

SUMMARY AND CONCLUSION

This thesis dealt the synthesis, structural characterization and biological activities of Schiff bases transition metal complexes derived from (i) Salicylidene-4-iminoantipyrine and 2-aminothiazole, (ii) Benzalidene-4-iminoantipyrine and 2-aminothiazole, (iii) Benzylidene-curcuminyl-4-iminoantipyrine and 2,6-diaminopyridine, (iv) Salicylidene-4-imino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one and Histidine, (v) Diphenyldi-(imino-4-nitro) benzene and 2, 2'-bipyridyl. Here, also report DNA interactions of some selected complexes using electronic absorption spectroscopy and cyclic voltammetry.

This thesis comprised of seven chapters which are discussed below:

Chapter - I

INTRODUCTION

In this chapter, the survey of the earlier work in this field covers the period from the early sixties to the end of 2017. At the end of the chapter, the scope of the present work, justifying the choice and significance of the work reported in the thesis.

Chapter - II

GENERAL EXPERIMENTAL METHODS AND TECHNIQUES

This chapter describes the general experimental methods, materials employed, purification of solvents, analytical procedures, CHNS (O) analysis, Magnetic susceptibility measurements, Molar conductance, X-ray diffraction studies, SEM, FESEM, Spectral studies (IR, UV-Vis., Mass, NMR and ESR spectroscopy), Electrochemical Study (CV) and Photoluminescence. Also, Characterisation for the interaction of Calf-Thymus DNA with copper complexes is done by using absorption

(UV-Vis) spectra and cyclic voltammetry (CV) studies. Procedures for *in vitro* antibacterial and antifungal activities of synthesized compounds were also reported.

Chapter - III

SYNTHESIS, CHARACTERIZATION, DNA INTERACTION AND STATISTICAL ANALYSIS OF BIOCIDAL INVESTIGATION OF SCHIFF BASE METAL COMPLEXES DERIVED FROM SALICYLIDENE-4-IMINOANTIPYRINE AND 2-AMINOTHIAZOLE

In this chapter, we reported the synthesis of new Schiff base Cu(II), Co(II), Ni(II), VO(II) and Zn(II) complexes by condensing salicylidene-4-iminoantipyrine with 2-aminothiazole. The ligand system coordinates with the metal ion in tetradentate manner through the two azomethine group of Schiff base, phenolic –OH group of the salicylaldehyde moiety and sulphur atom of the thiazole ring. Analytical data of the synthesized compounds reveals that the general formula of all the complexes are [ML]Cl. Monomeric nature of the complexes was confirmed from their magnetic susceptibility data. The higher conductance value of the chelate supports their mono electrolytic nature which is consistent with other reported complexes. Spectroscopic data of all the complexes suggest that they are square planar geometry except [VOL]Cl complex which shows square pyramidal geometry.

DNA interaction studies of [CuL]Cl complex indicate that the binding takes place through intercalation mode between the complex and the DNA binding. The *in-vitro* antimicrobial activities of the investigated compounds tested against the bacterial and fungal strains were monitored by well diffusion method. The MIC values against the growth of microorganisms indicate that the complexes have much larger antimicrobial activities than the free ligand. This is reduction in size of Ligand in metal chelates due to coordination. These results are supported by FESEM and

powder XRD data. From statistical analysis, the results confirmed for preparing samples of bacteria and fungi that highly control the *Klebsiella pneumoniae* and *Staphylococcus aureus* bacterial species.

Chapter - IV

BIOLOGICAL SCREENING STUDIES OF DNA RELATE METAL COMPLEXES FROM BENZALIDENE-4-IMINO-2,3-DIMETHYL-1-PHENYL-3-PYRAZOLIN-5-ONE AND 2-AMINOTHIAZOLE

This chapter discussed the synthesis of terdentate Schiff base derived from Benzalidene-4-imino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one and 2-aminothiazole. The Schiff base was used for complexation to metal ions like Cu(II), Ni(II), Co(II), Mn(II) and Zn(II). The structural features of the chelates have been confirmed by microanalytical data, FAB-Mass spectra, Powder XRD, SEM, FTIR, UV-Vis, ¹H-NMR, EPR, CV and thermal analysis techniques. The analytical and mass spectral data of the complexes correspond well with the general formula [ML₂]Cl₂. The high conductance data of the chelates support their electrolytic nature. The spectral data of the complexes indicate that they are octahedral geometry around the central metal ion. The cyclic voltammogram of [CuL₂]Cl₂ complex in MeCN solution at 300 K shows two couples for Cu(II)/Cu(I) and Cu(I)/Cu(0) in the region. The ESR parameters for the [CuL₂]Cl₂ complex indicate that g_{\parallel} (2.31) > g_{\perp} (2.075) which is akin to axially elongated octahedral geometry and unpaired electron lies predominantly in the $d_{x^2-y^2}$ orbital. The bonding parameters α^2 and β^2 indicate that the in-plane σ -bonding is more covalent than the in-plane π -bonding. Powder XRD data and SEM images persist that the complexes are nano size grain with polycrystalline structure. DNA interaction studies of [CuL₂]Cl₂ complex have been done by electronic spectral and cyclic voltammetric measurements which reveal that the binding occurs through

intercalation between complex and DNA interaction of $[\text{CuL}_2]\text{Cl}_2$ complex with CT-DNA leads to hypochromism. The MIC values of complexes against the growth of microorganisms are lower than the ligand. This is mainly due to lipophilicity of metal ion in complexes.

Chapter - V

SYNTHESIS, CHARACTERIZATION, ANTIMICROBIAL AND ANTICANCER ACTIVITIES OF 14-MEMBERED FULLY CONJUGATED MACROCYCLIC SCHIFF BASE METAL COMPLEXES FROM BENZYLIDENE-CURCUMINYL-4-IMINOANTIPYRINE AND 2,6-DIAMINOPYRIDINE

Here, we described the synthesis of pentaaza 14-membered macrocyclic Schiff base transition metal complexes derived by the condensation between benzylidene-curcuminy-4-iminoantipyrine and 2,6-diaminopyridine. The analytical and mass spectral data of the complexes correspond well with the general formula $[\text{ML}]\text{Cl}_2$. The magnetic susceptibility value of the complexes at room temperature is consistent with that of square planar geometry around the central metal ion except for $[\text{VOL}]\text{Cl}_2$ complex which shows octahedral geometry. The higher conductance values of the chelates support their electrolytic nature of the metal complexes. It also indicates that the chloride anions present in the ionization sphere. The decreased crystalline size for complexes was observed in XRD data. SEM images of complexes confirmed that they have well known different morphologies.

IR, UV-Vis. spectral data of complexes suggested that the complexes are square planar geometry except $[\text{VOL}]\text{Cl}_2$ which shows octahedral geometry due to axial oxygen atom. The ESR parameters for copper complex clearly indicate that $A_{\parallel} (153 \times 10^{-4} \text{ cm}^{-1}) > A_{\perp} (67 \times 10^{-4} \text{ cm}^{-1})$ and $g_{\parallel} (2.36) > g_{\perp} (2.08) > 2$, the complex coincide

well with square planar geometry and the system is axially symmetric while for [VOL]Cl₂ complex [$A_{||}$ ($181 \times 10^{-4} \text{ cm}^{-1}$) $>$ A_{\perp} ($74 \times 10^{-4} \text{ cm}^{-1}$) and g_{\perp} (1.98) $>$ $g_{||}$ (1.94)] indicates that the complex is octahedral geometry.

The Schiff base and [CuL]Cl₂ complex were tested against the growth of breast cancer (human) cell line (MCF-7) using the MTT assay method. IC₅₀ values for ligand and [CuL]Cl₂ were 75.7 μM and 47.98 μM respectively. The % cell inhibition of Schiff base at 100 μM is 57.64605 and [CuL]Cl₂ at 100 μM is 62.45704. The minimum inhibitory concentration values of metal chelates for antimicrobial activities have lower than the free ligand.

Chapter - VI

DNA INTERACTION AND IN VITRO MICROBIAL STUDIES OF SOME FIRST ROW TRANSITION METAL COMPLEXES FROM SALICYLIDENE-4-IMINO-2,3-DIMETHYL-1-PHENYL-3-PYRAZOLIN-5-ONE AND HISTIDINE

This chapter elucidated the synthesis of neutral tetradentate N₂O₂ donor type Schiff base transition metal complexes have been derived from histidine and salicylidene-4-imino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one. The synthesized compounds were characterized by using elemental analysis, molar conductance, magnetic susceptibility measurements, IR, FAB-MS, ¹H-NMR, UV, EPR, CV, Fluorescence emission, Powder XRD and SEM techniques. FAB mass and analytical data of the metal complexes correspond well with the general formula [ML]. The paramagnetic nature of the complexes was confirmed from their magnetic susceptibility data. The lower conductance of the complexes supports their non-electrolytic nature. Powder XRD data and SEM image persist that the complexes are nano size grains with polycrystalline structure.

The spectroscopic evidence shows all the metal chelates are square planar geometry except vanadyl complex which shows square pyramidal geometry. CV data for [CuL] and [VOL] complexes in MeCN solution indicates that the redox potential of metal ions is affected by the coordinated ligand. ESR spectra of [CuL] and [VOL] complexes were well coinciding with proposed geometries and other reported complexes. Cyclic voltammogram of [CuL] complex at 300 K in the presence and absence of DNA in Tris-HCl buffer (pH 7.2) shows a direction reduction peak at $E_{pc} = 0.60$ V for Cu(II) \rightarrow Cu(I) in the cathodic region. At anodic side, oxidation peak was observed at $E_{pa} = 0.37$ V for Cu(I) \rightarrow Cu(II) region. The strong stripping peak at $E_{pa} = -0.79$ V is due to the oxidation of $-C=N$ group in the Schiff base. This pattern was totally altered by the CT-DNA interaction with the metal ion. Decrease in intensity and increase in peak potential of an oxidation peak at $E_{pa} = -0.79$ V region, reveals that DNA also interacts with azomethine nitrogen atom of the Schiff base. The *in vitro* antimicrobial activity of the investigated compounds were tested and reported.

Chapter - VII

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES ON SCHIFF BASE TRANSITION METAL COMPLEXES DERIVED FROM BENZIL, 4-NITROANILINE AND 2, 2'-BIPYRIDYL

Synthesis of new biologically active transition metal complexes of Cu(II), Ni(II), Co(II), Zn(II) and VO(II) ion derived from the Diphenyldi-(imino-4-nitro)benzene and 2,2'-bipyridyl is described in this chapter. The structural features of the synthesized complexes have been arrived from their elemental analyses, FAB-mass, IR, UV-Vis., $^1\text{H-NMR}$ and ESR spectral studies. FAB-Mass and analytical data shown that the general formula for the complexes are $[\text{ML}(\text{bipy})]\text{Cl}_2$. The high molar conductance value of the complexes reveals their electrolytic nature. Magnetic

moment values of the complexes in the solid state show that copper, cobalt and vanadyl complexes are paramagnetic whereas $[\text{NiL}(\text{bipy})]\text{Cl}_2$ and $[\text{ZnL}(\text{bipy})]\text{Cl}_2$ are diamagnetic at room temperature.

Spectral data evidences revealed that the all complexes are square planar geometry except $[\text{VOL}(\text{bipy})]\text{Cl}_2$ complex which shows square pyramidal geometry. The cyclic voltammogram of the $[\text{CuL}(\text{bipy})]\text{Cl}_2$ complex in MeCN solution shows a quasi-reversible peak for the couple: $\text{Cu(II)} \rightarrow \text{Cu(III)}$ at $E_{p_a} = 0.61$ V with the direct cathodic peak for $\text{Cu(III)} \rightarrow \text{Cu(II)}$ at $E_{p_c} = 0.38$ V. Further, it exhibits another couple in the negative region characteristic for $\text{Cu(II)} \rightarrow \text{Cu(I)}$ ($E_{p_c} = -0.58$ V) reduction and $\text{Cu(I)} \rightarrow \text{Cu(II)}$ ($E_{p_a} = -0.18$ V) oxidation.

The binding mode of copper complex with CT-DNA was analyzed by electronic absorption spectra and cyclic voltammetry. The *in vitro* biological screening effects of the investigated compounds were tested against bacteria: *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Bacillus subtilis* and *Klebsiella pneumoniae*. All the compounds exhibit their resistance against growth of microbes.