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Novel Nickel Complex Compound Reactivates the Apoptotic Network, Cell Cycle Arrest and Cytoskeletal Rearrangement in Human Colon and Breast Cancer Cells

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Abstract : Colon and breast cancers are categorized as the most prevalent types of cancer worldwide. Recently, the broad clinical application of metal complex compounds has led to the discovery of potential therapeutic drugs. The aim of this study was to evaluate the cytotoxic action of a selected nickel complex compound (NCC) against human colon and breast cancer cells. In this context, we determined the potency of the compound in the induction of apoptosis, cell cycle arrest, and cytoskeleton rearrangement. HT-29, WiDr, CCD-18Co, MCF-7 and Hs 190.T cell lines were used to determine the IC50 of the compound using the MTT assay. Analysis of apoptosis was carried out using immunofluorescence, acridine orange/ propidium iodide double staining, Annexin-V-FITC assay, evaluation of the translocation of NF-kB, oxygen radical antioxidant capacity, quenching of reactive oxygen species content , measurement of LDH release, caspase-3/-7, -8 and -9 assays and western blotting. The cell cycle arrest was examined using flowcytometry and gene expression was assessed using qPCR array. Results showed that our nickel complex compound displayed a potent suppressive effect on HT-29, WiDr, MCF-7 and Hs 190.T after 24 h of treatment with IC50 value of 2.02±0.54, 2.13±0.65, 3.76±015 and 3.14±0.45 µM respectively. This cytotoxic effect on normal cells was insignificant. Dipping in the mitochondrial membrane potential and increased release of cytochrome c from the mitochondria indicated induction of the intrinsic apoptosis pathway by the nickel complex compound. Activation of this pathway was further evidenced by significant activation of caspase 9 and 3/7.The nickel complex compound (NCC) was also shown activate the extrinsic pathways of apoptosis by activation of caspase-8 which is linked to the suppression of NF-kB translocation to the nucleus. Cell cycle arrest in the G1 phase and up-regulation of glutathione reductase, based on excessive ROS production were also observed. The results of this study suggest that the nickel complex compound is a potent anti-cancer agent inducing both intrinsic and extrinsic pathways as well as cell cycle arrest in colon and breast cancer cells.

Keywords : nickel complex, apoptosis, cytoskeletal rearrangement, colon cancer, breast cancer
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