SUMMARY

Schiff base metal complexes have been considered as the ‘Current Work Horse’ in the development of Co-ordination chemistry. Flexibility of metal ions in an environment of a nucleophilic molecule or anions gave birth to large number and varieties of complexes. Recent explosion in the field of metal complex chemistry was not only due to the economic inspiration but also of the intrinsic curiosity and intellectual challenges confronted in Quantitative Structure – Activity Relationship (QSAR Analysis) of many of their compounds. This investigation is expected to provide valuable insight into the nature of metal ligand bonds and their thermal stability. High degree of biochemical interest in Schiff base Chemistry stems from their suitability in designing metal centred model systems, their mimic biologically active system. Many transition metal complexes play a crucial role in living systems. Hence it is proposed to study the biological mechanisms and also to find out some significant applications of Schiff bases and their metal chelates in biology.

In view of the versatile importance of Schiff base metal chelates we herein describe the study of the metal complexes of Schiff bases derived from 2-Hydroxyacetophenone 2-Aminothiophenol (HAPATP), 2-Hydroxy-
acetophenone 2-Aminophenol (HAPAP), Benzil 2-Aminothiophenol (BATP) and Benzil 2-Aminophenol (BAP) and their transition metal chelates. They have been synthesised and characterised with the help of analytical as well as physico-chemical methods. Co(II), Ni(II), Cu(II) and Zn(II) are the metal ions used for the complexation.

The thesis is divided into 4 parts. Part I deals with the synthesis and characterisation of the metal complexes derived from some new Schiff base ligands. There are 6 Chapters in Part I. The first chapter consists of an introduction and a critical review of the published work on metal complexes of Schiff bases derived from hydroxyketones, 1,2-diketones, aminophenols and aminothiophenols. Materials, methods and instruments used for the various studies during this work are given in Chapter II.

Synthesis and characterisation of Co(II), Ni(II), Cu(II) and Zn(II) complexes of HAPATP are described in Chapter III. Structural elucidation of these complexes has been made on the basis of microanalytical, magnetic and spectral data. These data suggest that HAPATP behave as a neutral bivalent tridentate ligand during complexation. All these complexes possess 1:1 metal ligand stoichiometry and are non electrolytes. Based on the above physico-chemical studies an octahedral geometry is suggested for all the
complexes. Co(II), Ni(II) and Cu(II) complexes showed para magnetism while Zn(II) chelate is purely diamagnetic in nature.

Chapter IV deals with the preparation and characterisation of the Co(II), Ni(II), Cu(II) and Zn(II) metal chelates of the ligand HAPAP. Microanalytical data reveals that there exists 1:1 stoichiometry between metal and the ligand. Conductance data explains the non electrolytic nature of all these complexes. During the magnetic studies, it is observed that complexes of Co(II), Ni(II) and Cu(II) are paramagnetic while Zn(II) complex is diamagnetic. The spectral data suggest an octahedral structure for all the metal chelates. All the above results confirm that the ligand acts as a bivalent tridentate in all the metal complexes.

Chapter V describes the preparative as well as physico-chemical investigations of the metal complexes of the Schiff base, BATP. All the metals were found to form 1:1 complexes with the ligand. Conductance data explain the non electrolytic behaviour of the metal complexes.

Chapter V explains the preparation and characterisation of the metal complexes of BAP. Micro analytical data reveals that there exist an 1:1 stoichiometry between the metal and the ligand in all these complexes. These
complexes were found to be non-electrolytes in methanol. Except Zn(II), all other complexes were found to be paramagnetic in nature.

In both the above cases the ligands act as dianionic tetradentate type ligand. Part I ends with references.

Part II deals with the thermal studies of 8 metal complexes of the above Schiff bases. There are 4 chapters in this part. The first chapter gives an introduction about thermogravimetric analysis. Chapter II deals about the materials, methods and instruments used for the thermogravimetric studies.

Thermal decomposition studies of Cu(II) and Zn(II) complexes of HAPATP and HAPAP are discussed in Chapter III. A three stage decomposition pattern was observed for CuL1(H2O)3, whereas the Zn(II) complex of the same ligand showed a two stage decomposition. The temperature regions and the probable assignments are presented in Table II.3.1. In the case of HAPAP a two stage decomposition pattern was observed for both Cu(II) and Zn(II) complexes. Results of this studies are summarised in Tables II.3.2.

Chapter IV explains the thermal decomposition studies of Cu(II) and Zn(II) chelates of BATP and BAP. Table II.4.1 and II.4.2 gives a detailed
information regarding the temperature ranges and probable assignments for each decomposition stages of the metal chelates. Part II concludes with references.

Part III and IV consists of biological studies of some complexes.

In Part III antitumour activity of the metal chelates was discussed in detail. The studies include in vivo and in vitro antitumour study and acute toxicity studies in BALB/c Mice. Chapter I and II give an introduction to cancer and materials and methods employed in the present study. Chapter III explains the results of the above mentioned screening studies in detailed manner. Tables III.3.1-III.3.5 and Figures III.3.1-III.3.9, given the information about the antitumour screening of the transition metal complexes.

The screening studies confirm that Zn-HAPATP and Cu-BAP are the most active metal chelates with lowest IC$_{50}$ value for DLA and HeLa cells. The low molecular weight and lipid solubility of the Zn and Cu complexes facilitate their penetration of cell membrane. The cell death due to apoptosis was further confirmed as assessed by Acridine orange/Ethidium bromide dual staining and DNA laddering. Depending upon the specific type of complexes used treatment has resulted enhanced immune response to tumours, decreased tumour growth and increased survival of the mice as
evidenced by its extended life span. Experimental evidence indicates that the complex Zn-HAPATP achieved a sizable peripheral pool of PHA-sensitive naive T-lymphocytes which ensure an improved immune response. This shows that the Zn(II) complex is able to induce lymphocytes clonal proliferation in normal as well as tumour bearing mice, thus making them more reactive to neoplastic challenges. The abnormality observed with other complexes can be attributed to the steric hindrance of the complexes and also due to their membrane impermeable character.

Part IV deals with antibacterial studies of some selected complexes towards 4 clinically important bacterial strains. This part is divided into 3 chapters. Chapter I gives an introduction about antibacterial study. In Chapter II materials, methods and instruments used in the present study were discussed. In Chapter III results of antibacterial study was explained. It is important to note that metal complexes exhibit enhanced antibacterial activity than their free ligands (ie., 2-Hydroxyphenone2-Aminothiophenol and Benzil 2-Aminophenol). Among the metal complexes studied, Cu-BAP showed better antibacterial activity against all the bacterial strains studied especially towards the Gram negative organism, P.aerugenosa. This is because of an increase in the cell permeability of the metal complex. The lipid membrane which surrounds the cell favours the passage of only lipid
soluble material and it is known that liposolubility is an important factor that controls antimicrobial activity. The variation in the activity of different metal complexes against different bacteria depends either on the impermeability of the cells of the microbes or difference in ribozomes in microbial cells.

Part III and IV conclude with references.