Abstract

The design, synthesis and supramolecular assemblies in coordination compounds have received much emphasis in the field of crystal engineering due to their potential applications in wide range of fields. The work in the present thesis focuses on the synthesis, crystal structures and supramolecular asemblies of a few transition metal coordination solids involving N- and O-donor ligands. The compounds have been synthesized by using transition metal salts of manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II). The single crystal X-ray structures of all the compounds have been determined. The compounds were further characterized using vibrational and electronic spectroscopies, PXRD, elemental analysis, magnetic moment and TGA. The supramolecular assemblies involving the unconventional synthons in the compounds have been analyzed theoretically using various computational tools. Antiproliferative evaluation of the compounds in cancerous cell lines has lead to a better understanding of the action of these classes of coordination complexes and can be used as potential candidates to design new anti-cancer metallo-drugs.

Chapter 1 contains the general introductory discussions about the supramolecular chemistry, non-covalent interactions, self-assembly, metallo-supramolecular chemistry and computational methods for studying non-covalent interactions. This chapter also reviews the anticancer activities of transition metal complexes. The aims and objectives of the present thesis are highlighted at the end of the chapter.

Chapter 2 describes the synthesis, crystal structures and properties of three isostructural coordination compounds of Co(II), Mn(II) and Zn(II) involving 2,5-pyridinedicarboxylato ligand *viz*. $[Co(2,5\text{-}PDC)(H_2O)_4]\cdot 2H_2O$ (**1**), $[Mn(2,5\text{-}PDC)(H_2O)_4]\cdot 2H_2O$ (**2**) and $[Zn(2,5\text{-}PDC)(H_2O)_4]\cdot 2H_2O$ (**3**) [where, 2,5-PDC = 2,5-pyridinedicarboxylate]. Crystal structure analysis of compounds **1**, **2** and **3** reveals the significant contribution of anion–π and unconventional antiparallel CO···CO interactions towards the stability of the solid state structures. The unconventional interactions have been further analyzed theoretically by using DFT calculations, molecular electrostatic potential (MEP) surface and non-covalent interaction (NCI) plot

computational tools. The isostructurality parameters of the three compounds have been highlighted using Fabian and Kalman approach. The antiproliferative activities of compounds **1** and **2** have been explored in Dalton's lymphoma (DL) cancer cell line by using MTT based cytotoxicity study, fluorescence based apoptosis assay, molecular docking and pharmacophore modelling. The compounds significantly induced cytotoxicity through apoptotic cell death in DL cells with negligible cytotoxicity in normal cells. Both the compounds interact well with the anti-apoptotic cancer target proteins with higher binding affinities. Furthermore, the significant pharmacophore features of the structures of the compounds responsible for biological activities have been identified to establish structure activity relationship (SAR).

Chapter 3 focuses on the synthesis and crystal structures of three Mn(II) coordination complexes involving 4-nitrobenzoate, 1,3,5-benzenetricarboxylic acid, 4-cyanopyridine and benzoate ligands *viz*. $[Mn(4\text{-}NBz)_2(4\text{-}CNpy)_2]_n$ (**4**), $[Mn(4\text{-}CNpy)_2(H_2BTC)_2]_n$ (**5**) and $[Mn(Bz)_2(H_2O)_4](4\text{-}CNpy)\cdot 2H_2O$ (**6**). Single crystal X-ray structure analysis reveals that **4** and **5** are coordination polymers with interesting 3D network architectures assisted by unconventional antiparallel nitrile···nitrile interactions which have been further studied theoretically using quantum theory of atoms in molecules (QTAIM) and molecular electrostatic potential (MEP) surface analysis. The crystal structure analysis of compound **6**, an unusual cocrystal hydrate of Mn(II), reveals the enclathration of guest 4-CNpy molecules in the Mn(II) host tetramer involving energetically significant C–H···C contacts. The symmetry adapted perturbation theory (SAPT) analysis reveals that both electrostatics as well as dispersion interactions are the most dominant contributors towards the stabilization of the C–H···C interactions.

Chapter 4 discusses three isostructural coordination compounds of Co(II), Mn(II) and Zn(II) involving 3-cyanopyridine and 2-chlorobenzoate ligands *viz*. $[M(3\text{-}CNpy)_2(2\text{-}ClBz)_2(H_2O)_2]$ [where, M = Co(**7**), Mn(**8**) and Zn(**9**); 3-CNpy = 3-cyanopyridine, 2-ClBz = 2-chlorobenzoate]. Electrostatically enhanced π-π interactions are observed between the phenyl rings of 2-ClBz and pyridine rings of 3-CNpy involving the monomeric units of the complexes. These interactions have been theoretically explored by using DFT calculation, MEP surface and NCI plot computational tools. The

cytotoxic potential of the compounds in DL cells have been investigated considering MTT assay, apoptosis assay and molecular docking studies. The complexes exhibit cytotoxicity through apoptotic cell death with negligible cytotoxicity in normal PBMC cells. The docking simulation results also confirm the interaction of the complexes with the active sites of the target anti-apoptotic proteins. Furthermore, the pharmacophore features embedded with the structures of the synthesized complexes may play important roles in biological activities.

Chapter 5 describes the synthesis and crystal structures of three monomeric Co(II), Ni(II) and Cu(II) complexes involving 2,6-pyridinedicarboxylato and pyridine ligands *viz*. [Co(py)(2,6-PDC)(H_2O)$_2$]·H_2O (**10**); [Ni(py)(2,6-PDC)(H_2O)$_2$]·H_2O (**11**) and [Cu(py)(2,6-PDC)(H_2O)]·2H_2O (**12**) [where, py = pyridine, 2,6-PDC = 2,6-pyridinedicarboxylate]. A closer look on the crystal structures reveal the formation of self-assembled supramolecular dimers assisted by antiparallel π-stacking interactions involving pyridine rings. The strength of the biologically relevant antiparallel π-stacking interactions has been evaluated theoretically using DFT calculations and the influence of the pyridine coordination to the strength of the stacking assembly has also been confirmed. The compounds significantly inhibit cell viability by inducing apoptotic cell death in DL cell lines with negligible cytotoxicity in normal cells. The molecular docking study reflects that the compounds interact and accommodated well in the active site of anti-apoptotic BCL-2 protein that might lead to apoptotic cell death. The pharmacophore features responsible for the biological activities based on structure activity relationship (SAR) of the compounds have also been identified.