PREFACE

In this thesis the various facets of the chemistry of photocytotoxic iron and cobalt complexes have been investigated along with their syntheses, characterization, evaluation of the photocytotoxic activities in various cancer cell lines, mechanism of cell death, the cellular uptake, localization inside cells, photo release, the interaction with double stranded DNA and their ability to induce DNA photocleavage.

Chapter I describes a general introduction on application of transition metal complexes for photochemotherapeutic activity. A brief introduction regarding Photodynamic Therapy (PDT) as a new alternative to chemotherapy for treating cancer has been made. The different modes of interaction of small molecules with duplex DNA are described. Recent reports on metal-based photocytotoxicity, photo-induced DNA cleavage activity and cellular localization are presented in detail. Recent advancement in the field of PDT has been elaborated. Objective of the present investigation is also dealt in this Chapter.

Chapter II describes the syntheses, characterization, evaluation of visible light induced cytotoxicity, mode of cell death and interaction with DNA of a series of iron(II) bispyridylphen / bispyridyldppz(phen, 1, 10-phenanthroline; dppz dipyrido phenazine) complexes. The DNA binding affinities of the complexes discussed. The importance of this work lies in the remarkable photocytotoxic behaviour of the iron(II) complexes with visible light which was not reported earlier.

Chapter III deals with the syntheses of two iron(III) benzhydroxamate complexes which upon irradiation with red light can initiate photoreactions to generate cytotoxic species and induce death in HeLa and HaCaT cells. The mechanisms of cell

death, effect of the complexes on the cell cycle under various conditions, the uptake inside cells with ICE-OES study, generation of reactive oxygen species and localization of the molecules inside the cell are described. The DNA binding affinities of the complexes and their ability to induce DNA photocleavage in red light are also described here.

Chapter IV presents an iron(III) complex with cytosolic localization in cancer cells, with preferential uptake into the MCF-7 cells in comparison to HeLa cells. The synthesis, characterization, photocytotoxicity in HeLa and MCF-7 cells, cell death mechanisms and cellular uptake and localization of the iron(III) complexes are presented.

Chapter V describes the syntheses, characterization and biological activities of BODIPY appended iron(III) catecholate complexes. These complexes contain all the necessary requirments of a molecule to be called an ideal PDT agent. They localize in the mitochondria of cancer cells. They can be activated with red light to generate singlet oxygen as the reactive oxygen species (ROS) causing apoptotic cell death.

Chapter VI presents the syntheses, characterization of a series of cobalt(III) complexes of curcumin and mitocurcumin and their cellular uptake in cancer cells. Light induced release of curcumin and its derivative has been observed. The visible light induced cytotoxicities of the complexes in HeLa and MCF-7 cells, their effect on the progression of the cell cycle in dark and light generation of reactiva oxygen species and the localization of the complexes inside the cells are studied.

The references have been compiled at the end of each chapter and given as superscripts in the text. The complexes presented in this thesis are indicated by bold-faced numbers. Crystallography data of the complexes that are structurally

characterized by single crystal X-ray diffraction method are given in CIF format in the enclosed CD (Appendix-I). Due acknowledgements have been made wherever the work described is based on the findings of other investigators. Any unintentional omission that might have happened due to oversight is regretted.

INDEX WORDS: Iron complexes • Cobalt Complex • Crystal structure • Red light induced cytotoxicity • Cellular imaging • DNA binding • PDT • DNA photo-cleavage • Curcumin.

Date:

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