ARSENIC-INDUCED OXIDATIVE STRESS AND APOPTOSIS IN HUMAN LIVER CARCINOMA (HEPG₂) CELLS

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Abstract: Arsenic is a toxic and carcinogenic agent associated with various human malignancies. Arsenic intoxication may result in hepatic toxicity, including toxic hepatitis and elevated liver enzyme levels. It has been shown that this agent induced apoptosis in a variety of malignant cell lines, but the precise mechanisms involved are not well elucidated. From ongoing investigations underlying the mechanisms of arsenic toxicity, evidence suggests that oxidative stress plays an important role in arsenic induced cell death or apoptosis. The purpose of this study was to evaluate the effects of arsenic trioxide on oxidative stress and apoptosis in human liver carcinoma (HepG₂) cells. Thiobarbituric acid test and flow cytometric analysis using annexin V/propidium iodide kit were used to assess oxidative stress and apoptosis following 24hr of exposure, respectively. The results of the thiobarbituric acid test demonstrated that arsenic trioxide significantly increase (p <0.05) the production of MDA, an end product of lipid peroxidation and a biomarker of oxidative stress. Our preliminary results of the flow cytometric assessment (Annexin V FITC/PI) showed a strong dose-response relationship between arsenic trioxide exposure and annexin V positive cells undergoing early stage apoptosis in HepG₂ cells. Overall, we conclude that arsenic trioxide induces cell death in HepG₂ cells and its apoptotic mechanism functions through oxidative stress. Further investigations are ongoing to identify the intracellular targets of oxidative stress induced following the exposure to arsenic trioxide.

Keywords: Arsenic trioxide, oxidative stress, apoptosis, annexin V, HepG₂ cells

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