ARSENIC TRIOXIDE-INDUCED CYTOTOXICITY AND GENOTOXICITY IN COLON CANCER 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. Hence, the aim of the present research was to evaluate cytotoxicity and genotoxicity induced by arsenic trioxide in human colon cancer (HT-29) cells in in vitro. In this study, [³H] thymidine incorporation and MTT [3-(4,5 dimethylthiazoyl-2-yl)-2,5- diphenyltetrazolium bromide] assays to assess cell proliferation and cell viability, respectively have been used. The genotoxic effect of arsenic-induced DNA damage in a human colon cancer cell line (HT-29) was determined by the alkaline single cell gel electrophoresis (Comet) assay. HT-29 cells were cultured according to the standard protocols following by exposure to various doses (0, 2, 4, 6, 8, 10, 12 and 14 µg/ml) of arsenic trioxide for 24, 48 and 72 h depending on the assay. Experimental data indicated that arsenic trioxide is cytotoxic to colon cancer cells showing LD₅₀ values of 9.8, 9.4 and 9.0 µg/ml upon 24, 48 and 72 h of exposure, respectively. There was a dose-dependent response with regard to As₂O₃ toxicity in HT-29 cells. Although there was a reduction in LD₅₀ value with increasing exposure time, this decrease was not statistically significant. We demonstrated that arsenic trioxide affected DNA synthesis in HT-29 cells. The data clearly showed a biphasic response to arsenic trioxide in the colon cancer cells which indicated cell proliferation at a lower levels and a cytotoxic effect at higher levels of exposure. The Comet assay was carried out to determine DNA damage as represented by comet tail-length. The study confirms that arsenic trioxide causes significant DNA damage at the doses used as revealed by the comet assay. In conclusion, the results show that arsenic trioxide exhibits both cytotoxic and genotoxic effects to colon cancer cells.

Keywords: Arsenic trioxide, colon cancer (HT-29) cells, cytotoxicity, genotoxicity, MTT assay, [³H] thymidine incorporation assay, Comet assay

Acknowledgements: This research supported by a grant from the National Institutes of Health (NIH) (Grant #1G12RR13459), through the NCRR-RCMI-Center for Environmental Health at Jackson State University (JSU). We thank Dr. Abdul K. Mohamed, Dean Emeritus and RCMI Program Director at JSU, for his support of this research.