Summary

Hydrazones and their metal complexes display diverse biological and pharmaceutical activities, such as anticancer, antitumor and antioxidative as well as inhibition of lipid peroxidation etc. Transition metals are particularly suitable for this purpose because they can adopt a wide variety of coordination numbers, geometries and oxidation states. The development of interaction models and the elucidation of the mechanisms of interaction of transition metal complexes with biomolecules and their subsequent application in molecular biology continue to attract significant attention in the recent years. In particular, considerable interest has been shown on the experiments involving DNA binding and DNA cleavage by metal complexes in order to explore the sequence specificities of DNA binding using a variety of intercalating ligands. The efficiency of a drug such as metal complexes can be altered by the degree to which it binds to the proteins within blood plasma. Protein binding can influence the drug's biological half-life in the body in which the bound portion may act as a reservoir from which the drug is slowly released as the unbound form and hence protein binding is of much importance.

Keeping these facts in mind, we synthesised different hydrazones that included both bidentate and tridentate types. A bidentate ligand can coordinate to the metal ion in a neutral or monoanionic fashion. In order to increase the chelating ability of the hydrazones, tridentate ligands were chosen in such a way that the third donor atom may either be a neutral or negative one.

The present thesis dealt with the study on the coordination behaviour of various hydrazone ligands with the transition metal ions such as Co, Ni and Cu. Synthesis of new complexes was followed by detailed investigations towards the interactions of them with biomolecules such as nucleic acids and proteins, free radical scavenging ability and cytotoxic potencies. Further, a particular series of metal hydrazones were also tested for their acid sensing and non-linear optical abilities.
In the second chapter, we reacted bidentate hydrazone ligands (HL\textsubscript{1} or HL\textsubscript{2}) with the precursor complex, [CuCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2}]. The product obtained in these experiments were found to have the composition [Cu(L\textsubscript{1})(PPh\textsubscript{3})\textsubscript{2}] and [Cu(L\textsubscript{2})(PPh\textsubscript{3})\textsubscript{2}] with tetrahedral geometry. Additionally, [CuCl(PPh\textsubscript{3})\textsubscript{3}] was also obtained as a minor product along with the hydrazone complexes. A noticeable feature in these reactions was the reduction of copper ion from its oxidation state of +2 in the precursor to +1 in the hydrazone complexes.

Another hydrazone ligand that possessed an additional neutral donor site (N) was reacted with the starting precursors of the type [MCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2}] (where, M = Co(II) or Ni(II) or Cu(II)) in 1:1 stoichiometric ratio, wherein complexes of the type [M(L)\textsubscript{2}] with two units of coordinated ligand and hence with octahedral geometry were realized. In this case also, we obtained a minor byproduct [CuCl(PPh\textsubscript{3})\textsubscript{3}] with a reduced oxidation state along with the copper(II) hydrazone complexes, but not with cobalt and nickel systems.

Reactions carried out using a tridentate ligand containing an anionic oxygen (O) atom as a third donor with nickel and cobalt precursors afforded complexes of the type [Ni(L)(PPh\textsubscript{3})] and [Co\textsubscript{1}(L)\textsubscript{2][Co\textsubscript{2}(H\textsubscript{2}O)\textsubscript{4}(OPPh\textsubscript{3})\textsubscript{2}]. Here, the ligands coordinated to metal ion in a dianionic tridentate fashion leading to a square planar and octahedral structure with nickel and cobalt ions, respectively. Single crystal XRD of the cobalt complex mentioned above revealed the presence of two different complexes in an unit cell with non-equivalent coordination arrangements in such a way that one of them acted as a counter-ion to compensate the cationic charge raised due to the other complex.

In addition, a series of dianionic tridentate ligands similar to that of the one utilized in the previous chapter but with a more planar naphthyl ring attached to the azomethine bond and different heterocyclic moieties at the hydrazide part were reacted with [NiCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2}]. All these hydrazones afforded O,N,O chelated nickel(II) square planar complexes.

In the last chapter, reactions made between a set of bidentate hydrazones incorporating ferrocenyl moieties at the carbonyl centers with and without hetero atoms
at the hydrazide parts and [CuCl$_2$(PPh$_3$)$_2$] and [NiCl$_2$(PPh$_3$)$_2$] in 1:1 stoichiometry yielded complexes of the type [Cu(L$_n^0$(PPh$_3$)$_2$] and [Ni(L$_n^0$)$_2$]. Herein, copper was reduced from the cupric ionic state to cuprous and resulted in the less planar tetrahedral geometry with 1:1 stoichiometry between the metal and ligand. However, in the case of nickel, no such reduction took place upon treatment with the same hydrazones and also 1:2 ratio was found between the metal and ligand to afford more planar square planar structure for them. Additionally, the complex, [CuCl(PPh$_3$)$_3$] was obtained as a minor byproduct together with the copper(I) hydrazones, [Cu(L$_n^0$(PPh$_3$)$_2$] but not in the case of nickel hydrazones.

Among the various hydrazones utilized, only [N’-(phenyl(pyridine-2-yl)methylidene)benzohydrazide] ligand yielded copper(II) hydrazones upon reaction with [CuCl$_2$(PPh$_3$)$_2$]. All other hydrazones did reduce the cupric ion to cuprous ion during the complex formation. However, in the case of nickel and cobalt ions, no such reduction was observed by treatment with hydrazones. Similarly, wherever we utilized [CuCl$_2$(PPh$_3$)$_2$] as the precursor for the synthesis of new copper hydrazone complexes, [CuCl(PPh$_3$)$_3$] was formed as a byproduct with very low yield in all the reactions irrespective of the hydrazones employed.

Towards bioinorganic approach, investigations towards nucleic acid binding and cleavage were made and the results suggested a groove or intercalating behaviour and dose dependent cleavage abilities. Protein interaction study revealed that there occurred different types of interaction at the tyrosine and tryptophan microenvironments. Free radical scavenging ability of the synthesised complexes towards DPPH, OH, NO, ABTS cationic, O$_2^-$ radicals, FRAP and lipid peroxidation revealed selective dose dependent outputs. Finally, preliminary studies on anticancer activities have been undertaken using different dosages of the newly synthesised metal hydrazone complexes reported in this thesis.

The outcome of the biomolecular interactions did throw some light on the influence of molecular geometry and planarity along with the composition of ligands in particular case. Also, significant alterations in the biological properties of the synthesised
complexes demonstrated the effect of specific metal ion as well as the hetero atoms presented in the hydrazone with interesting electronic effects.