Summary and Conclusions

Transition metals play an important place in medicinal biochemistry. Research has shown significant progress in utilization of transition metal complexes as drugs to treat several human diseases like carcinomas, lymphomas, infection control, anti-inflammatory, diabetes, and neurological disorders. Many of the reports in the literature show their biological applications as anticancer, antimicrobial, anti-inflammatory, antitubercular, antiviral, antioxidant and so on. Transition metals exhibit different oxidation states and can interact with a number of negatively charged molecules. This activity of transition metals has started the development of metal based drugs with promising pharmacological application and may offer unique therapeutic opportunities. The present work is focused on the synthesis of some novel quinoxaline, pyrimidine and benzothiazole derivatives and their metal complexes and to evaluate their antimicrobial, anticancer, antioxidant, antitubercular activities. The discussion made in the various chapters have been summarized below:

The introductory aspects of the present investigation have been presented in Chapter I. It gives the introduction about the transition metal complexes in therapeutic uses, the biological importance of heterocyclic compounds and their applications. The biological applications of especially Pt(II) complexes and Ru(III) complexes has been highlighted. Other applications like sensors and catalytic activity has also been discussed.

Chapter II gives the elaborate background discussion about the transition metal complexes with the quinoxaline, pyrimidine and benzothiazole based heterocyclic ligands. Chapter III describes about the synthesis, characterization and biological applications of Cr(III), Mn(II), Cu(II), Co(II), Ni(II) complexes of quinoxaline based Schiff base ligand. The structure of the ligand and the complexes optimized by UB3LYP methods with 6-31G (d) basis set and the structure has been reported.

- The HOMO-LUMO gap calculated from the DFT calculations show -4.14eV for the ligand and -0.0043eV for the Cu(II) complexes. This property can be tuned for the optoelectronic applications.
- The complexes were evaluated for their biological activity like antimicrobial, anticancer, antioxidant studies and have been found to be good.

- Co(II) and Mn(II) complexes were found to have better biological activity than the other complexes.

Chapter IV describes the synthesis, characterization and biological applications of pyrimidine based Schiff bases and their Cu(II), Co(II) and Ni(II) complexes.

- The crystal data and the structural refinement parameters of the ligand $C_{14}H_{16}N_5O_3S$ with formula weight 334.38 have been discussed. The synthesized pyrimidine Schiff base ligands and their Cu(II), Co(II) and Ni(II) complexes were found to possess square planar [Ni(II) and Cu(II) complexes] and octahedral geometry [Co(II) complexes]. These structures have been optimized by DFT calculations.
- The HOMO-LUMO energy gap for the Cu(II) and Ni(II) complexes are in the range of -0.31eV to -0.77eV. These can be tuned for their photophysical properties.
- The MIC values for the ligands against *T. thidurance, E. coli* and *C. albicans* were 500, 125, 250 μg/ml and 250, 125 and 250 μg/ml respectively.
- The K_b values of all the complexes were in the order of 10^4 M^{-1}.
- The DNA cleavage activity has been studied and the formations of two forms in the presence of hydrogen peroxide showed that the mechanism is non-hydrolytic pathway.
- The molecular docking of the Schiff bases was done against six different active sites and compared with the experimental results.

Chapter V describes the synthesis, characterization and biological applications of pyrimidine based Schiff bases and Ru(III) complexes with triphenylphosphine as the co-ligand. The catalytic applications of the Ru(III) complexes have been reported.

- The Ru(III) complexes has been synthesized and characterised using various spectral techniques and from all the spectral data octahedral geometry has been proposed.
- The low HOMO-LUMO gap (0.4127eV) in the complex is responsible for the optoelectronic properties.
- The IC_{50} values of the complexes range from 25.85μg/ml to 79.77 μg/ml.

- The IC_{50} values indicated that the compounds showed antioxidant activity but lesser than that of the standard.
- From docking studies, the binding energy of the the complex is -8.56 Kcal/mol with a pIC_{50} value of 533.55 nanomolar concentration.
- The nuclease activity of the Ru(III) complexes does not involve hydrolytic pathway.
- The catalytic activity of the alcohols in the presence of Ru(III) complex has been studied and reported and their order of reactivity is reported.

Chapter VI describes the synthesis, characterization and applications of the 2-amino-6-methyl-benzothiazole and its Co(II) complex.

- The single crystal XRD of the Co(II) complex shows that the complex has the empirical formula $C_{16}H_{16}Cl_2CoN_4S_2$ with formula weight 458.28. The intermolecular interactions contribute to the packing stabilization.
- The observed magnetic moment value of the Co(II) complex was 4.12BM.
- The coercivities of the Co(II) complexes were 410.35G.The low saturation magnetization and the presence of coercivities for the samples indicate that these complexes are weakly ferromagnetic.
- The cobalt complex showed a very good activity against *Aspergillus niger*, *Thiobacillus thidurance* and *Serratia marcescens*.
- The IC_{50} values of ligand and the complex are 80.19μM and 14.12μM respectively.
- Co(II) complex had a MIC value of 6.2μg/ml in anti-tubercular which is equal to the tested standard Streptomycin.
- The observed binding constant value was lesser than that of the classical intercalators and hence it was concluded that the Co(II) complex is a minor groove binder.
- The binding energy of the complex is -6.0Kcal/mol with a pIC_{50} value 39.02 micromolar concentration (docking analysis).

Chapter VII describes the synthesis, characterization and applications of the benzothiazole Schiff bases and its Ru(III) complexes.

- The single crystal XRD study of the Schiff base revealed that it has the empirical formula $C_{15}H_{12}N_2OS$ with formula weight 268.33.

- The synthesized complexes have been characterized using various spectral techniques and proposed octahedral geometry.
- The sensor applications of the benzothiazole Schiff bases has been studied and found to sense Hg^{2+} ion and Cr^{3+} to a small extent.
- The minimum inhibitory concentration of the complexes range from 31.25 to 125 μg/ml against *P. aeruginosa, E. coli* and *C. albicans*. The synthesized complexes showed a pronounced activity than the ligands.
- The *in-vitro* anticancer activity showed the IC_{50} values of the Ru(III) complexes as 36.85 and 25.68μg/ml respectively.
- The binding constants of the Ru(III) complexes were in the order of 10^5 M^{-1}.
- The molecular docking of the Schiff bases was done against six different active sites and compared with the experimental results.

Chapter VIII describes the Co(II) complexes of the fused heterocyclic systems, their synthesis, characterization and antimicrobial activity.

- From the results of the spectral data, a tetrahedral geometry has been suggested for the complexes.
- The emission properties of the ligand and the complexes has been studied and compared.
- The synthesized complexes were checked with antimicrobial activity and found to be excellently active against *S. aureus.*

Chapter IX describes the single crystals we obtained during laboratory trials. Their structural description and their biological importance are presented as published papers in international journals.

SCOPE FOR FUTURE WORK

- More series of quinoxaline, pyrimidine and benzothiazole derivatives can be studied because they have very good pharmaceutical applications.
- For complexes having good activity toxicity studies can be done.
- The quinoxaline complexes have very low HOMO LUMO energy gap. These complexes can be tuned for their optoelectonic applications. The Co(II) complexes of the fused heterocyclic systems, the luminescent property can be tuned for the photophysical applications.
- Protein binding studies can be done for all the complexes.
- For complexes which has more pharmaceutical applications the particle size can be studied and bring them to then nanolevel for drug delivery applications.
- The anion sensing and cation sensing properties can be studied in detail.