Chrysophyllum cainito stem bark extract induces HepG2 apoptosis and cell death by ROS generation

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Cancer is a major public health problem in both developed and developing countries, worldwide. Over the past decade, medicinal plants have attracted much interest due to their diverse range of biological and therapeutic properties. Accumulating evidence has suggested that medicinal plants can be used as alternative medicines for cancer treatment. It is widely known that several current chemotherapeutic drugs for cancer treatment are molecules isolated or derived from plants. The objective of this study was to examine the possible anticancer properties of *Chrysophyllum cainito* against human hepatocarcinoma HepG2 cells. Stem bark of *Chrysophyllum cainito* was extracted with deionized water at room temperature for 8 hr (50 g in 200 ml for 4 times, 2 hr each), and then lyophilized before used. The cytotoxic effects of *Chrysophyllum cainito* stem bark extract (CE) were determined using MTT and trypan blue assays. Cell death and cell apoptosis were detected by Tali image-based cytometer, staining by propidium iodide (PI) and annexin V-Alexa Fluor 48, respectively. Reactive oxygen species (ROS) level was assessed using 2', 7'-dichlorofluorescin diacetate (DCFH) staining. CE exhibited dose-dependent cytotoxic activity against HepG2 cells with IC_{50} of 104.75 (MTT assay) and 113.24 µg/ml (trypan blue method). Morphological changes of the cells treated with CE at the concentration of 50 µg/ml or higher were observed. At the highest concentration used in this experiment (100 µg/ml), majority of HepG2 cells treated with CE became round and shrunken and could not be affixed to the cultured plate and floating in the medium (Figure 1). After 24 hr period of incubation with CE, cytometry analyses of PI and V-Alexa Fluor 48 staining revealed that CE increased cell death and apoptosis in the dose-dependent fashion. Fluorescence images using the fluorescent probe DCFH indicated that CE induced intracellular ROS generation in HepG2 cells in the concentration-dependent manner (Figure 2). The present study demonstrated that CE mediated HepG2 cell growth inhibition via induction of cell death and apoptosis at least partly through ROS generation. This is the first report to demonstrate *in vitro* anticancer activity of the stem bark extract of *Chrysophyllum cainito* in relation to liver cancer.

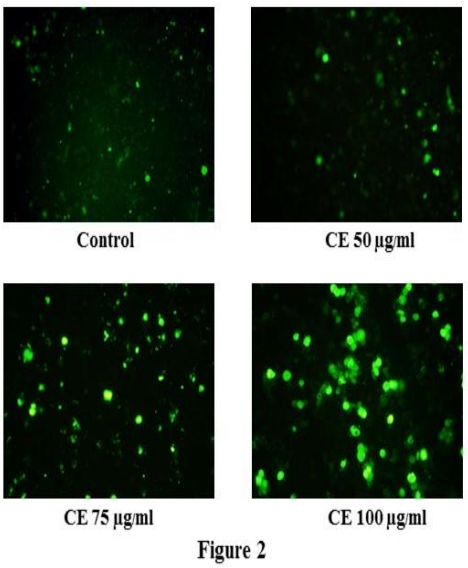

Figure 2

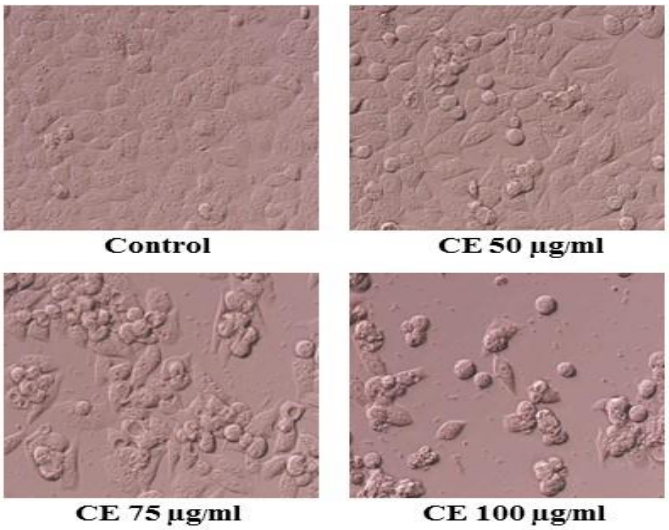

Figure 1