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## Selective Toxicity of Persian Gulf Sea Cucumber (*Holothuria Parva*) Methanolic Extract on Liver Mitochondria Isolated from Animal Model of Hepatocellular Carcinoma

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### Abstract

**Introduction:** Natural products isolated from marine environment are well known for their pharmaco-dynamic potential in diversity of disease treatments such as cancer or inflammatory conditions. Sea cucumbers are one of the marine animals of the phylum Echinoderm and the class Holothuroidea, with a leathery skin and gelatinous body. Many studies have shown that the sea cucumber and sponge contains antioxidants and anti-cancer compounds. This study was designed to figure out the selective toxicity of Persian Gulf sea cucumber (*Holothuria parva*) methanolic extract on liver mitochondria isolated from animal model of hepatocellular carcinoma as part of a national project which hopes to come across novel potential anticancer candidates in Iranian Persian gulf Flora and fauna.

**Methods:** To induce hepatocarcinogenesis, rats were given diethylnitrosamine (DEN) injections (i.p., 200 mg/kg, by single dose), and then cancer promoted by 2-acetylaminofluorene (2-AAF) (0.02 w/w) for two weeks. Histopathological evaluations and levels of liver injury markers and liver cancer specific marker, alpha-fetoprotein (AFP), were determined for confirmation of hepatocellular carcinoma induction. Finally mitochondria were isolated from cancerous and non cancerous hepatocytes. In this study, cytotoxicity was measured by a complex II activity assay using MTT test, mitochondrial membrane depolarization was determined by fluorescence spectrophotometry, cytochrome c release by Sigma kit, mitochondrial swelling by spectrophotometry, mitochondrial ROS measurement by fluorescent probe DCFH.

**Results:** Our results showed that *Holothuria parva* (*H.parva*) methanolic extract (250,



500 and 1000 µg/ml) increased reactive oxygen species (ROS) formation, mitochondrial membrane potential (MMP), mitochondrial swelling , cytochrome c release and decreased complex II activity only in the mitochondria obtained from cancerous BUT NOT non-cancerous liver hepatocytes.

**Conclusion:** Our results suggest that *H.parva* may be promising therapeutic candidates for the treatment of HCC patients following further confirming in vivo experiments and clinical trials. Also, mass spectrometer showed a compound with molecular weight of 205.

**Keywords:** Hepatocellular carcinoma, *Holothuria Parva*, sea cucumber, Persian Gulf.