In vitro Anticancer Activity of New Iridium and Ruthenium Arene Complexes on different Human Cancer Cell Lines and *in vivo* Tumour Regression in Dalton's Lymphoma Bearing Mice

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Abstract—*Interest in transition metal complexes as anticancer agents is increasing with new complexes being reported and their mechanisms of action being discovered. In this work we investigated the effects of iridium and ruthenium arene complexes on cancer cells. Their identities have been established by satisfactory physical and electrochemical studies (elemental analyses, electrospray ionization-mass spectrometry (ESI-MS), FT-IR, NMR (1H, 13C), UV/vis, emission spectral). Structure has been authenticated by X-ray single crystal analyses and complexes effectively bind with calf thymus DNA (CT DNA) through intercalative/electrostatic interactions. After various physicochemical techniques, Complexes were tested in vitro on different cancer cell lines (DL cells, HeLa, MCF-7 and A549 cell lines) as well as in vivo on Dalton's Lymphoma (DL) bearing mice. In MTT assay, iridium complexes displayed highest cytotoxicity and antiproliferative activity or lowest IC_{50} value in 24 h exposure. Different parameters also have been checked for mode of cell death and action of drugs. In morphological study of cells, complexes appear to induce blebbing and nuclear fragmentation which are dependable markers of apoptosis. Apoptosis as well as cell cycle delay were further confirmed by cell cycle analysis and complexes also increases intracellular ROS generation that may be a factor to induce apoptosis. Mode of interaction of the complexes with DNA/protein has also been supported by molecular docking. Further in vitro data was validated on in vivo experiments and Treated/Control (T/C) value of each complex was calculated. In this study, iridium complex significantly increases in life span of the tumor bearing mice and reduced the belly size. From these data, we conclude that complexes exert remarkable anticancer activity against cancer cells.*

Keywords*: Dalton's Lymphoma (DL), A-549, MCF-7, HeLa, Cytotoxicity, MTT, Cell cycle, Reactive Oxygen Species (ROS)*