the type [Ni (L) (H₂O)] Cl₂.nH₂O, where L = [(pyridine-2-carboxaldehyde)-3-isatin]-bishydrazone (cpish), [(2-acetyl pyridine)-3-isatin]-bishydrazone (apish) and [(2-benzoyl pyridine)-3-isatin]-bishydrazone (bpish) have been synthesized and characterized by Mostafa K. Rabia and *et al*. [119]. Investigation of their interaction with CTDNA under physiological conditions, using spectroscopic (UV-visible) and hydrodynamic techniques (viscosity measurements). Binding constant 'Kb' obtained from spectroscopic methods revealed significant binding of compounds with DNA via intercalation, Furthermore, free energies of compounds-DNA interactions indicated spontaneity of their binding.

Mixed-ligand Cu(II), Ni(II), Co(II), and Zn(II) complexes using a tryptophan-derived Schiff base (obtained by the condensation of tryptophan and benzaldehyde) as the primary ligand and 1,10-phenanthroline as the co-ligand were

synthesized and characterized by D. Shiva leela *et al* [118]. The binding properties of metal complexes with DNA (Figure 20) were investigated by electronic absorption spectroscopy, cyclic voltammetry, and by performing viscosity

measurements, and the results showed that these complexes have the ability to interact with DNA *via* an intercalative mode. The DNA cleavage efficiencies of these complexes with pUC19 DNA were investigated by gel electrophoresis. The

complexes were found to promote the cleavage of pUC19 DNA from the supercoiled form I to the open circular form II and the linear form III in the presence of ascorbic acid.

2.3. Antitumor Activity

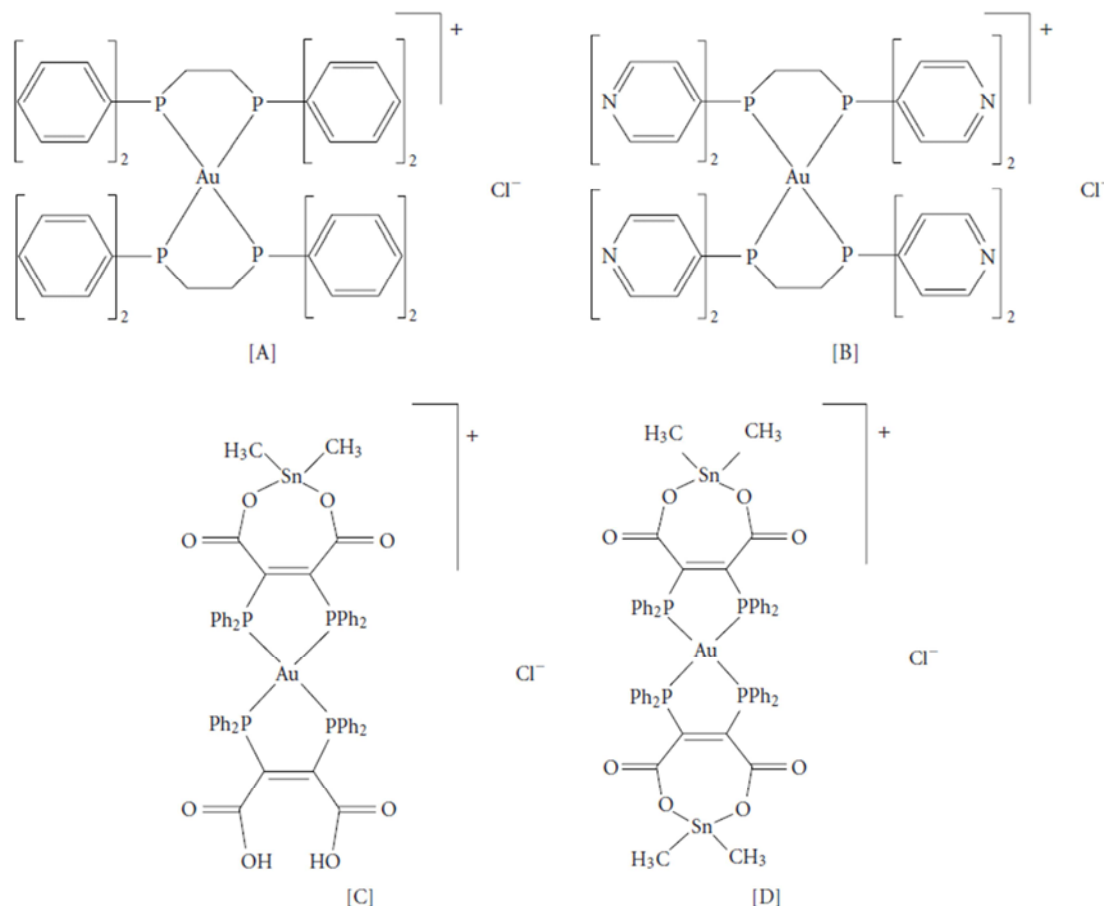


Figure 21. Structure of the experimental compounds: $[Au(dppe)_2]Cl$ [A], $[Au(d4pype)_2]Cl$ [B], $[Au(dpmaaSnMe_2)(dpmaaH_2)]Cl$ [C], and $[Au(dpmaaSnMe_2)_2]Cl$ [D]. (50 μM).

The *in vitro* cytotoxicities of a number of gold(I), silver(I) and copper(I) complexes containing chiral tertiary phosphine ligands have been examined by Mark J. McKeage *et al.* [120] against the mouse tumour cell lines P815 mastocytoma, B16 melanoma [gold(I) and silver(I) compounds] and P388 leukaemia [gold(I) complexes only] with many of the complexes having IC₅₀ values comparable to that of the reference compounds cis-diamminedichloroplatinum(II), cisplatin, and bis[1,2-bis(diphenylphosphino) ethane]gold(I) iodide. M. P. Sathisha *et al.* [121] synthesized Co(II), Ni(II), Cu(II), and Zn(II) complexes of thiocarbohydrazone ligand. The ligand was synthesized starting from thiocarbohydrazone and isatin. The compounds showed considerable cytotoxic activity in the trypan blue exclusion method. In the *in vivo* cancer model (Ehrlich ascitic carcinoma model), the compounds significantly ($P < .05$) reversed the tumor-induced changes in the parameters monitored *viz*, percentage increase in body weight, percentage increase in lifespan, tumor-viable count, and hematological parameters (total and DLC of WBC,

total RBC, and Hemoglobin count). These effects were almost comparable to cisplatin—the standard drug used in the study. The compounds, however, were found to have good effect in prolonging the lifespan (ILS) as compared to standard drug cisplatin. These findings imply that the compounds might be having some anticancer principles. Sodium N-[(trimethylamineboryl)-carbonyl]-L-phenylalanine 2 and {N-[(trimethylamineboryl)-carbonyl]-L-phenylalanine-2-carboxylate} - bis - {N-[(trimethylamineboryl)-carbonyl]-L-phenylalanine} dicopper(II) 3 were successfully synthesized. The compounds demonstrated *in vitro* cytotoxicity primarily in suspended tumor cell lines (e.g. murine L1210 lymphoid leukemia, human Tmolt3 T cell acute lymphoblastic leukemia, and HeLa-S suspended human uterine cervical carcinoma) with variable activity in human solid tumor cell cultures. Murine L1210 cytotoxicity assays demonstrated good activity for compound 2 (ED₅₀ 2.68 $\mu g/ml$) which was more effective than the parent 1 (ED₅₀ 3.34 $\mu g/ml$) [35]. Rat osteogenic sarcoma UMR-106 activity was noted for only compound 3 (ED₅₀ 3.24

lag/ml). Against the growth of Tmolt3 only the parent 1 was active (EDs0 1.31 g/ml). Compounds 2 (EDs0 2.37 lag/ml) and 3 (EDs0 1.91 lag/ml) were active against human HeLa-S suspended cervical carcinoma growth while the parent compound was inactive. In contrast compounds 1 (EDs0 3.38 lag/ml) and 2 (EDs0- 1.82 lag/ml) were active against solid HeLa cervical carcinoma growth while compound 3 was inactive [122]. Sherika Mahepal and *et al.* [123] described antimitochondrial gold complexes, that is, [A] $[\text{Au}(\text{dppe})_2]\text{Cl}$ and [B] $[\text{Au}(\text{d4pype})_2]\text{Cl}$ with two novel lipophilic cations, that is, [C] $[\text{Au}(\text{dpmaaH2})(\text{dpmaaSnMe2})]\text{Cl}$ and [D] $[\text{Au}(\text{dpmaaSnMe2})_2]\text{Cl}$ as antimitochondrial agents. The results of this study indicate that [C] and [D] have intermediate partition coefficients and exhibited a selective uptake by cells. They exhibited a higher selectivity for the various cell lines than [A] but were more cytotoxic than [B]. There is a significant correlation between the cytotoxic potential of [A], [B], [C], and [D] (Figure 21) and their octanol/water partition coefficients in both MCF-7 (breast cancer) and MCF-12A (nonmalignant breast) cells, whereas their cytotoxic potential and ability to induce the release of cytochrome c correlated only in the case of the MCF-12A cells. Complexes [C] and [D] are promising new chemotherapeutic drugs. These compounds target the mitochondrial membranes of certain cancer cells exploiting the differences between the mitochondrial membrane potential of these cells and normal cells. Although the concentrations of these compounds necessary to eradicate cancer cells are very high, the results provide a basis for the synthesis of a new family of compounds with intermediate partition coefficients compared to [A] and [B] but with increased activity against cancer cells.

Metal complexes of 5-carboxy-2-thiouracil with Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) ions were synthesized, characterized, and subjected to a screening system for evaluation of antitumour activity against Sarcoma-180 (S-180) tumour cells (Udai P and *et al.* [124].

2.4. Anticancer Activity

The diverse anticancer utility of cisplatin has stimulated significant interest in the development of additional platinum-based therapies, resulting in several analogues receiving clinical approval worldwide. However, due to structural and mechanistic similarities, the effectiveness of platinum-based therapies is countered by severe side-effects, narrow spectrum of activity and the development of resistance. Nonetheless, metal complexes offer unique characteristics and exceptional versatility, with the ability to alter their pharmacology through facile modifications of geometry and coordination number. This has prompted the search for metal-based complexes with distinctly different structural motifs and non-covalent modes of binding with a primary aim of circumventing current clinical limitations. This review discusses recent advances in platinum and other transition metal-based complexes with mechanisms of action involving intercalation. Cisplatin [*cis*-diamminedichloroPt(II)] (Figure 22) is an important chemotherapeutic drug used in the therapy of a broad spectrum of human malignancies such as ovarian, testicular, head and neck, and lung cancers, and in combination with a wide range of other drugs for the treatment of other malignancies. For this reason, it is one of the most widely utilized antitumor drugs in the world. Unfortunately, its use is greatly limited by severe dose-limiting side effects (nephrotoxicity, ototoxicity, and peripheral neurotoxicity) and intrinsic or acquired drug resistance. Thus, numerous Pt derivatives have been further developed with more or less success to minimize toxic effects. Over the last 30 years, 23 other Pt-based drugs have entered clinical trials with only two of these (carboplatin and oxaliplatin), gaining international marketing approval, and another three (nedaplatin, lobaplatin and heptaplatin) approved in individual nations [125]. Currently, there are only four Pt drugs in the various phases of clinical trial (satraplatin, picoplatin, LipoplatinTM and ProLindacTM).

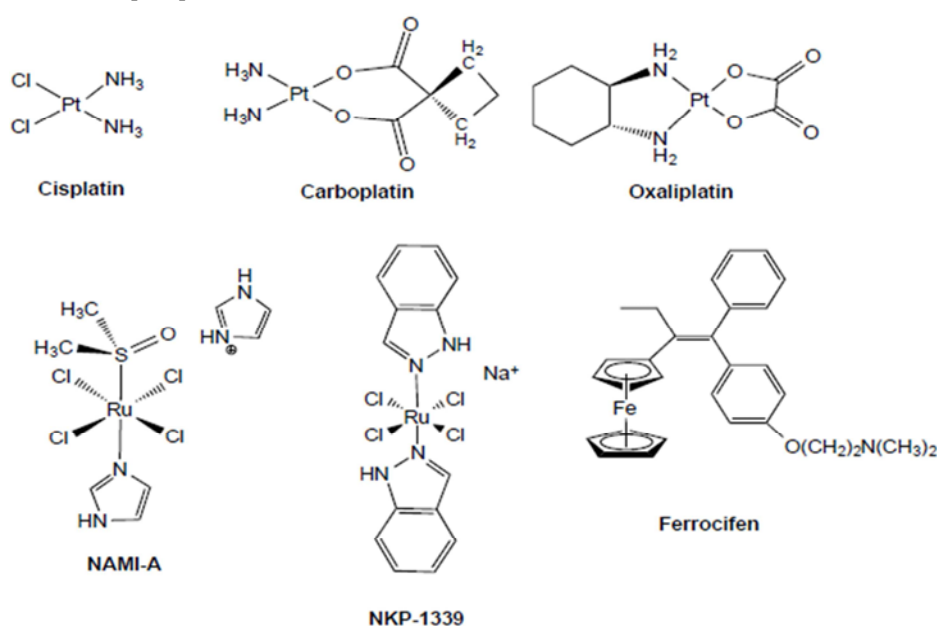


Figure 22. Chemical structures of clinical and experimental metal-based anticancer agents.

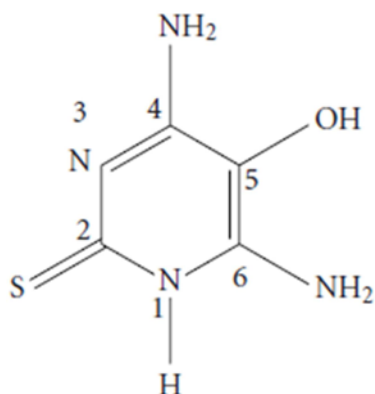


Figure 23. 4,6-diamino-5-hydroxy-2-mercaptopyrimidine (Hdahmp).

Over the years, research on innovative anticancer metallodrugs has produced several ruthenium-based compounds as alternatives to Pt compounds. The Ru(III) complex *trans*-[tetrachloro (DMSO) (imidazole) ruthenate(III)] (NAMI-A) was demonstrated to have cisplatin-resistant human colon carcinoma cell lines and *in vivo* in various tumor types [126]. Due to its higher water solubility, NKP-1339 has now been selected as a lead candidate for further clinical development. Besides these coordination compounds, several classes of other metal complexes and organometallic compounds, based on different metals such as Au, Fe, Ag, Ga, Rh, and Ti, exhibit promising anticancer activity at least in preclinical studies [127–131]. Notably, Jaouen and co-workers have developed organometallic ferrocene-modified tamoxifens (named ferrocifens, Figure 22) as estrogen-targeting molecules effective in hormone-independent breast cancer cells, where hydroxytamoxifen and ferrocene are inactive. In this compound class the β -phenyl ring of tamoxifen has been substituted by a ferrocenyl moiety using classical organic/organometallic synthetic methods. Such structural modifications lead to more lipophilic compounds able to easily cross cell membranes, and, therefore, provide stronger cytotoxic effects, high selectivity for solid tumor metastases and low toxicity at pharmacologically active doses [132]. This is the first ruthenium complex to enter clinical trials. A related Ru(III) compound, indazolium *trans*-[tetrachlorobis (1*H*-indazole) ruthenate(III)] (KP1019) and its sodium salt analogue NKP-1339, also entered clinical trials after they were found to exhibit cytotoxic activity *in vitro* in cisplatin-resistant human colon carcinoma cell lines and *in vivo* in various tumor types [126]. Due to its higher water solubility, NKP-1339 has now been selected as a lead candidate for further clinical development. The Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) ion complexes with novel Schiff base ligand 2,20-((1*Z*,10*Z*)-(1,3-phenylenebis (azanylylidene)) bis (phenylmethanylylidene)) dibenzoic acid (H_2L) was obtained by the condensation of *m*-phenylenediamine with *o*-benzoylbenzoic acid by Walaa H. Mahmoud [133]. The newly synthesized ligand and its metal complexes were screened against a number of bacteria organisms as *Bacillus*

subtilis, *Staphylococcus aureus*, *Escherichia coli*, and *Neisseria gonorrhoeae* and against one fungus, *Candida albicans*, to assess their inhibiting potential by using the disc diffusion method. The results showed that in some cases the antimicrobial activity of complexes was more biologically active than the Schiff base ligand. Anticancer activity of the ligand and its metal complexes were evaluated in human cancer (MCF-7 cells viability). It was found that $[Cd(H_2L)(H_2O)_2Cl_2] \cdot 2H_2O$ complex showed lowest IC_{50} than the others, and hence was the more active. A series of gold(I) complexes of the general composition $[Au(naza)(PPh_3)]$ (1–8) was prepared and thoroughly characterized (e.g., electrospray ionization (ESI) mass spectrometry and multinuclear nuclear magnetic resonance (NMR) spectroscopy) by Pavel Starha *et al.* [134]. The N1-deprotonated anions of 7-azaindole or its derivatives (naza) are coordinated to the metal centre through the N1 atom of their pyrrole ring, as proved by a single crystal X-ray analysis of the complexes $[Au(3I5Braza)(PPh_3)]$ (7) and $[Au(2Me_4Claza)(PPh_3)] \cdot 1/2H_2O$ (80). The *in vitro* cytotoxicity of the complexes 1–8 was studied against both the cisplatin-sensitive and -resistant variants of the A2780 human ovarian carcinoma cell line, as well as against the MRC-5 human normal fibroblast cell line. The complexes 4, 5, and 8, containing deprotonated 3-iodo-7-azaindole, 5-bromo-7-azaindole, and 2-methyl-4-chloro-7-azaindole (2Me4Claza), respectively, showed significantly higher potency ($IC_{50} = 2.8–3.5$ M) than cisplatin ($IC_{50} = 20.3$ M) against the A2780 cells and markedly lower effect towards the MRC-5 non-cancerous cells ($IC_{50} = 26.0–29.2$ M), as compared with the mentioned A2780 cancer cells. The results of the flow cytometric studies of the A2780 cell cycle perturbations revealed a G2-cell cycle phase arrest of the cells treated by the representative complexes 1 and 5, which is indicative of a different mechanism of action from cisplatin (induced S-cell cycle phase arrest). New platinum(II) complexes $[PtCl(O,O\text{-}acac)(L)]$ (1) and $[Pt(O,O\text{-}acac)(\gamma\text{-}acac)(L)]$ (2) ($L =$ DMSO, a; DMS, b) containing a single chelated ($O,O\text{-}acac$) (1), or one chelated and one σ -bonded ($\gamma\text{-}acac$) acetylacetonate (2) have been synthesized by Sandra Angelica De Pascali and *et al.* [135]. The new Pt(II) complexes exhibited high *in vitro* cytotoxicity on *cisplatin* sensitive and resistant cell lines and showed negligible reactivity with nucleobases (Guo and 5-GMP) but selective substitution of DMSO/DMS with soft biological nucleophiles, such as L-methionine. In order to assess the ability of the new complexes with respect to cisplatin to induce apoptosis by interaction with nongenomic targets, the Ames' test, a standard reverse mutation assay, was carried out on two *Salmonella typhimurium* strains (TA98 and TA100). Sahar I. Mostafa and Farid A. Badria [136] were synthesized two new water-soluble mixed ligand $[Pd(bpy)(dahmp)]Cl$ and $[Ag(bpy)(Hdahmp)]NO_3$ complexes (dahmp and Hdahmp are the deprotonated monoanion and the protonated neutral 4,6-diamino-5-hydroxy-2-mercaptopyrimidine, resp.) is reported. The composition of the reported complexes was discussed on the bases of IR, 1H NMR, and mass spectra, as

well as conductivity and thermal measurements. The reported complexes display a significant anticancer activity against *Ehrlich ascites* tumor cells (EACs). The higher activity of these complexes with their higher conductivity values corresponds to their complete ionization in aqueous solution. The structure of (Hdahmp) (Figure 23) and their Ag(I), Pd(II) complex (Figure 24, 25).

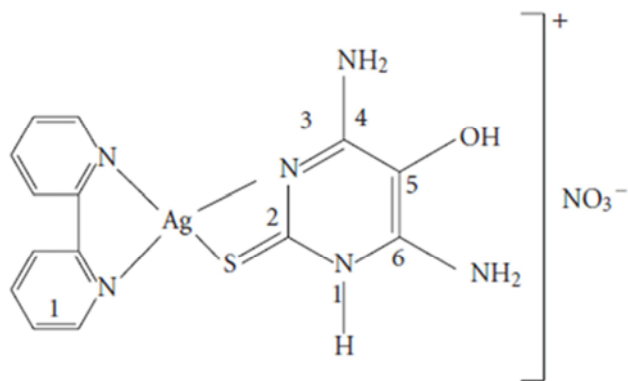


Figure 24. Structure of $[Ag(bpy)(Hdahmp)_2]NO_3$.

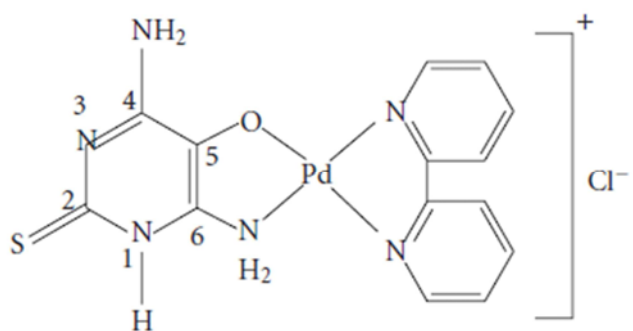


Figure 25. Structure of $[Pd(bpy)(dahmp)]Cl$.

Maryam Hajrezaie *et al.* [137] examined the antiproliferative effect of a copper(II) complex on HT-29 colon cancer cells. The $Cu(BrHAP)_2$ Schiff base compound demonstrated a potent antiproliferative effect in HT-29 cells, with an IC_{50} value of $2.87 \mu g/ml$ after 72 h of treatment. HT-29 cells treated with Cu(II) complexes underwent apoptosis death, as exhibited by a progressive elevation in the proportion of the G1 cell population. At a concentration of $6.25 \mu g/ml$, the $Cu(BrHAP)_2$ compound (Figure 26) caused significant elevation in ROS production following perturbation of mitochondrial membrane potential and cytochrome *c* release, as assessed by the measurement of fluorescence intensity in stained cells. Furthermore, the activation of caspases 3/7 and 9 was part of the Cu (II) complex-induced apoptosis, which confirmed the involvement of mitochondrial-mediated apoptosis. Meanwhile, there was no significant activation of caspase-8. Taken together, these results imply that the $Cu(BrHAP)_2$ compound is a potential candidate for further *in vivo* and clinical colon cancer studies to develop novel chemotherapeutic agents derived from metal-based agents.

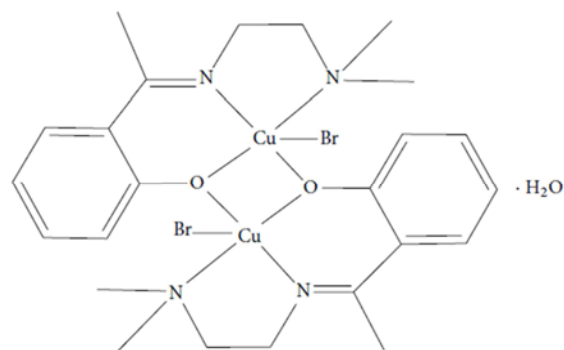


Figure 26. Chemical structure of $Cu(BrHAP)_2$.

Dilip Kumar Saha *et al.* [138] synthesized a square planar copper complex of derivatized NSAID drug (Ketoprofen thiosemicarbazone [3-benzoyl-ct-methyl benzene acetic acid thiosemicarbazone] and characterized by elemental analysis, spectroscopy, electrochemistry and magnetic susceptibility studies which exhibits dose-dependent and enhanced antiproliferative effects on human breast cancer cell line T47D rich in progesterone receptors. The phthalocyanine analogue containing nonperipheral long alkyl-substituted benzenoid rings and pyridine rings, zinc bis (1,4- didecylbenzo)-bis (2,3-pyrido) porphyrazine, was synthesized by Keiichi Sakamoto and *et al.* [139]. The synthesized Zn(II) complexes was tested against IU-002 cells. Ahmad *et al.* [140] have synthesized a Co(II) complex, $[Co(mpca)_2] \cdot H_2O$, which is capable of recognizing a specific sequence in DNA minor groove to inhibit the expression of Topo-I (Figure 27) and thereby controlling the multiplication of tumor affected cells. 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.

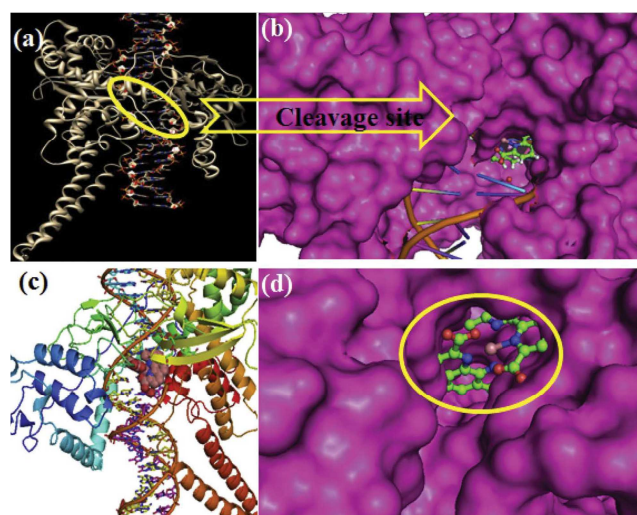


Figure 27. Diagram showing in (a) human-DNA-Topo-I (70 kDa) (PDB ID: 1SC7), (b) docked model of $[Co(mpca)_2] \cdot H_2O$ occupying cleavage active site of Topo-I, DNA is represented by the structure shown as stick representation, (c) docked model $[Co(mpca)_2] \cdot H_2O$ (surface representation) towards the cleavage site of Topo-I (cartoon representation) and (d) binding of $[Co(mpca)_2] \cdot H_2O$ in the Topo-I pocket, preventing the building of the topoisomerase I-DNA complex represented via surface presentation.

3. Conclusion

In this work, the pharmacological effects of a few metal complexes have been reviewed. The application of bioinorganic chemistry to medicine is a rapidly developing field. Novel therapeutic and diagnostic metal complexes are now having an impact on medical practice. Advances in bioinorganic chemistry are important for improving the design of compounds to reduce toxic side-effects and understand their mechanisms of action. This review reveals that the pharmacologically interesting metals such as chromium, vanadium, copper, cobalt, nickel, zinc, cadmium, palladium and platinum could be a suitable strategy to develop novel therapeutic tools for the medical treatment.

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