Enhancing Sensitization of Cervical Cancer Cells to γ-Radiation Ellagic Acid

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Abstract : Herbal polyphenols have gained significance because of their increasing promise in prevention and treatment of cancer. Therefore, development of a dietary compound as an effective radiosensitizer and a radioprotector is highly warranted for cervical cancer patients undergoing therapy. This study describes the cytotoxic effects of the flavonoid, ellagic acid (EA) when administered either alone or in combination with gamma radiation on cervical cancer HeLa cells in vitro. Apoptotic index and proliferation were measured by using trypan blue assay. Reproductive cell death was analyzed by clonogenic assay. Propidium iodide staining for flowcytometry was performed to analyze cell cycle modulation. Nuclear and mitochondrial changes were studied with specific dyes. DNA repair kinetics was analyzed by immunofluorescence assay. Evaluation and comparison of EA effects were performed with other clinically used breast cancer drugs. When tumor cells were exposed to 2 and 4 Gy of irradiation in presence of EA (10 µM), it yielded a synergistic cytotoxic effect on cervical cancer cells whereas in NIH3T3 cells it reversed the injury caused by irradiation and abetted in the regaining of normal healthy cells. At 24h ~25foci/cell was observed and 2.6 fold decrease in the mitochondrial membrane potential. Up to 40% cell were arrested in the G1 phase and 20-36% cells exhibited apoptosis. Our results demonstrate the role of increased apoptosis and cell cycle modulation in the mechanism of EA mediated radiosensitization of cervical cancer cells and thus advocating EA as an adjuvant for preclinical trials in cancer chemo- radiotherapy.
Keywords : cervical cancer, ellagic acid, sensitization, radiation therapy
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