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Article

Biological and Proteomic Characterization of the Anti-Cancer Potency of Aqueous Extracts from Cell-Free Coelomic Fluid of *Arbacia lixula* Sea Urchin in an In Vitro Model of Human Hepatocellular Carcinoma

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Abstract: Echinoderms are an acknowledged source of bioactive compounds exerting various beneficial effects on human health. Here, we examined the potential in vitro anti-hepatocarcinoma effects of aqueous extracts of the cell-free coelomic fluid obtained from the sea urchin *Arbacia lixula* using the HepG2 cell line as a model system. This was accomplished by employing a combination of colorimetric, microscopic and flow cytometric assays to determine cell viability, cell cycle distribution, the possible onset of apoptosis, the accumulation rate of acidic vesicular organelles, mitochondrial polarization, cell redox state and cell locomotory ability. The obtained data show that exposed HepG2 cells underwent inhibition of cell viability with impairment of cell cycle progress coupled to the onset of apoptotic death, the induction of mitochondrial depolarization, the inhibition of reactive oxygen species production and acidic vesicular organelle accumulation, and the block of cell motile attitude. We also performed a proteomic analysis of the coelomic fluid extract identifying a number of proteins that are plausibly responsible for anti-cancer effects. Therefore, the anti-hepatocarcinoma potentiality of *A. lixula*'s preparation can be taken into consideration for further studies aimed at the characterization of the molecular mechanism of cytotoxicity and the development of novel prevention and/or treatment agents.

Keywords: coelomic fluid; sea urchin; echinoderm; HepG2 cells; apoptosis; cell cycle; acidic vesicular organelles; mitochondrial transmembrane potential; reactive oxygen species; wound healing assay

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1. Introduction

The marine environment, which occurs in about 70% of the globe's surface and 90% of the biosphere, is the largest habitat of the Earth. It harbors a significant fraction of the world's biodiversity with many still unknown species and represents a little exploited treasure chest rich in bioactive natural products. In fact, animal adaptation processes to the different and often extreme aquatic environments have led to the establishment of unique bio-synthetic pathways [1]. Within this context, the development of interindividual signalization systems and defensive strategies, e.g., against predators, infectious agents and UV radiations, prompted sessile aquatic species to set up networks of chemical communication through a variety of exclusive marine species-specific metabolites, which can be available for extraction and characterization as a massive library of natural active compounds [2,3].

One of the acknowledged potential applications shared among several marine natural products is related to cancer prevention and treatment. Studies performed on compounds extracted from sponges, mollusks, soft corals and tunicates demonstrated their relevant