



Selective Toxicity of Caspian cobra (*Naja oxiana*) venom on liver cancer cell mitochondria

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Abstract

To explore the cytotoxicity effects of Caspian cobra (*Naja oxiana* or *N. Oxiana*) venom on hepatocytes and mitochondria obtained from the liver of HCC rats. In this study, HCC induced by diethylnitrosamine (DEN), as an initiator, and 2-acetylaminofluorene (2-AAF), as a promoter. Rat liver hepatocytes and mitochondria for evaluation of the selective cytotoxic effect of *N. Oxiana* venom was isolated and mitochondria and cellular parameters related to apoptosis signaling were then determined. Our results showed a raise in mitochondrial reactive oxygen species (ROS) level, swelling in mitochondria, decline in the mitochondrial membrane potential (MMP) and cytochrome c release after exposure of mitochondria only from the HCC group with the crude venom of the *N. Oxiana* (12/5, 25, and 50 µg/ml). This crude venom also induced caspase-3 activation ($p < 0.001$) in the hepatocytes obtained only from the HCC rat liver. Based on the overall results, we suggested that *N. Oxiana* may could be considered as a promising complementary therapeutic agent for the treatment of HCC.

Key words: *Naja Oxiana*; Apoptosis; Hepatocellular carcinoma; Hepatocytes; Mitochondria.