Chapter I

Introduction

Coordination and organometallic compounds

Coordination chemistry is undoubtedly the most active research area in inorganic chemistry that spans the entire spectrum from theoretical works on bonding to the synthesis of organometallic compounds. Several thousands of coordination complexes have been synthesized and investigated during the past decades. Research on coordination chemistry has emerged as an active and interesting field for chemists and biologists due to the reason that coordination compounds are largely utilized in the production of fragrances, semiconductors, pharmaceuticals, ceramic precursors etc. Ever since the importance of coordination phenomenon in biological processes was realized, large number of metal containing macromolecules have been synthesized and studied to understand the mechanism of complex biological reactions that has resulted in the emergence of an important branch of inorganic chemistry viz. bioinorganic chemistry. Similarly, coordination of substrate molecules to metal ions in catalysis was well understood and lot of research work is being carried out and published. Since structure and reactivity are interdependent, studies on molecular structure of transition metal complexes are of paramount importance to understand their properties. Excellent modern theories available on metal ligand bonding aid the researchers in interpreting the experimental data obtained using sophisticated instrumental techniques.

Metal complexes have played an important role since the early days of coordination chemistry. Indeed, a great deal of work has been carried out on the synthesis and characterization of transition metal compounds mainly due to their applications in various fields. However, the ability of a metal ion to participate in bonding to all possible coordination sites depends in part on its preferences for the donor atoms of the ligand, the flexibility and conformational adaptability of the ligand used, as well as on the competition from other Lewis acids and different entities capable of occupying the coordination pocket.
Medicinal inorganic chemistry is an area of growing interest owing to the fact that inorganic pharmaceuticals play a key role in clinical therapy. For these inorganic compounds, the metal serves as structural center for organizing the organic ligands in the biologically relevant chemical space. Transition metals appear more appealing for this purpose because they can support a multitude of coordination numbers and geometries that go far beyond sp, sp$^2$ and sp$^3$ hybridizations of carbon. Another key aspect for using metal containing compounds as structural scaffolds is the kinetic stability of the coordination sphere in the biological environment.

Transition metal complexes act as homogeneous catalysts in many industrially important reactions such as hydrogenation, hydrosilation, hydroformylation, polymerisation, isomerisation, acylation and oxidative hydrolysis of olefins. Binuclear transition metal complexes have also received much attention in recent years as they may serve as model for variety of biological reactions such as oxygen transport, oxygen activation, photosynthesis water reduction, electron transfer process, metal-metal interactions and multi centered catalysis.

Transition metal ions with different oxidations state have a strong role in redox enzyme systems and may provide the basis of models for active sites. To mention a few, nickel is an essential component in at least 4 types of enzymes viz. urease, carbon monoxide dehydrogenase (CODH) or acetyl coenzyme A synthase, hydrogenase and methyl-S-coenzyme M reductase. Some polydentate Co(II) complexes with ligands capable of intercalation into DNA strands are capable of inducing DNA cleavage under photochemical conditions. Since the recognition of Vitamin B$_{12}$ and synthesis of cochalmines, responsible for erythrocytes (RBC) formation in human body, there has been much study of model systems. Copper complexes are known to play important role in the active site of many copper proteins in vivo as well as in homogeneous and heterogeneous catalysis for organic chemical reactions. A large body of evidence indicates that copper chelation is an effective method to inhibit tumor growth and copper chelators have become promising agents in the treatment of cancer. It has been found that some copper chelators acquire more effective or novel bioactivity after forming complexes. Recent
studies indicated that Cu\(^{2+}\) was critically needed for PDTC induced apoptosis in HL-60 cells and the copper complex of salicylaldehyde benzoylhydrazone (SBH) derivatives showed increased potency of growth inhibition in several cancer cell lines, compared with the metal-free organics. Copper-SBH complexes were significantly more cytotoxic than complexes of other transitional metals (Cu > Ni > Zn > Mn > Fe > Cr > Co) in MOLT-4 cells, an established human T-cell leukaemia cell line. It was noted that SBHs, especially their copper complexes appeared to be unusually potent inhibitors of DNA synthesis and cell growth in a variety of human cancer cell lines, including the human lung epithelial cancer cell line, SKMES-1 and rodent cancer cell lines. A series of, novel salicylaldehyde pyrazole hydrazone (SPH) derivatives were found capable of inhibiting the growth of A549 lung carcinoma cells.

Hydrazones

In a brilliant series of investigations in the 1930’s and the beginning of the 1940’s, which were reviewed in,\(^{2-4}\) Pfeiffer and his co-workers developed principle methods for synthesizing azomethine complexes and studied their physicochemical and structural properties. The first paper describing a metal-containing product of the reaction of ammonia with salicylaldehyde and cupric acetate appeared in 1840\(^{5}\) and in subsequent years, hundreds of papers on complexes of azomethine were published. Many of these complexes were included in the review articles\(^{6-9}\) and the subject of azomethine was represented by 15 papers in the proceedings of the 29\(^{th}\) International Conference on Coordination Chemistry (Lausanne, Switzerland, July 1992).\(^{10}\)

The architectural beauty of coordination complexes arises from the interesting ligand systems containing different donor sites. Among the ligand systems, hydrazide and hydrazone occupy special place because complexes of these compounds with transition metals are nowadays extensively used for the treatment of several diseases, in synthetic and analytical chemistry as novel heterogeneous catalysts in oxido-reduction processes and various chemical and photochemical reactions as well as numerous industrial applications of science and technology.\(^{11-15}\)
Aroyl hydrazones present a combination of donor sites such as protonated / deprotonated amide oxygen and the imine nitrogen of hydrazone moiety, very often additional donor site (usually N or O) is provided by the aldehyde or ketone forming the Schiff base. Aroyl hydrazones have been proved to be a strong chelating agent for transition metals, lanthanides as well as for main group elements. They have also been shown to be useful molecules to build up controllable supramolecular structures. Lehn and co-workers have demonstrated that suitably substituted hydrazones are capable of coordinating metals to give multimetallic square grid complexes, whose optical, photophysical and magnetic properties were modulated by the degree of protonation of the ligands.

**Structure, bonding and stereochemistry of the acid hydrazones**

Hydrazones contain two connected nitrogen atoms of different nature and a C=N bond that is conjugated with a lone electron pair of the terminal nitrogen atom. These structural fragments are mainly responsible for the physical and chemical properties of hydrazones (Fig. 1.1). Both the nitrogen atoms of the hydrazone group are nucleophilic, although the amino type nitrogen is more reactive. The carbon atom of hydrazone group has both electrophilic and nucleophilic character.

![Figure showing the reactivity of hydrazones.](image)

The chelating behavior of hydrazones depends on their amido-iminol tautomerism and in addition to this, the number and type of the substituents attached to the hydrazone framework also influences the coordination mode. The functional grouping causes these compounds to behave as bidentate ligands for metal ions and owing to the availability of – NH– C=O group, acid hydrazones show keto-enol (amido-iminol) tautomerism (Fig.
1.2). In aqueous or ethanolic solutions, these hydrazones show tautomeric structures which can be coordinated to the metal ion, probably through the N-atom either alone or in combination with O-atom of the enolic group.\textsuperscript{31} In solid state, hydrazones predominantly exist in form (I) (amido), but in solution they exist in form (II) (iminol). In hydrazones, it is well known that a proton transfer can occur between the hydrazinic-N and keto group of hydrazone part. Therefore, tautomerisation equilibrium exists between amido form and iminol form through intramolecular proton transfer. This proton transfer causes a change in the π-electron configuration and thus increases conjugation.

![Fig. 1.2 Tautomerisation of hydrazone ligands.](image1)

In general, hydrazones act as a bidentate chelating ligand by utilizing the available amide oxygen and azomethine nitrogen donor sites by which a five membered chelate ring is produced and some of the examples are provided in Fig. 1.3.\textsuperscript{32-34}

![Fig. 1.3 General bidentate coordination mode of acid hydrazones.](image2)

Further, the chelation can be increased by increasing the number of coordination sites on the hydrazone framework. If a heterocyclic ring or phenolic moiety is attached to the hydrazone framework as shown in Fig. 1.4, it can coordinate to the metal center with increased denticity.\textsuperscript{35-39}
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Fig. 1.4 Examples of tridentate behaviour of hydrazone ligands.

It is evident that the stereochemistry of the ligand is much decided by the steric effects of the various substituents in the hydrazone moiety and most of them are in cis form while coordinating to the metal ions. This phenomenon is assumed to be due to better electron delocalisation in the chelate ring system that increases the stability upon coordination with metal atoms. Hydrazones may also act as a unidentate ligand by bonding through enolate oxygen when they are existing in a trans form.

The amido form itself exists in syn or anti conformation depending on the groups attached with the azomethine bond (Fig. 1.5). In the syn form, as far as the azomethine bond is concerned two bulkier groups (R₂ and R₃) are on the same side, while in anti form the bulkier groups are on opposite side.

Fig. 1.5 Geometrical isomers of hydrazone system.

In addition to the steric effects of the various substituents in the hydrazone moiety, additional interactions such as intramolecular hydrogen bonding also play a role
to decide the stereochemistry of hydrazones. It is observed that the syn nature of the bond usually transforms to anti geometry, while coordinating to metal ions.\textsuperscript{41,42}

**Transition metal hydrazone complexes: Applications**

The coordination chemistry of hydrazones as ligand is an intensive area of study and numerous transition metal complexes of them have been investigated.\textsuperscript{43} Earlier, investigations on the hydrazone complexes were focused mainly on the synthesis and structural characterization, but nowadays these metal complexes were reported to serve some applications in various fields like non-linear optics, sensors, medicine etc.

**In bioactivities**

Metal complexes containing site-specific substructures and multiple reactive sites constitute a group of promising candidates for nuclease activity because of their electronic and structural advantages. Most of the first row transition metals either alone or in their complex form are biologically essential with a number of known bioactivities. Among them, nickel, cobalt and copper are especially notable as they involve in many biological processes.\textsuperscript{44-53} It is well known that cancer is currently the second leading cause of death in industrialized countries, accounting for roughly a quarter of total numbers.\textsuperscript{54} Hence, development of new anticancer therapies is one of the fundamental goals in medicinal chemistry. The interactions between biomacromolecules and drugs have attracted special interest among both chemistry and biology researchers recently.\textsuperscript{55-57} DNA is one of the main molecular targets in the design of anticancer compounds\textsuperscript{58} and the interaction between nucleic acids and other molecules is a fundamental issue in life science that relates the replication, transcription, mutation of genes and related variations of species in character, origin of some diseases and mechanism of interaction of some DNA-targeted drugs.\textsuperscript{59-62} Further, it has been demonstrated that free radicals can damage proteins, lipids and DNA of bio-tissues leading to increased rates of cancer and fortunately antioxidants can prevent this damage due to their free radical scavenging activity.\textsuperscript{63,64} Hence, it is very important to develop compounds with strong DNA binding, antioxidant and cytotoxic properties for effective cancer therapy. As known well, serum albumins are the class of proteins involved in the transport of metal ions and metal
complexes along with drugs through the blood stream.\textsuperscript{65} Many drugs, including anticoagulants, tranquilizers, antiinflammatory and general anaesthetics are transported in the blood via combination with albumin.\textsuperscript{66,67} The nature and magnitude of drug-albumin interaction significantly influence the pharmacokinetics of drugs and thus the binding parameters are useful in studying protein-drug binding as they greatly influence absorption, distribution, metabolism and excretion properties of typical drugs.

\textbf{In molecular sensors}

Recently, the development of molecular sensors has attracted lot of research activities for their use in processes that include food, clinical, environmental analysis and analytical applications. It was reported that a potentiometric aluminium sensor based on $N,N'$-bis(salicylidene)-1,2-cyclohexanediamine as a neutral carrier in poly(vinyl chloride) matrix was successfully applied for direct determination of aluminium(III) in biological, industrial and environmental samples\textsuperscript{68} in the pH range of 2.0-9.0. It has been used as an indicator electrode in potentiometric titration of aluminium ion with EDTA. The Schiff base, $N,N',N'',N'''$-1,5,8,12-tetraazadodecane-bis(salicylaldiminato), has been used as an ionophore for preparing Mn\textsuperscript{2+} selective sensor\textsuperscript{69} over a number of alkali, alkaline and heavy metal ions for the determination of manganese in various samples by direct potentiometry.

\textbf{In non-linear optical devices}

Non-linear optics (NLO) deals with the interactions of applied electromagnetic fields materials to generate new electromagnetic fields, altered in frequency, phase, or other physical properties. Such materials that are able to manipulate photonic signals efficiently are of importance in optical communication, optical computing and dynamic image processing.\textsuperscript{70-74} In this connection, transition metal complexes have emerged as potential building blocks for nonlinear optical materials due to various excited states present in these systems as well as their ability to tailor metal-ligand interactions.\textsuperscript{75-80} Compared to the more common organic molecules, metal complexes offer a large variety of novel structures, the possibility of enhanced thermal stability and a diversity of tunable electronic behaviours by virtue of the coordinated metal center and hence they may find
use as NLO materials with unique magnetic and electrochemical properties.\textsuperscript{81-83} Investigations on NLO properties of metal complexes are being pursued by several research groups.\textsuperscript{84-90} Di Bella and co-workers reported that bis(salicylaldiminato) metal Schiff base complexes exhibit good second order NLO properties.\textsuperscript{91-97}

Based on the above facts, studies on the chelating properties of hydrazone ligands and the effect of coordination of them on the composition and geometry of the complexes containing cobalt(II), nickel(II) and copper(I/II) ions were undertaken as the subject of the present work. Additionally, comparison on the biological properties of hydrazone complexes with respect to DNA / BSA interactions, free radical scavenging and cytotoxicity under in vitro conditions have been carried out.

**Survey of the previous work**

Though voluminous reports are available in the literature on the chemistry and other aspects of metal hydrazone complexes, some of them relevant to our work alone were reviewed and presented in this part of the Introduction chapter.

Yi-Heng Lu et al.\textsuperscript{98} reported the synthesis and characterization of Co(II) complexes containing salicylaldehyde benzoylhydrazone (SBH) and established that the ligand has three sites suitable for coordination bond formation. The UV-visible absorption spectra using deconvolution method showed that the structure of complex in solution is different from that in solid crystals. The nature of complexes in solution depends on acidity of the phenolic proton of SBH and on the medium. In neutral or slightly acidic medium, the SBH is a non-charged bidentate ligand and the free hydroxyl group on the SBH molecule makes it possible to form hydrogen bonds in solution. In basic medium, the SBH is a uninegatively charged tridentate ligand.
Recently, the first Co(III)/Co(III) ionic complex with hydrazone and azide ligands, \([\text{Co}(L)_2]^+\text{[Co}(L)(\text{N}_3)_3]^-\text{CH}_3\text{OH}\) was structurally and electrochemically characterized by Bikasa et al.\(^9^9\) in which \(\text{HL} = N'-(1E)-1\text{-pyridin-2-ylethylidene]}-2\text{-furohydrazide}\) was used as a ligand. In the cation \([\text{Co}(L)_2]^+\), two units of furanhydrazone, each of them with three donor atoms constitute a meridional arrangement around the cobalt atom. The coordination polyhedron is a \(\text{CoO}_2\text{N}_4\) distorted octahedron for the cation and a \(\text{CoON}_5\) distorted octahedron for the anion. Cyclic voltammetric experiments of the \([\text{Co}(L)_2]^+\text{[Co}(L)(\text{N}_3)_3]^-\) in DMSO revealed the reduction of ligand at \(-1.56\) V and two reduction potentials at \(-0.81\) and \(-1.28\) V respectively, for two different Co(III) ions.

A novel ligand 2-acetyl-2-thiazoline acetylhydrazone (ATHAc) and two new chloride-bridged dimeric nickel(II) complexes containing thiazoline hydrazone derivative ligands, \([[\text{Ni}(\text{ATsc})(\text{MeOH})]_2(\mu\text{-Cl})_2\text{Cl}_2\) (I) (ATsc = 2-acetyl-2-thiazoline semicarbazone) and \([[\text{Ni}(\text{ATHAc})(\text{H}_2\text{O})]_2(\mu\text{-Cl})_2\text{Cl}_2\) (2) were prepared and structurally characterized using elemental analysis, single crystal X-ray diffraction, IR and UV-visible spectroscopy by Vinuelas-Zahinos et al.\(^{10^0}\) The coordination geometry around each nickel ion was described as a distorted octahedron coordinated to one thiazoline
nitrogen atom, one imine nitrogen atom, one carbonyl oxygen atom, one oxygen atom (from a methanol molecule in 1 and from a water molecule in 2) and two bridging chloride ligands.

From the reaction between Cu(II) and Ni(II) salts and the Schiff base 6-amino-5-formyl-1,3-dimethyluracil-benzoylhydrazone (H$_2$BEZDO), in dimethylformamide (DMF)-water and ammonia media, the complexes [Ni(BEZDO)]·H$_2$O·NH$_3$ (1), [Cu(BEZDO)]·H$_2$O·NH$_3$ (2) and [Cu(BEZDO)(H$_2$O)]·H$_2$O (3) containing the dianionic organic ligand have been obtained. These compounds have been studied by IR, electronic and EPR spectroscopy and magnetic measurements. The structure of [Cu(BEZDO)(H$_2$O)]H$_2$O has been solved by means of X-ray diffraction method. The coordination environment around the Cu(II) was a square-plane structure in which the Schiff base acts as tridentate ligand through the N(6), N(51) and O(52) atoms, making both a five and six membered chelate rings. The coordination sphere is completed with the oxygen atom of a water molecule.$^{101}$

Galic et al.$^{102}$ reported the solution and solid-state complexation behaviour of first series transition metal cations, Cd(II) and Al(III) with two aroylhydrazones derived from nicotinic acid hydrazide and salicylaldehyde or o-vanillin at 25 °C in buffered dioxane / water 1 / 1 mixture (pH, 5.8) by means of spectrophotometric and spectrofluorimetric titrations. The addition of Mn(II) or Cd(II) ions to hydrazone solutions had no effect on their absorption spectra whereas the addition of Ni(II) and Cr(III) immediately caused precipitation.
Three new diorganotin(IV) complexes of the general formula \( R_2Sn[3-(OMe)-2-OC_6H_5CH=N-N=C(O)Ph] \) (\( R = \text{Ph}, \text{Ia}; R = \text{Me}, \text{Ib}; R = n-\text{Bu}, \text{Ic} \)) have been synthesised from the corresponding diorganotin(IV) dichlorides and the ligand, \( N'-(2\text{-hydroxy-3-methoxybenzylidene})\text{benzohydrazide} \) in methanol at room temperature in the presence of trimethylamine.\(^{103}\) All the complexes have been characterized by elemental analysis, IR and \(^1\text{H}, \, ^{13}\text{C}, \, ^{15}\text{N}, \, ^{119}\text{Sn} \) NMR spectra and their structures have been confirmed by single crystal X-ray diffraction analysis of the representative compound \text{Ia} in which the ligand \( N'-(2\text{-hydroxy-3-methoxybenzylidene})\text{benzohydrazide} \) \((\text{H}_2\text{L})\) coordinates to the metal centre in the enolate form via the phenolic \( \text{O} \), imino \( \text{N} \) and enolic \( \text{O} \) atoms. In the complex \text{Ia}, the central tin atom adopted a distorted trigonal bipyramidal coordination geometry with the oxygen atoms in axial positions, while the imino nitrogen atom of the Schiff base and the two phenyl groups occupy the equatorial sites.

A new aroyl hydrazone, \( N\text{-2-hydroxy-4-methoxybenzaldehyde-4-nitrobenzoyl hydrazone (H}_2\text{L}) \), its binuclear \([\text{Cu}_2\text{L}_2]\) \((\text{I})\) and mixed ligand copper(II) mononuclear complexes \([\text{CuLpy}] \) \((\text{2}) \) \([\text{py} = \text{pyridine}]\) have been prepared by Raj et al.\(^{104}\) The structures determined by single crystal X-ray diffraction showed that the ligand molecule exits in
the keto form in the solid state, while at the time of complexation, it tautomerises into the ligand molecule i.e., both the phenolic and the enolic protons.

“Tritopic” picolinic dihydrazone ligands with tridentate coordination pockets were designed to produce homoleptic [3×3] nonanuclear square grid complexes on reaction with transition metal salts and many structurally documented examples have been obtained with Mn(II), Cu(II) and Zn(II) ions. However, other oligomeric complexes with smaller nuclearities have also been identified structurally in some reactions involving Fe(II), Co(II), Ni(II) and Cu(II) with certain tritopic ligands. This illustrates the dynamic nature of the metal-ligand interaction and the conformationally flexible nature of the ligands and points to the possible involvement of some of these species as intermediates in the [3×3] grid formation process. Examples of mononuclear, dinuclear, hexanuclear, heptanuclear and nonanuclear species involving Fe(II), Co(II), Ni(II) and Cu(II) salts with a series of potentially heptadentate picolinic dihydrazone ligands with pyrazine, pyrimidine and pyridine end groups were described in the same study.105

Cobalt(III) complexes of diacetyl monooxime benzoyl hydrazone (dmoBH₂) and diacetyl monooxime isonicotinoyl hydrazone (dmoInH₂) have been synthesized and characterized by elemental analyses and spectroscopic methods by Naskar et al.106 The X-ray crystal structure of the hydrazone ligands, as well as that of the cobalt(III) complex [Co³⁺(dmoInH₂)Cl·2H₂O (1) were also reported in which the amide and the oxime hydrogens are deprotonated for both the ligands, while the isonicotinone nitrogens are
protonated. In the \([\text{Co}^{\text{III}}(\text{dmoBH})_2]\text{Cl}\) (2) complex, only the amide nitrogens are deprotonated. It was shown that the additional hydrogen bonding capability of the

isonicotine nitrogen resulted in different conformation and supramolecular structure for dmoInH₂, compared to dmoBH₂, in the solid state. Comparing the structure of the \([\text{Co}^{\text{III}}(\text{dmoInH})_2]\text{Cl·2H}_2\text{O}\) with that of the Zn(II) complex of the same ligand reported earlier, it is seen that the metal ion has a profound influence on the supramolecular structure due to change in geometrical dispositions of the chelate rings.

Synthesis, structural investigation by elemental analyses, magnetic susceptibility measurements, electronic, IR, NMR and EPR spectral techniques and corrosion inhibition studies on cobalt(II), nickel(II), copper(II) and zinc(II) complexes with 2-acetylthiophene benzoylhydrazone (Hatbh) was investigated by Singh et al. The molecular structures of ligand and its copper(II) complex have been determined by single crystal X-ray diffraction technique. The Cu(II) complex possesses a CuN₂O₂ chromophore with a considerable delocalization of charge. The structure of the complex was stabilized by intermolecular π–π stacking and C–H···π interactions. Hatbh acts as a monobasic bidentate ligand in all the complexes bonding through a deprotonated C–O⁻ and C=N groups. Electronic spectral studies indicated an octahedral geometry for the Ni(II) complex while square planar geometry for the Co(II) and Cu(II) complexes. EPR spectrum of the Cu(II) complex exhibits a square planar geometry in both solid and in DMSO solution. The trend \(g_|| > g_\perp > 2.0023\) indicates the presence of an unpaired electron
in the d_{x^2-y^2} orbital of Cu(II). The electrochemical study of Cu(II) complex revealed a metal based reversible redox behavior.

A new series of macrocyclic unsymmetrical binuclear copper(II) [CuL_{a,b}] complexes was prepared by Sengottuvelan et al.\textsuperscript{108} using 6,6'-piperazine-1,4-diyldimethylenebis(4-methyl-2-formyl)phenol (L\textsubscript{a}) and 6,6'-piperazine-1,4-diyldimethylenebis(4-bromo-2-formyl)phenol (L\textsubscript{b}) and [Cu(oxen)](ClO\textsubscript{4})\textsubscript{2} or [Cu(oxpn)](ClO\textsubscript{4})\textsubscript{2} (where oxen = N,N'-bis(2-aminoethyl)oxamide and oxpn = N,N'-bis(3-aminopropyl)oxamide). The binuclear copper(II) complexes contain three different compartments: the first compartment has two piperazinyl nitrogens and two phenolic oxygens (N\textsubscript{2}O\textsubscript{2}), the second compartment has two phenolic oxygens and two imine nitrogens (O\textsubscript{2}N\textsubscript{2}) and the third compartment has two imine nitrogens and two amide nitrogens (N\textsubscript{4}) as coordinating sites. Apart from the three compartments, the complex has two oxamide oxygen atoms for further coordination. The copper(II) ion in the complex is

\[
\text{where, } L^{1a}: R = (\text{CH}_2)_2, X = \text{CH}_3; L^{1b}: R = (\text{CH}_2)_2, X = \text{Br}; \\
L^{2a}: R = (\text{CH}_2)_3, X = \text{CH}_3; L^{2b}: R = (\text{CH}_2)_3, X = \text{Br}
\]
tetracoordinated with two tertiary nitrogen atoms and two phenoxy oxygen atoms coordinated in the equatorial plane to the copper(II) ion and the geometry around the copper nuclei is distorted square planar. Both mono and binuclear copper(II) complexes were characterized by elemental, electronic, EPR, etc., Further, the electrochemical studies of the mono- and binuclear copper(II) complexes were also are discussed.

Dioxo- and oxovanadium(V) complexes of biomimetic, ONO and NNS donor hydrazone ligands and their catalytic reactivity was reported by Monfared et al. Oxo- and dioxovanadium(V) complexes of hydrazone ONO donor ligands with the formula \([\text{VO}(\mu_{2}-\text{OCH}_3)(\text{L}^1)]_2\) (1) and \([\text{VO}_2(\text{L}^2)\cdot\text{H}_2\text{O}\) (2) were synthesized by the reaction of \([\text{VO}(\text{acac})_2]\) with proton transfer complexes of benzenetricarboxylic acid / benzoxyldiazide and benzenetricarboxylic acid / isonicotinohydrazone, respectively (\(\text{H}_2\text{L}^1 = \text{monocondensation of benzoxyldiazide and acetylacetone, } \text{H}_2\text{L}^2 = \text{monocondensation of isonicotinohydrazone and acetylacetone}\). Dioxo complex of V(V), \([\text{VO}_2(\text{L}^3)]\) (3), was synthesized by the reaction of equimolar amounts of \(\text{VO}(\text{acac})_2, 2\)-acetylpyridine and thiosemicarbazide (\(\text{H}_2\text{L}^3 = \text{hydrazone Schiff base of acetylpyridine and thiosemicarbazide and Hacac = acetylacetone}\) and characterized by FT-IR, UV-visible and NMR spectroscopic methods. The crystal structures of 1 and 2 were determined by X-ray analyses. The \(^1\text{H}\) NMR spectrum of the complex 1 in CDCl\(_3\) solution indicated that this dimeric complex is converted appreciably into its respective monomeric form. The catalytic potential of the complexes has been tested for the oxidation of alkene, alkane and aromatic hydrocarbons using \(\text{H}_2\text{O}_2\) as the terminal oxidant.
New macrocyclic binuclear nickel(II) complexes have been synthesized by using the bicompartimental mononuclear complex \([\text{NiL}]_1\) \([3,3'-(1E,7E)-3,6\text{-dioxo-2, 7-diazaocta-1,7-diene-1,8-diyl]bis(3-formyl-5-methyl-2-diolato)nickel(II)}\) with various diamines like 1,2-bis(aminooxy)ethane \((L^1)\), 1,2-diamino ethane \((L^2)\), 1,3-diamino propane \((L^3)\), 1,4-diamino butane \((L^4)\), 1,2-diamino benzene \((L^5)\) and 1,8-diamino naphthalene \((L^6)\). The complexes were characterized by elemental analysis and spectroscopic methods. The molecular structures of the symmetrical binuclear complex \([\text{Ni}_2L^1(H_2O)_4](\text{ClO}_4)_2\) \((1)\) and unsymmetrical binuclear complex \([\text{Ni}_2L^3(H_2O)_4](\text{ClO}_4)_2\cdot(H_2O)_4\) \((3)\) were determined by single-crystal X-ray diffraction which revealed that geometry around both the nickel(II) ions in each molecule is a slightly distorted octahedral. The influence of the coordination geometry and the ring size of the binucleating ligands on the electronic, redox, phosphate hydrolysis, DNA binding and cleavage properties have been studied.\(^{110}\)

A novel difunctional acylhydrazone has been synthesized by the reaction of 5-methylisoxazole-4-carbonyl hydrazine with benzaldehyde and characterized by X-ray crystallography and spectroscopy by Jin et al.\(^{111}\) Moreover, the spectroscopic properties were evaluated through density functional theory (DFT) and time-dependent density functional theory (TD DFT) calculations. In addition, the results of antibacterial activities indicated that the title compound has certain modest antibacterial activity as well as the broad-spectrum bacteriostasis, which can be supported by the molecular electrostatic potential (MEP). Therefore, it is concluded that the title compound possess both antibacterial activity and photoluminescent property, which has potential applications in many fields such as material science and photodynamic therapy.

A new bis-phenanthroline dicopper(II) complex has been synthesized and characterized by elemental analysis and spectroscopic methods by Anbu et al.\(^{112}\) The molecular structure of the dinuclear Cu(II) complex \([\text{Cu}_2(\mu-\text{CH}_3\text{COO})(\mu-\text{H}_2\text{O})(\mu-\text{H}_2\text{O})]_2\text{Cl}_2\) \((2)\) is shown.

\[
\begin{align*}
\text{N} \quad \text{O} \quad \text{N} \\
\text{H}_2\text{C} \quad \text{O} \quad \text{N} \\
\text{H}_3\text{C}
\end{align*}
\]
OH)(phen)$_2^{2+}$ (phen = 1,10-phenanthroline) (1) was determined by single crystal X-ray diffraction technique. The coordination environment around each Cu(II) ion in complex 1 was described as slightly distorted square pyramidal geometry. The electronic, redox, phosphate hydrolysis, DNA binding and DNA cleavage have been studied. The antiproliferative effect of complex 1 was confirmed by the lactate dehydrogenase (LDH) enzyme level in MCF-7 cancer cell lysate and content media. The dicopper(II) complex inhibited the LDH enzyme as well as the growth of the human breast cancer MCF7 cell line in minimum concentration level.

A series of mono and binuclear copper(II) complexes, of general formulae [CuL$_1$(ClO$_4$)] and [Cu$_2$L$_2$(ClO$_4$)$_2$], respectively, have been synthesized from lateral macrocyclic ligands that have different compartments, originated from their corresponding precursor compounds 3,4:9,10-dibenzo-1,12-[N,N'-bis{(3-formyl-2-hydroxy-5-methyl)benzyl}diaza]-5,8-dioxacyclotetradecane (PC-1) and 3,4:9,10-dibenzo-1,12-[N,N'-bis{(3-formyl-2-hydroxy-5-methyl)benzyl}diaza]-5,8-dioxacyclopentadecane) (PC-2). The structure of the precursor compound PC-1, mononuclear copper(II) complex [CuL$_{1a}$](ClO$_4$) and binuclear copper(II) complex [Cu$_2$L$_{2c}$](ClO$_4$)$_2$ were determined using single crystal XRD. In addition, electrochemical, magnetic moment and EPR studies evidenced the mono and binuclear nature of them.
The observed initial rate constant values of catechol oxidation, using complexes as catalysts, range from $4.89 \times 10^{-3}$ to $5.32 \times 10^{-2}$ min$^{-1}$ and were higher for binuclear complexes than for the corresponding mononuclear complexes.$^{113}$

Five new copper(I) complexes containing PPh$_3$ and [2,3]-pyrazino-[1,10]phenanthroline-2,3-dicarbonitrile (C$_{16}$H$_6$N$_6$) [Cu(PPh$_3$)(C$_{16}$H$_6$N$_6$)Cl]·H$_2$O (1), [Cu(PPh$_3$)(C$_{16}$H$_6$N$_6$)Br]·CH$_3$CN (2), [Cu(PPh$_3$)(C$_{16}$H$_6$N$_6$)I]·CH$_3$CN (3), [Cu(PPh$_3$)(C$_{16}$H$_6$N$_6$)(CN)]·0.5 CH$_2$Cl$_2$ (4) and Cu(PPh$_3$)(C$_{16}$H$_6$N$_6$)(SCN) (5) have been synthesized for the first time$^{114}$ by the reactions of CuX (X = Cl, Br, I, CN, SCN) with the bidentate ligand C$_{16}$H$_6$N$_6$ and the monodentate ligand PPh$_3$ in the molar ratio of 1:1:1 in the mixed solvent of CH$_2$Cl$_2$ and CH$_3$CN (5 mL / 5 mL). They are characterized by X-ray crystallography, luminescence, IR, $^1$H NMR and $^{31}$P NMR. All the complexes exhibit intense luminescence in solid state at room temperature.

The macrocyclic symmetrical and a series of unsymmetrical binuclear copper(II) complexes have been synthesized by using mononuclear complex [CuL] [3,30-((1$E$,7$E$)-3,6-dioxa-2,7-diazaocta-1,7-diene-1,8- diyl)bis(3-formyl-5-methyl-2-diolato)copper(II)]. Another compartment of the [CuL] have been condensed with various diamines like 1,2-bis(aminooxy)ethane (L$^1$), 1,2-diamino ethane (L$^2_a$), 1,3-diamino propane (L$^2_b$), 1,4-diamino butane (L$^2_c$), 1,2-diamino benzene (L$^2_d$), 1,8-diamino naphthalene (L$^2_e$) and characterized by elemental analysis, spectroscopic and X-ray crystallographic methods. The influence of the coordination geometry and the ring size of the binucleating ligands on the electronic, redox, magnetic, catecholase activity, DNA binding and cleavage properties have been studied. The molecular structures of the symmetrical binuclear complex [Cu$_2$L$^1$(H$_2$O)$_2$](ClO$_4$)$_2$ (1) and unsymmetrical binuclear complex [Cu$_2$L$^{2b}$(ClO$_4$)(H$_2$O))ClO$_4$ (2b) were determined by X-ray crystallography. The aromatic diamine condensed macrocyclic ligands of copper(II) complexes display better DNA interaction and significant chemical nuclease activity than the aliphatic diamine condensed macrocyclic Cu(II) complexes$^{115}$. 
Two types of copper(II) and nickel(II) complexes derived from benzophenone anthranoylhydrazone (L₁), 2-acetonaftanone anthranoylhydrazone (L₂), 4-phenylacetonaftronone anthranoylhydrazone (L₃), benzophenone salicyloylhydrazone (L₄), 2-acetonaftanone salicyloylhydrazone (L₅), 4-phenylacetonaftronone salicyloylhydrazone (L₆) and bidentate heterocyclic base [1,10-phenanthroline (phen)] with general stoichiometry [M(L)₂] and [ML(phen)]Cl have been synthesized and characterized by Gup et al.¹¹⁶

Cytotoxicity, quantitative structure-activity relationships of salicylaldehyde benzooylhydrazone analogs and their transition metal complexes have been discussed by Ainscough et al.¹¹⁷ For this discussion, a series of salicylaldehyde benzooylhydrazone derivatives, their copper(II) complexes and a range of transition metal complexes of the unsubstituted ligand have been synthesized and evaluated for cytotoxicity against a human adenocarcinoma cell line. The QSAR analysis revealed a strong correlation between the ligand cytotoxicity with electronic and transport factors that can be modeled by treating each ‘half’ of the molecule as an isolated unit. Activity increases when substituents in the benzoyl ring were electron withdrawing whereas for the salicylaldehyde ring electron donation was required. However, the activity of the transition metal complexes of the unsubstituted ligand mirrored charge density on the metal.

[Chemical structure image]

The key role of hydrogen bonding in the nuclearity of three copper(II) complexes with hydrazone derived ligands and nitrogen donor heterocycles were reported by Shit et al.¹¹⁸ Three new Cu(II) complexes of formula [Cu(L₁)(pyz)(CH₃OH)]ClO₄ (1), [Cu(L₁)(4,4'-bpy)(ClO₄)]·0.5H₂O (2) and [Cu(L₂)(ClO₄)₂(μ-4,4'-bpy)] (3) have been synthesised by using pyrazine (pyz) and 4,4'-bipyridine(4,4'-bpy) and tridentate O,N,O-donor hydrazone ligands, L₁H and L₂H, obtained by the condensation of 1,1,1-trifluoro-
2,4-pentanedione with salicyloylhydrazide and benzhydrazide, respectively. The ligands and their complexes have been characterized by elemental analyses, FT-IR and UV-visible spectroscopies. Single crystal X-ray structure analysis revealed the metal ion in a slightly distorted square pyramidal geometry in all the complexes. However, complexes 1 and 2 are mononuclear with pyz and 4,4'-bpy, respectively showing an unusual monodentate behavior while complex 3 is dinuclear with 4,4'-bpy adopting the typical bridging coordination mode.

Wang et al.\textsuperscript{119} reported the synthesis, characterisation and calf-thymus DNA interaction studies of neutral mononuclear Ln(III) complexes with 7-methoxychrom-one-3-carbaldehyde-isonicotinoyl hydrazone ligand. The antioxidant activities of the ligand and its Ln(III) complexes were also investigated.

Schleife et al.\textsuperscript{120} investigated the metal complexation properties of a functionalized N$_3$O$_2$ donor ligand H$_2$L$_2$, where H$_2$L$_2$ stands for 2,6-diacetyl-4-
carboxymethyl-pyridine bis(benzoylhydrazone). The ligand H₂L₂ is observed to react essentially in the same fashion as its unmodified parent H₂L₁ producing mixed-ligand [M(H₂L₂)(Cl₂)] complexes (M = Mn²⁺ (1), Co²⁺ (3)) upon treatment with MCl₂. Complexes [M(HL₂)(H₂O)(EtOH)]BPh₄⁻ (M = Mn²⁺ (2), M = Co²⁺ (4)), incorporating the supporting ligand in the partially deprotonated form (HL₂⁻), are formed by salt elimination of the [M(H₂L₂)(Cl₂)] compounds with NaBPh₄. Compounds 2 and 4 are isostructural featuring distorted pentagonal-bipyramidal coordinated Mn²⁺ and Co²⁺ ions, with the H₂O and EtOH ligands bound in axial positions.

The reactions between bis(acetylacetonato)dioxomolybdenum(VI) and Schiff base ligands derived from 5-chlorosalicylaldehyde or 3-ethoxy-salicylaldehyde and 3-methoxybenzoic hydrazide (m-anisic hydrazide), 2-furoic hydrazide or 2,4-dihydroxy-benzoic hydrazide in the presence of donor solvents yielded cis-dioxomolybdenum(VI) complexes with the general formula MoO₂L(D), where L = tridentate Schiff base ligand and D = dimethylsulfoxide, hexamethylphosphoramide, dimethylformamide, imidazole or methanol. The complexes were characterized by elemental analysis, electronic spectra, IR, ¹H and ¹³C NMR spectroscopies, thermogravimetric analysis, cyclic voltammetry and the molecular structures of five of the dioxomolybdenum complexes were elucidated by single crystal X-ray diffraction studies. In general, the complexes adopt an octahedral environment around the Mo center with a cis-oxo configuration. The other coordination sites are occupied by the imino nitrogen, phenoxy oxygen, hydroxyl oxygen of the tridentate Schiff base and the donor atom of the solvent molecule. The structural data
revealed that the labile coordination site, which is occupied by N or O atoms from the donor solvents, has a longer Mo–O or Mo–N bond distance.

Two new copper(II) complexes have been synthesized by reacting 2-oxo-1,2-dihydroquinoline-3-carbaldehyde-(benzoyl)-hydrazone (H₂L) with CuCl₂·2H₂O or Cu(NO₃)₂·3H₂O. The structure of the complexes have been determined by single crystal X-ray diffraction studies. Results obtained using spectroscopic methods strongly suggested that the ligand and its Cu(II) complexes interacted with calf thymus DNA through intercalation. In the case of protein binding, the obtained results indicated that all the three compounds could quench the intrinsic fluorescence of bovine serum albumin through static quenching process. In addition, antioxidant activity tests showed that H₂L and its copper(II) complexes possess significant scavenging effect against free radicals. Further, the two copper(II) complexes exhibited effective cytotoxic activity against a panel of human cancer cell lines.

Six new copper complexes of di-2-pyridyl ketone nicotinoylhydrazone and their versatile binding properties (HDKN) have been studied by Mangalam et al. The
complexes have been characterized by a variety of spectroscopic techniques and the structure of \([\text{Cu(DKN)}_2] \cdot \text{H}_2\text{O}\) (1) determined by single crystal X-ray diffraction was proved to be distorted octahedral geometry. The EPR spectra of compounds \([\text{Cu}_2(\text{DKN})_2(\mu-\text{N}_3)_2]\) (2) and \([\text{Cu}_2(\text{DKN})_2(\mu-\text{NCS})_2]\) (3) in polycrystalline state suggested a dimeric structure as they exhibited a half field signal, which indicate the presence of a weak interaction between two Cu(II) ions in these complexes.

![Diagram of complex 1]

A new series of stable transition metal complexes of the formula \([\text{M(L)X-S}]\) (where M = Cu(II), Ni(II), Co(III), Cr(III) and Fe(III) and L is the deprotonated ligand of 4-hydroxy-coumarin-3-thiocarbohydrazone, X = Cl\(^{-}\), NO\(_3\)\(^{-}\) or CH\(_3\)COO\(^{-}\) and S = H\(_2\)O and / or EtOH) have been prepared\(^{124}\). The ligand HL acts as a monobasic tridentate ONS donor in all metal complexes and coordinated through the phenolic OH, azomethine nitrogen and thione sulfur. The formed complexes after releasing the solvent were investigated and their structures are suggested to have square planar or octahedral arrangement. Pharmacodynamic of cobalt(III) complex on some biochemical parameters and histological studies in serum and heart tissue in rats have been studied. Although the complexes demonstrated a significant effect at low dose than the high dose, the ligand showed significant good effects in both high and low doses on the biochemical analysis in serum and heart tissue. Cobalt complex was screened in order to evaluate its antifungal activity against the filamentous fungi *Aspergillus niger*, *Aspergillus fumigatus* and *Aspergillus flavus* and antibacterial activity against the *Candida albicans*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. 
The coordination behavior of a new dihydrazone ligand, 2,6-bis[(3-methoxysalicylidene) hydrazinocarbonyl]pyridine towards manganese(II), cobalt(II), nickel(II), copper(II), zinc(II) and cadmium(II) has been described by Vadavia et al. The metal complexes were characterized by magnetic moments, conductivity measurements, spectral (IR, NMR, UV-visible, FAB mass and EPR) and thermal studies. IR spectral studies revealed the nonadentate behavior of the ligand. The X-band EPR spectra of copper(II) complex at both room temperature and liquid nitrogen temperature showed unresolved broad signals with $g_{iso} = 2.106$. Cyclic voltammetric studies of copper(II) complex at different scan rates revealed that all the electrochemical reactions are irreversible in nature.

Six copper(II) complexes of 2-hydroxy-4-methoxybenzaldehyde nicotinoylhydrazone (H$_2$hmbn), 2-hydroxy-4-methoxyacetophenone nicotinoylh ydrazone (H$_2$hman), 2-hydroxy-4-methoxybenzaldehyde benzoilhydrazone (H$_2$hmbb) and 2-hydroxy-4-methoxyacetophenone benzoilhydrazone (H$_2$hmab) have been synthesized by Mathew et al. The complexes viz. [Cu(hmbn)]$_2$·2H$_2$O (1), [Cu(hman)]$_2$ (2), [Cu(hmbb)]$_2$·2H$_2$O (3), [Cu(hmbb)phen]·1(1/2)H$_2$O (4), [Cu(hmbb)(bipy)·H$_2$O] (5) and [Cu(hmab)phen] (6) were characterized by different physicochemical techniques. The crystal structure of complex 6 showed that it possesses a distorted square pyramidal geometry with π–π stacking interactions and significant C–H···π interactions.
A number of indolo[3,2-c]quinolines were synthesized and modified at the lactam unit to provide a peripheral binding site to accommodate metal ions. Potentially tridentate ligands HL\textsuperscript{1a}-HL\textsuperscript{4a} and HL\textsuperscript{1b}-HL\textsuperscript{4b} were reacted with copper(II) chloride in isopropanol/methanol to afford novel five-coordinate copper(II) complexes [Cu(HL\textsuperscript{1a-4a})Cl\textsubscript{2}] and [Cu(HL\textsuperscript{1b-4b})Cl\textsubscript{2}]. In addition, a new complex [Cu(HL\textsuperscript{5b})Cl\textsubscript{2}] and two previously reported compounds [Cu(HL\textsuperscript{6a})Cl\textsubscript{2}] and [Cu(HL\textsuperscript{6b})Cl\textsubscript{2}] with modified paullone ligands HL\textsuperscript{5b}, HL\textsuperscript{6a} and HL\textsuperscript{6b} which can be regarded as close analogues of indoloquinolines HL\textsuperscript{1b}, HL\textsuperscript{4a} and HL\textsuperscript{4b} in which the pyridine ring was formally substituted by a seven-membered azepine ring, were synthesized and compared. The new ligands and copper(II) complexes were characterized by \textsuperscript{1}H and \textsuperscript{13}C NMR, IR and electronic absorption spectroscopy, ESI mass spectrometry, magnetic susceptibility measurements in solution at 298 K ([Cu(HL\textsuperscript{1a})Cl\textsubscript{2}] and [Cu(HL\textsuperscript{4b})Cl\textsubscript{2}]) and X-ray crystallography ([Cu(HL\textsuperscript{3b})Cl\textsubscript{2}]-3DMF, [Cu(HL\textsuperscript{4b})Cl\textsubscript{2}]-2.4DMF, HL\textsuperscript{5b} and [Cu(HL\textsuperscript{5b})Cl\textsubscript{2}]-0.5CH\textsubscript{3}OH). All complexes were tested for cytotoxicity in the human cancer cell lines CH1 (ovarian carcinoma), A549 (non-small cell lung cancer) and SW480 (colon carcinoma). The compounds are highly cytotoxic, with IC\textsubscript{50} values ranging from nanomolar to very low micromolar concentrations. Substitution of the seven-membered azepine ring in paullones by a pyridine ring resulted in a six to nine fold increase of cytotoxicity in SW480 cells. Electron-releasing or electron-withdrawing substituents in position 8 of the indoloquinoline backbone do not exert any effect on cytotoxicity of copper(II) complexes, whereas copper(II) compounds with Schiff bases obtained from 2-acetylpyridine and indoloquinoline hydrazines are 10 to 50 times more...
Introduction

P. Krishnamoorthy, 2011

cytotoxic than those with ligands prepared from 2-formylpyridine and indoloquinoline hydrazines.

Complexes of Co(II), Ni(II), Cu(II), Mn(II), Cd(II), Zn(II), Hg(II) and U(IV)O$_2$ with $N'$-(1-(4-hydroxyphenyl)-ethylidene)-2-oxo-2-(phenylamino)acetohydrazide H$_3$OPAH) are reported and have been characterized by various spectroscopic techniques like IR, UV-visible, $^1$H NMR and EPR as well as magnetic and thermal (TG and DTA) measurements.\textsuperscript{128} It was found that the ligand behaves as a neutral bidentate, monoanionic tridentate or tetradeionate and dianionic tetradentate. An octahedral geometry for [Mn(H$_3$OPAH)$_2$Cl$_2$], [Co$_2$(H$_2$OPAH)$_2$Cl$_2$(H$_2$O)$_4$] and [(UO$_2$)$_2$(HOPAH)(OAc)$_2$(H$_2$O)$_2$] complexes, a square planar geometry for [Cu$_2$(H$_2$OPAH)Cl$_3$(H$_2$O)]-H$_2$O complex, a tetrahedral structure for [Cd(H$_3$OPAH)Cl$_2$], [Zn(H$_3$OPAH)(OAc)$_2$] and [Hg(H$_3$OPAH)Cl$_2$]H$_2$O complexes. The binuclear [Ni$_2$(HOPAH)Cl$_2$(H$_2$O)$_2$]-H$_2$O complex contains a mixed geometry of both tetrahedral and square planar structures.

The design of novel Fe chelators with high Fe mobilization efficacy and low toxicity remains an important priority for the treatment of Fe overload disease. Some new methyl pyrazinylketone isonicotinoyl hydrazone (HMPIH) analogs were designed and synthesised based on previously investigated aroylhypdrazone chelators. The HMPIH series demonstrated high Fe mobilization efficacy from cells and showed limited to moderate antiproliferative activity. Importantly, this novel series demonstrated irreversible electrochemistry which was attributed to the electron-withdrawing effects of the non-coordinated pyrazine N-atom. The latter functionality played a major role in forming redox-inactive complexes that prevent reactive oxygen species generation. In fact, the Fe complexes of the HMPIH series prevented the oxidation of ascorbate and hydroxylation of benzoate. It was determined that the incorporation of electron-withdrawing groups is an important feature in the design of $N,N,O$-arylahydrazones as candidate drugs for the treatment of Fe overload disease.\textsuperscript{129}
A novel hydrazone, $N'-(2,4$-dimethoxy benzylidene)-2-hydroxybenzohydrazide (DBH), which is an analogue of isonicotinic acid (3-hydroxy-naphthalen-2-ylmethylene)-hydrazide possessing potent anticancer activity has been synthesized and characterized. The interaction between DBH and bovine serum albumin (BSA) was investigated systematically by fluorescence, molecular docking, circular dichroism, UV-visible absorption and electrochemical impedance spectroscopy methods under physiological conditions. The fluorescence quenching observed is attributed to the formation of a complex between BSA and DBH and the reverse temperature effect of the fluorescence quenching has been found and discussed. The effects of iron on the system of DBH-BSA have also been investigated and found that iron could compete against BSA to bind DBH. All of these results are supported by a docking study using a BSA crystal model. It is shown that DBH can efficiently bind with BSA and be transported to the focuses needed.

The syntheses and characterization of six copper(II) complexes of 2-benzoylpyridine benzhydrazone (BPB) in the form of $[\text{Cu}(\text{BPB})_2]$, $[\text{Cu}(\text{BPB})\text{Cl}].\text{H}_{2}\text{O}$, $[\text{Cu}(\text{BPB})\text{Br}]$, $[\text{Cu}_2(\text{BPB})_2](\text{ClO}_4)_2.4\text{H}_{2}\text{O}$, $[\text{Cu}(\text{BPB})\text{N}_3].\text{H}_{2}\text{O}$ and $[\text{Cu}(\text{BPB})\text{NCS}].\text{H}_{2}\text{O}.\text{CH}_3\text{OH}$ were reported by Mangalam et al. The crystal structural analysis revealed that the hydrazone adopts the $E$ conformation about the azo bond and attached to the metal through the $\text{N}_\text{py}–\text{N}_\text{azo}–\text{O}$ chelating system.

A new series of homo, heterodinuclear and homotrinuclear copper(II) complexes containing a new Schiff base ligand (L) and 1,10-phenanthroline were synthesized. Based on the results of elemental analyses, FT-IR, $^1\text{H}$ and $^{13}\text{C}$ NMR spectra, conductivity measurements and magnetic susceptibility measurements, the complexes were assigned general compositions $\{[\text{Cu}(L)(\text{H}_{2}\text{O})\text{M}(\text{phen})_2](\text{ClO}_4)_2 \ [\text{M} = \text{Cu}(\text{II}), \text{Mn}(\text{II}), \text{Co}(\text{II})]\}$ and $\{[\text{Cu}_3(L)_2(\text{H}_{2}\text{O})_2](\text{ClO}_4)_2\}$ with metal:L:phen ratio of 2:1:2 for the dinuclear copper(II) complexes whereas the metal:L ratio for the trinuclear copper(II) complex was 3:2. The interaction between these complexes and DNA has also been investigated by agarose gel electrophoresis and it was found that the homo and heterodinuclear copper complexes can cleave supercoiled pBR322 DNA to nicked and linear forms in the presence of $\text{H}_2\text{O}_2$. 
Nickel, copper and zinc complexes of both isatin ($\text{H}_2\text{L}_1$) and N-methylisatin 3-picolinoyl hydrazone ($\text{HL}_2$) were synthesized and characterized by means of spectroscopic techniques including X-ray diffractometry by Maria et al. Biological studies carried out in vitro on human leukemic cell lines TOM 1 and NB4, have shown that both ligands and some copper and nickel complexes are active to inhibit cell proliferation.

Srinivasan et al. studied the spectral and redox properties of mixed ligand complexes of cobalt(III) phenanthroline / bipyridyl-benzoylhydrazones [$\text{Co(N-N}_2\text{L})\text{(ClO}_4)_2\cdot\text{H}_2\text{O}$ [where L = anionic form of para-substituted benzaldehyde-benzoylhydrazone (BHBR); $R = \text{H}, \text{Me, OMe, OH, Cl or NO}_2$; N-N = 2,2'-bipyridine (bpy) or 1,10-phenanthroline (phen)] along with their DNA binding and antimicrobial activity. Binding of these complexes with herring sperm DNA displayed a lower binding constant value of these complexes with respect to the $[\text{Co(phen/bpy)}_3]^{3+}$ due to the polar interaction of the substituted benzoylhydrazone moiety with the sugar-phosphate backbone of the DNA. The experimental results indicated that phenanthroline mixed ligand complexes bound to DNA through an intercalative mode more effectively than their bipyridine counterparts. These complexes were also found to have good antimicrobial activity.
Anticancer activity, structure and theoretical calculation of \(N\)-(1-phenyl-3-methyl-4-propyl-pyrazolone-5)-salicylidene hydrazone (H\(_2\)L) and its copper(II) complex [Cu\(_2\)L\(_2\)CH\(_3\)OH]-2CH\(_3\)OH has been studied by Zhang et al.\(^{135}\) The crystallographic structural analysis of the complex revealed that the two Cu centers display two different coordination patterns. The pharmacological result showed that the coordination effect improves the antitumor activity of the ligand. The calculated Fukui function for H\(_2\)L and its deprotonated form L\(_2\) predicts that the most probable reactive sites for electrophilic attack are oxygen atoms and the theoretical data were in good agreement with the experimental data.

Binuclear complexes [Zn\(_2\)(HL\(_1\))^\(_2\)(CH\(_3\)COO)\(_2\)] (1) and [Zn\(_2\)(L\(_2\))^\(_2\)] (2) were synthesized with salicylaldehyde semicarbazones (H\(_2\)L\(_1\)) and salicylaldehyde-4-chlorobenzoyl hydrazone (H\(_2\)L\(_2\)) respectively by Parrilha et al.\(^{136}\) Upon recrystallization of previously prepared [Zn\(_2\)(HL\(_2\))^\(_2\)(Cl)\(_2\)] (3) in 1:9 DMSO:acetone crystals of
[Zn₂(L²)₂(H₂O)₂]·[Zn₂(L²)₂(DMSO)₄] (3a) were obtained. The crystal structure of 3a was also determined. All crystal structures revealed the presence of phenoxo-bridged binuclear zinc(II) complexes.

Complexation of iron(III) with the heterodonor chelating agent 3,5-di-tert-butylsalicylidene benzoylhydrazone (H₂(3,5-¹Bu₂)salbh), in the absence or presence of a base afforded the complex cation [Fe{H(3,5-¹Bu₂)salbh}₂]⁺ (1) or the neutral compound [Fe{H(3,5-¹Bu₂)-salbh}((3,5-¹Bu₂)salbh)] (2) respectively as revealed by single-crystal X-ray analyses. Such a synthetic and crystallographic demonstration of the coordination versatility of an aroylhydrazone towards iron is uncommon. The oxidation and spin states of the iron have been verified with magnetic and spectroscopic measurements.¹³⁷

Novel Ln(III) complexes with hesperetin-4-one-(benzoyl) hydrazone (H₄L) have been synthesized and characterized.¹³⁸ Electronic absorption spectroscopy, fluorescence spectra, ethidium bromide displacement experiments, iodide quenching experiments, salt
effect and viscosity measurements indicated that the ligand and Ln(III) complexes, especially the Nd(III) complex strongly bind to calf thymus DNA presumably via an intercalation mechanism. The intrinsic binding constants of the Nd(III) complex and ligand with DNA were 2.39×10^6 and 2.7×10^5 M⁻¹, respectively. Further,, the in vitro antioxidant activity of the ligand and Ln(III) complexes was determined by superoxide and hydroxyl radical scavenging method indicated that the ligand and Ln(III) complexes have the activity to suppress O₂⁻ and HO⁻ and the Ln(III) complexes were more effective than the free ligand.

A macrocyclic hydrazone Schiff base synthesized by reacting 1,4-dicarbonyl phenyl dihydrazide with 2,6-diformyl-4-methyl phenol was treated with Co(II), Ni(II) and Cu(II) salts and the new complexes have been characterized by elemental analyses, IR, ¹H NMR, UV-visible, FAB mass, EPR spectra, fluorescence, thermal, magnetic and molar conductance data. The electrochemical behavior of the copper(II) complex was investigated by cyclic voltammetry. EPR spectra of the complex showed the presence of
a considerable covalent character in the metal-ligand bond. The brine shrimp bioassay was also carried out to study their in vitro cytotoxic properties. The Schiff base and its complexes have also been screened for their antibacterial and antifungal activities (Escherichia coli, Staphylococcus aureus, Shigella dysentery, Micrococcus, Bacillus subtilis, Bacillus cereus, Pseudomonas aeruginosa, Aspergillus niger, Penicillium and Candida albicans) by MIC method.

Two novel 2-oxo-quinoline-3-carbaldehyde-(4'-hydroxybenzoyl) hydrazone thiosemicarbazone ligands and their corresponding water soluble Cu(II) complexes were synthesized and characterised by single crystal X-ray diffraction. Interaction of these Cu(II) complexes with calf thymus DNA (CT DNA) was investigated by electronic absorption spectroscopy, fluorescence spectroscopy and viscosity measurement. Further, the in vitro antioxidant activity of the above complexes were determined using hydroxyl and superoxide radicals.

Metal complexes of 2-methyl-1H-benzimidazole-5-carboxylic acid hydrazide and its Schiff base, 2-methyl-N-(propan-2-ylidene)-1H-benzimidazole-5-carboxyhydrazide with copper, silver, nickel, iron and manganese were prepared and their antitumor activity has
been studied. Among the complexes, the silver containing one displayed cytotoxicity (IC$_{50}$ = 2 μM) against both human lung cancer cell line A549 and human breast cancer cell line MCF 7.\textsuperscript{141}
Reference


