ARSENIC TRIOXIDE MODULATES GENOTOXICITY, CELL CYCLE REGULATION, AND APOPTOSIS IN COLON CARCINOMA (HT-29) CELLS

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Abstract: Arsenic trioxide is a well known environmental toxicant and carcinogen. However, arsenic trioxide has also been used clinically to treat some forms of human cancer (e.g., leukemia). Although its therapeutic effects have been studied extensively, the cellular and molecular mechanisms of its action on cancer cells are not fully elucidated. Recent studies in our laboratory have demonstrated that arsenic trioxide is cytotoxic in human colon cancer (HT-29) cells. Our present study focuses on the genotoxicity and the dose-dependent effect of arsenic trioxide on the induction of sub-G1 phase in HT-29 cells. HT-29 cells were cultured according to standard protocol followed by exposure to various doses (0, 2, 4, 6, 8, 10, and 12 μg/mL) of arsenic trioxide for 24 and 48 h. The genotoxic effects of arsenic-induced DNA damage in a human colon cancer cell line was determined by the alkaline single cell gel electrophoresis (Comet) assay. Cell cycle analysis was performed using propidium iodide (PI) staining. The study confirmed that arsenic trioxide caused DNA damage as revealed by the significance increase in comet tail-lengths of chemical-treated cells compared to control cells; indicating that arsenic trioxide exhibited genotoxic effects to colon cancer cells. Flow cytometric analysis of cell cycle distribution showed the appearance of sub-G1 peak and cell arrest at the G1 phase in the presence of arsenic trioxide. A dose-dependent effect of arsenic trioxide in the induction of the sub-G1 phase was observed and clearly demonstrated that the arsenic trioxide induced apoptosis in HT-29 cells.

Keywords: Arsenic Trioxide, HT-29 cells, genotoxicity, comet assay, flow cytometry, and cell cycle

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