MOLECULAR MECHANISMS OF CADMIUM-INDUCED TOXICITY IN HUMAN LIVER CARCINOMA (HEPG2) CELLS

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Abstract: Cadmium is a heavy metal that has been shown to manifest its toxicity in humans and animals. Many documented in vitro studies have shown that cadmium produces various genotoxic effects such as DNA damage and chromosomal aberrations. Diseases like autoimmune thyroidism are thought to be caused, in large part, by overexposure to cadmium. Although there have been numerous studies examining the effects of cadmium in animal models and a few case studies involving communities where cadmium contamination has occurred, the mechanisms of the carcinogenic activity of cadmium is not clearly defined. Therefore, the purpose of this study was to elucidate some of the molecular mechanisms that are involved in cadmium–induced toxicity in human liver carcinoma (HepG2) cells. To achieve this goal, we performed the MTT assay to measure cell viability. Annexin V assay and DNA fragmentation analysis were performed for early and late apoptosis, respectively. The result of MTT assay indicated that cadmium induces toxicity to HepG2 cells in a dose-dependent manner, showing a 24 h-LD50 of 3.6 µg/mL cadmium chloride. Similarly, a strong dose-response relationship (p < 0.05) was obtained in connection with cadmium chloride-induced apoptosis. Cadmium chloride-induced apoptosis was characterized by a significant increase in the percentages of annexin-V positive cells, as well by the occurrence of nucleosomal DNA fragmentation. In summary, this study indicated cadmium chloride is highly cytotoxic to HepG2 cells. This cytotoxic effect may be mediated at least in part through phosphatidylserine externalization and occurrence of nucleosomal DNA fragmentation.

Key words: Cadmium, cytotoxic, apoptosis, Annexin V, HepG2 cells, DNA fragmentation

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