PREFACE

The present thesis work deals with the studies involving synthesis of vanadium-based complexes as photoactivated chemotherapeutic as well a photodynamic therapeutic agent. Their interactions with DNA, as double-stranded DNA crosslinkers, visible light induced cytotoxic effect on cancerous cells, mechanistic aspects of cell death, and cellular localization behavior were studied.

Chapter I presents a brief introduction to the metal-based photochemotherapeutic and DNA crosslinking agents. Importance of vanadium metal in medicinal as well as biological aspects is discussed. The significance of photoactivated chemotherapy (PACT) and photodynamic therapy (PDT) in cancer treatment is discussed. A discussion on the opportunities and motivation for the development of metal-based anticancer agents is also made. DNA crosslinks and its relation to cancer and cancer treatment are presented. Objective of the present investigation is also dealt in this chapter.

Chapter II of the thesis deals with the synthesis, characterization and DNA damaging ability of a dioxovanadium(V) complex of vitamin-B6 Schiff base. The complex exhibited significant reactive oxygen species (ROS) mediated apoptotic photocytotoxicity in the cancer cells, while being essentially non-toxic in the dark. Alkaline Comet assay showed damage of nuclear DNA.

Chapter III presents synthesis and characterization of two oxovanadium(IV) complexes, viz. $[VO(pyphen)Cl_2]$ (**2**) and $[VO(pydppz)Cl_2]$ (**3**), where pyphen is 2-(2′-pyridyl)-1,10-phenanthroline and pydppz is 3-(pyridin-2-yl)dipyrido[3,2-a:2′,3′-c]phenazine. The complexes exhibited photo-induced DNA crosslinking property and photo-cytotoxicity.

Chapter-IV deals with oxovanadium (IV) complexes, viz. $[VO(L_1/L_2)Cl_2]_{n+}$ (**4**, **5**) of anthracenyl terpyridine and triphenyl phosphonium-appended anthracenyl terpyridine. Upon photo-irradiation with visible light (400-700 nm), The complexes showed significant photocytotoxicity in visible light with low dark toxicity in HeLa and MCF-7 cells. FACScan analysis showed cellular apoptosis when treated with the complex in visible light in comparison to their dark controls. The photocytotoxicity of the complexes was attributed to their DNA crosslinking ability. Fluorescence microscopic studies revealed mitochondrial localization of the complex within the cancer cells.

Chapter V deals with the synthesis, characterization, photo-induced DNA crosslinking ability and photocytotoxicity of the oxovanadium (IV) complexes, viz. $[VO(dpa/L_1/L_2)Cl_2]$ (**7-9**) of glucose or biotin appended ligands. Cell death mechanism was found out to be apoptic in nature. The complexes displayed enhanced cellular uptake in cancerous cells. The cytotoxicity of the complexes is comparable with the already available DNA crosslinking drug cis-platin.

In **Chapter VI** we have designed the oxovanadium (IV) complexes of BODIPY appended dipicolyl amine. The complexes, viz. $[VO(bzdpa/L_1/L_2)Cl_2]$ (**10-12**) were synthesized, characterized and their cellular uptake, photocytotoxicity, DNA crosslinking ability and mode of photo-induced cell death in cancer cells was studied. Mitochondria targeting photocytotoxic property of the complexes has been studied in details.

Finally, the summary of the dissertation and conclusions drawn from the present investigations are presented.

The references in the text have been indicated as superscript numbers and assembled at the end of each chapter. The complexes presented in this thesis are represented by bold-faced numbers. Due acknowledgements have been made wherever the work described is based on the findings of other investigators. Any omission that might have happened due to oversight or mistake is regretted.