



**The Chinese University of Hong Kong**  
**Non-confidential Abstract of Technology Disclosure**

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**Title:**

**Development of a Small-molecule as a Cancer Drug for Management of Liver Cancer**

**CUHK Ref. No.:**

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**Inventor(s):**

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**Non-confidential abstract:**

One of the major glucosinolates that is present in seeds of a herbal medicine showed unmatched anti-cancer properties in liver cancer in rats. However, the detail of the biologic activity of these small-molecules is lacking. Our study involved investigation of their potential therapeutic benefits both in vitro in human normal liver and cancer cell lines. In vivo study with rats with liver cancers was studied after treatment of rats via oral administration of the compound for two years. In vitro treatments of HepG2, Clone 9 and WRL-68 cell lines with the compound were performed in a time-course study. Results showed that the small-molecule inhibited the growth of the cancer cell line but showed almost no toxicity to the normal cells. Cell cycle analysis demonstrated that the growth of treated HepG2 cells were inhibited by G0/G1 phase arrest mechanism, and DNA fragmentation confirmed the apoptotic event.

In vivo studies of their effects on tumor development were investigated during cancer development in Sprague Dawley (SD) rats. Hepatocellular carcinoma (HCC) in the rat was induced by diethylnitrosamine (DEN) and promoted by carbon tetrachloride (CCl<sub>4</sub>). Solid liver cancer were developed in rats after 6 months of treatment prior to treatment of rats. Health conditions of the treated group (15mg/kg; once daily), positive control group (DEN-CCl<sub>4</sub> treated) and negative control group were monitored in promotion and progression cancer stages for 6 or 12 months, respectively. At the end of studies, all rats were sacrificed. Serum AST/ALT assay and histological analysis of rat livers including liver section staining, Hemotoxylin and Eosin (H&E) staining and immunostaining of GST-pi for detection of cancer, were performed to evaluate the effects of these pure compounds on carcinogen-induced tumor in rats. Results showed that AST and ALT levels were reduced in the treated group at both promotion and progression stages. The basic hexagonal structure was restored and the immunostaining of GST-p in the liver sections showed reduction in foci after treatment. However, the GST-p positive area ratio at the progression stage of cancer development was higher than that of the promotion stage. All rats of the positive control group showed regain of normal health conditions after treatment for 6 months while tumors in the negative control group spread to lungs and other organs.



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Molecular biology studies showed that Mdm2 as well as the wild type p53 protein expression was increased in the treated rats. Bax protein level was higher and Bcl-2 protein level was lower in the treated group resulting in apoptosis of tumor cells. p21, the cell cycle check point protein, was up-regulated in the treated rats and PCNA protein level was down regulated. Consequently, the compound-mediated gene over-expression allowed a sufficient time for DNA repairing. Specific genes associated with the cell growth, mitosis and apoptosis were also studied by microarray analysis.

The present findings clearly showed that some of the small-molecules we have identified can inhibit cancer cell growth by inducing G0/G1 phase arrest and subsequently apoptosis. It has protective and therapeutic benefits to the liver in vivo. Individual compounds can reduce carcinogen-induced toxicity by activating detoxification enzyme and to suppress the cancer cell growth by activating p53-dependent apoptosis. These molecules have never been reported in any studies or used in any of the commercial products for all intents or purposes.

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