MOLECULAR MECHANISMS OF CADMIUM CHLORIDE 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. Ailments such as bone disease, renal damage, and several forms of cancer are attributed to overexposure of 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, its molecular mechanisms of toxicity are not fully elucidated. Therefore, the purpose of this study was to elucidate the possible molecular mechanisms involved in cadmium chloride–induced toxicity in human liver carcinoma (HepG₂) cells. To achieve this goal, MTT assay was performed for cell viability, lipid hydroperoxide and comet assays for estimating the level of oxidative stress and DNA damage. Annexin V assay and DNA fragmentation analysis were also performed for apoptosis. The result of MTT assay indicated that cadmium chloride induces toxicity to HepG₂ cells in a dose-dependent manner, showing a 24 h-LD50 of 3.6 µg/mL cadmium chloride. There was a slight increase in MDA concentrations in cadmium chloride-treated cells compared to the control, with statistically significant (P < 0.05) at the higher tested. We observed a significant increase (p < 0.05) in comet tail-length, tail arm and tail moment, as well as in percentages of DNA cleavage in cadmium chloride-treated cells compared to the control. However, above 4µg/mL of exposure there was a reduction in DNA damage. Cadmium chloride-induced apoptosis was characterized by a significant increase (p < 0.05) in the percentages of annexin-V positive cells and the occurrence of nucleosomal DNA fragmentation. In summary, this study indicated cadmium chloride is highly cytotoxic to HepG2 cells. Based on this study, the mechanisms of cadmium induced toxicity is mediated through induction of oxidative stress, DNA damage, phosphatidylserine externalization, and induction nucleosomal DNA fragmentation.

Keywords: Cadmium chloride, HepG₂ cells, oxidative stress, DNA damage, apoptosis

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