SUMMARY

Chapter – 1 starts with the history and the development of platinum(II) complexes for the treatment of anticancer activity and also the cellular uptake of cisplatin (CDDP). Metal complexes with diimine ligands and other important factors for the anticancer activity were discussed. Interaction modes of these metal complexes with DNA were discussed and the types of cytotoxicity assays used in general were discussed here.

Chapter – 2 describes the aim of the present work.

Chapter – 3 deals with the synthesis and anticancer activity of six water soluble cobalt(III) complexes with ligands of the type [Co(N-N)₂Cl₂]Cl, where N-N = 5,6-dimethyl-1,10-phenanthroline (5,6-dmp) (1), 4,7-dimethyl-1,10-phenanthroline (4,7-dmp) (2), 3,4,7,8-tetramethyl-1,10-phenanthroline (tmp) (3), 5-methyl-1,10-phenanthroline (5-mp) (4), 4-methyl-1,10-phenanthroline (4-mp) (5) and 1,10-phenanthroline (phen) (6). The structures of the complexes were determined by elemental analysis, NMR, FAB-MS, IR and electronic spectroscopy. In addition, the structure of complexes 1, 2 and 3 were refined by single crystal X-ray diffraction. Combination of circular dichroism (CD), UV-Vis spectroscopy titration, and ethidium bromide (EthBr) displacement assay studies suggest that interaction of these complexes with CT-DNA is weak and therefore this interaction will not play a key role in the anticancer activity of these complexes. Anticancer activity of these complexes was assessed on HeLa and PC-3 cancer cell lines by MTS assay and PI staining assay using flow cytometry. Comparison of the anticancer activity of these complexes with their
hydrophobicity suggests that moderate rather than lower or higher hydrophobicity of the metal complexes is a necessary condition for the anticancer activity of these complexes.

**Chapter – 4** describes the synthesis of four cobalt(III) complexes with ligands of the type [Co(n-n)2Cl2]Cl, where n-n = 2-2′-bipyridine (bpy) (7), 4,4′-dimethoxy-2-2′-bipyridine (dmb) (8), 4,4′-di-tert-butyl-2,2′-bipyridine (dtbb) (9), 5,5′-dicarboxylic acid-2,2′-bipyridine (dcb) (10). The structures of these complexes were determined by elemental analysis, NMR, ESI-MS, IR and electronic spectroscopy. DNA binding interaction studies were carried out by UV-Vis spectroscopy titration method. Anticancer activity of these complexes was assessed on PC-3 cancer cell lines by MTS assay and PI staining assay using flow cytometry. UV-Vis spectroscopy titration studies suggest that these complexes interact weakly with DNA than the phenanthroline complexes indicated in Chapter 3, indicating this DNA binding is not playing a key role in the anticancer activity. Both MTS and flow cytometry assay methods suggest that the anticancer activity of substituted bipyridine complexes has been dramatically increased compared to un-substituted bipyridine complexes. The complex 9 compared to other complexes of this series shows more anticancer activity due to the presence of tertiary butyl groups that increases the hydrophobicity.

**Chapter – 5** deals with the importance of ionicity (charge) and presence of labile ligands on the anticancer activity of cobalt complexes. Five water soluble cobalt(II) complexes of the type of [Co(N-N)2Cl2] where N-N is 5,6-dimethyl-1,10-phenanthroline (5,6-dmp) (11), 4,7-dimethyl-1,10-phenanthroline
(4,7-dmp) (12), 3,4,7,8-tetramethyl-1,10-phenanthroline (tmp) (13) and two complexes of the type[Co(N-N)₃]³⁺/²⁺ with 4,7-dmp were synthesized (14 and 15) have been reported. These complexes were characterized by elemental analysis, NMR, EPR, ESI-MS, IR and electronic spectroscopy. In addition, the structure of complexes 11 and 13 were refined by single crystal X-ray diffraction and the anticancer activity was tested on PC-3 cancer cell lines by MTS assay and PI staining assay using flow cytometry. Both these anticancer studies suggest that mono cationic dichlorocobalt(III) complex shows higher anticancer activity than complexes with 0, 2+, 3+ charge. Also this higher anticancer activity is due to the additional feature of this complex like moderate hydrophobicity as well as the presence of two labile chloride ligands.

Collectively, this present work provides new direction to the anticancer activity of cobalt complexes. Targeting the DNA is not the only reason for anticancer activity and other factors such as hydrophobicity; ionicity and presence of labile ligands in the metal complexes are also important.