SYNOPSIS OF THE THESIS ENTITLED

SYNTHESIS, STRUCTURAL, ANTITUMOUR AND ANTIBACTERIAL STUDIES ON SOME TRANSITION METAL COMPLEXES OF SCHIFF BASES

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By

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SYNOPSIS

The field of co-ordination chemistry is one of the most intellectual, attractive and experimentally demanding frontiers in modern chemical sciences. Schiff bases constitute an important class of nitrogen donor ligands and occupy prominent position amongst the recent achievement in the field of co-ordination chemistry. The azomethine group (>C=N) which is the functional group of a Schiff base is aided in forming a stable complex. Schiff base ligands and their metal complexes have claimed increasingly greater attention in analytical chemistry, industry and in medicinal field. In the field of medicine these compounds have various applications as antitumour, antiviral and antibacterial drugs.

In the present work some new Schiff bases namely 2-Hydroxyacetophenone 2-Aminothiophenol (HAPATP), 2-Hydroxyacetophenone 2-Aminophenol (HAPAP), Benzil 2-Aminothiophenol (BATP), Benzil 2-Aminophenol (BAP) and their transition metal chelates have been synthesised and characterised on the basis of analytical and physico-chemical studies. Thermogravimetric studies were carried out to identify the decomposition pattern and hence the stoichiometry as well as the geometry of the metal complexes. Antitumour and antibacterial activities of some selected complexes have also been reported.
The thesis is divided into 4 parts. Part I consist of synthesis and structural studies of various Schiff bases and their metal complexes. Part II deals with thermoanalytical studies. Part III and Part IV explains the antitumour and antibacterial studies of some selected complexes respectively.

Part I is divided into 6 chapters. Chapter I consist of an introduction and review of the published work on the present investigation. In Chapter II, materials, methods and instruments used for the various studies during this work are described. Chapter III and Chapter IV deals with the work done using the ligands 2-Hydroxyacetophenone 2-Aminothiophenol and 2-Hydroxyacetophenone 2-Aminophenol. The metal chelates of these Schiff base ligands were synthesised and characterised on the basis of microanalytical, magnetic and spectral data. The transition metal ions used for the complexation are Co(II), Ni(II), Cu(II) and Zn(II). All these complexes were found to be non electrolytes and they possess 1:1 metal – ligand stoichiometry. Spectral and magnetic data suggest an octahedral geometry for all the complexes.

In the present work some new metal complexes of Schiff base ligands such as Benzil 2-Aminothiophenol and Benzil 2-Aminophenol were also synthesised and characterised. The details of their study were included in Chapter V and Chapter VI respectively. From the analytical studies it is clear
that the ligands behaved as dianionic tetradeutate type during complexation. Co(II), Ni(II), Cu(II) and Zn(II) are the metal ions used for the formation of complexes. All the metal chelates showed a general formula ML(H₂O)₂ [M = Metal ion, L = ligand moiety]. Conductance data revealed the non electrolytic nature of all the complexes. Co(II), Ni(II) and Zn (II) complexes showed paramagnetic behaviour while the Zn(II) chelates in both the cases were purely diamagnetic.

Part II contains the results of thermogravimetric studies of some selected complexes based on thermogravimetric data. This part is divided into 4 chapters. Chapter I gives an introduction and Chapter II describes materials, methods and instruments used for the present study. Chapter III deals with the thermal behaviour of Cu(II) and Zn(II) complexes of 2-Hydroxyacetophenone 2-Aminothiophenol and 2-Hydroxyacetophenone 2-Aminophenol. A three stage decomposition pattern was observed for the Cu(II) complex of the ligand 2-Hydroxyacetophenone 2-Aminothiophenol whereas the Zn(II) complex of the same ligand showed a two stage decomposition. In the case of 2-Hydroxyacetophenone 2-Aminophenol, both Cu(II) and Zn(II) chelates showed a two stage decomposition pattern.

In Chapter IV thermal decomposition studies of Cu(II) and Zn(II) complexes of Benzil 2-Aminothiophenol and Benzil 2-Aminophenol were incorporated. In all the above complexes, the decomposition started only
above 110°C and the absence of decomposition at the temperature range 60-90°C indicates that the water molecules present in the metal chelates are not in the lattice but co-ordinated to the central metal ion.

Part III explains the screening studies of metal complexes of Schiff bases as antitumour agents. This part is divided into 3 chapters. Chapter I deals with introduction to cancer and a general outlook on antitumour studies. Chapter II deals with materials, methods and instruments used for the study. *In vitro* antitumour study, *In vivo* antitumour study and acute toxicity studies in BALB/c Mice were included in Chapter III. The screening studies confirm that Zn-HAPATP and Cu-BAP are the most active metal chelates with lowest IC$_{50}$ values for DLA and HeLa cells. The low molecular weight and lipid solubility of the Zn and Cu complexes would have facilitated 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.

Part IV contains the results of antibacterial studies of some selected complexes towards 4 clinically important bacterial strains. The organisms selected for the study are *E.coli, P. aerugenosa, P.vulgaris* and *S.aureus*. This
Part is divided into 3 chapters. Chapter I gives an introduction to antibacterial study and Chapter II deals with materials, methods and instruments used for this investigation. Results of the antibacterial study of the metal chelates were included in Chapter III. It is important to note that metal complexes exhibit enhanced antibacterial activity than their free ligands. Among the metal complexes studied, Cu-BAP showed better antibacterial activity against all the bacterial strains studied especially towards the negative organism, *P. aerugenosa*. This is because of an increase in the cell permeability of the transition 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 micro-organisms depends either on the impermeability of the cells of the microbes or difference in ribozomes in microbial cells.

The thesis concludes with summary.

A detailed list of references arranged in serial order is given at the end of each part.