ARSENIC TRIOXIDE MODULATES APOPTOSIS IN LUNG CARCINOMA (A549) CELLS

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Abstract: Apoptosis is termed programmed cell death. Its role is to maintain tissue homeostasis and to eliminate excess or dysfunctional cells. Apoptosis is characterized by biochemical features such as activation of a caspase cascade, DNA fragmentation into nucleosomal fragments (the classical “ladder” pattern on DNA electrophoresis), and cleavage of various caspase substrates (caspases 3 and 9 activities). The primary objectives of this research were to determine whether arsenic trioxide induced apoptosis in lung carcinoma (A549) cells is mediated via caspase activation and p39 mitogen–activated protein kinase (MAPK) pathway, and to evaluate whether arsenic trioxide exposure causes cell cycle arrest in these cells. To achieve these aims, A549 cells were cultured following standard protocols, and exposed to various doses (0, 2, 4, 6, 8 µg/ml) of arsenic trioxide for 48 h. Apoptosis was determined by agarose gel electrophoresis (DNA laddering), fluorescein isothiocyanate (FITC) assay (caspase 3), and immunoblot analysis (p38 MAP kinase activity). The cell cycle analysis was evaluated by flow cytometry. Findings from the DNA laddering assay indicated that arsenic trioxide induced apoptosis in the lung carcinoma cells. Our results also revealed that arsenic trioxide modulated caspase 3 activity and induced p38 map kinase activation in A549 cells. The cell cycle analysis revealed no cell cycle arrest. Future studies are underway to elucidate the genotoxic effect and determine whether p53 and bcl proteins are upregulated or down regulated in lung cancer cell in response to arsenic trioxide.

Key words: Arsenic trioxide (ATO), apoptosis, DNA fragmentation, p38 map kinase, caspase-3 FITC and cell cycle regulation.

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