ARSENIC TRIOXIDE-INDUCED TOXICITY AND CELL DEATH THROUGH NECROSIS IN HUMAN LEUKEMIA (HL-60) CELLS

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Abstract: The treatment of acute promyelocytic leukemia (APL) has been based on the administration of all-trans retinoic acid plus anthracycline chemotherapy, which is very effective as first line therapy; however 25 to 30% of patients will relapse with their disease becoming refractory to conventional therapy. Therefore, the aim of the present study was to investigate whether arsenic trioxide (ATO) induced cell death is associated with necrosis. To achieve this goal, HL-60 cells were treated with different concentrations of ATO for 24 h prior to cell viability using MTT, trypan blue, and propidium iodide assays respectively. The results obtained from the MTT, trypan blue, propidium iodine assay indicated that at very low concentration, ATO has a stimulatory effect on the growth of HL-60 cells. A significant ($p < 0.05$) gradual decrease in brightfield negative cells (live cells) was observed when exposed to high level of ATO between the range dose of (2-20 ug/mL). Data generated from the propidium iodide indicated that ATO exposure significantly ($p < 0.05$) increased the proportion of fluorescence positive cells (necrotic death cells) compared to the control. In summary, these studies demonstrated that ATO exerts dual effects on HL-60 promyelocytic leukemia cells. At low doses, it plays a stimulatory effect on the growth of HL-60 cells whereas at high dose tested, it becomes highly cytotoxic. This cytotoxicity was found to be associated with necrosis as revealed by a significant increase in dead cell concentration (Fluorescence) with increasing of ATO doses.

Keywords: Arsenic trioxide, HL-60 cells, cytotoxicity, MTT assay, trypan blue, propidium iodine, cellometer vision

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