THE EFFECTS OF ARSENIC TRIOXIDE ON DNA SYNTHESIS AND GENOTOXICITY IN HUMAN COLON CANCER CELLS

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Abstract: Colon cancer is the third leading cause of cancer-related deaths worldwide. Recent studies in our laboratory have demonstrated that arsenic trioxide is cytotoxic in human colon cancer (HT-29), lung (A549) and breast (MCF-7) carcinoma cells. The purpose of the present study is to investigate the effects of arsenic trioxide on DNA synthesis and the possible genotoxic effects on human colon cancer 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 h. The proliferative response (DNA synthesis) to arsenic trioxide was assessed by [³H]thymidine incorporation. The genotoxic effects of arsenic-induced DNA damage in a human colon cancer cell line was evaluated by the alkaline single cell gel electrophoresis. Results indicated that arsenic trioxide affected DNA synthesis in HT-29 cells in a biphasic manner; showing a slight but not significant increase in cell proliferation at lower levels of exposure (2, 4 and 6 µg/mL) followed by a significant inhibition of cell proliferation at higher doses (i.e., 8 and 10 µg/mL). The study also confirmed that arsenic trioxide exposure caused genotoxicity as revealed by the significant increase in DNA damage, comet tail-lengths, and tail moment when compared to non-exposed cells. Results of the [³H]thymidine incorporation assay and comet assay revealed that exposure to arsenic trioxide affected DNA synthesis and exhibited genotoxic effects in human colon cancer cells.

Keywords: Arsenic trioxide, HT-29 cells, [³H]thymidine incorporation assay, genotoxicity, comet assay

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