

# **Frankincense essential oil prepared from hydrodistillation of *Boswellia sacra* gum resins induces human pancreatic cancer cell death in cultures and in a xenograft murine model.**

## **BACKGROUND:**

Regardless of the availability of therapeutic options, the overall 5-year survival for patients diagnosed with pancreatic cancer remains less than 5%. Gum resins from *Boswellia* species, also known as frankincense, have been used as a major ingredient in Ayurvedic and Chinese medicine to treat a variety of health-related conditions. Both frankincense chemical extracts and essential oil prepared from *Boswellia* species gum resins exhibit anti-neoplastic activity, and have been investigated as potential anti-cancer agents. The goals of this study are to identify optimal condition for preparing frankincense essential oil that possesses potent anti-tumor activity, and to evaluate the activity in both cultured human pancreatic cancer cells and a xenograft mouse cancer model.

## **METHODS:**

*Boswellia sacra* gum resins were hydrodistilled at 78°C; and essential oil distillate fractions were collected at different durations (Fraction I at 0-2 h, Fraction II at 8-10 h, and Fraction III at 11-12 h). Hydrodistillation of the second half of gum resins was performed at 100°C; and distillate was collected at 11-12 h (Fraction IV). Chemical compositions were identified by gas chromatography-mass spectrometry (GC-MS); and total boswellic acids contents were quantified by high-performance liquid

chromatography (HPLC). Frankincense essential oil-modulated pancreatic tumor cell viability and cytotoxicity were determined by colorimetric assays. Levels of apoptotic markers, signaling molecules, and cell cycle regulators expression were characterized by Western blot analysis. A heterotopic (subcutaneous) human pancreatic cancer xenograft nude mouse model was used to evaluate anti-tumor capability of Fraction IV frankincense essential oil in vivo. Frankincense essential oil-induced tumor cytostatic and cytotoxic activities in animals were assessed by immunohistochemistry.

## **RESULTS:**

Longer duration and higher temperature hydrodistillation produced more abundant high molecular weight compounds, including boswellic acids, in frankincense essential oil fractions. Human pancreatic cancer cells were sensitive to Fractions III and IV (containing higher molecular weight compounds) treatment with suppressed cell viability and increased cell death. Essential oil activated the caspase-dependent apoptotic pathway, induced a rapid and transient activation of Akt and Erk1/2, and suppressed levels of cyclin D1 cdk4 expression in cultured pancreatic cancer cells. In addition, *Boswellia sacra* essential oil Fraction IV exhibited anti-proliferative and pro-apoptotic activities against pancreatic tumors in the heterotopic xenograft mouse model.

## **CONCLUSION:**

All fractions of frankincense essential oil from *Boswellia sacra* are capable of suppressing viability and inducing apoptosis of a panel of human pancreatic cancer cell lines. Potency of essential oil-suppressed tumor cell viability may be associated with the greater abundance of high molecular weight compounds in Fractions III and IV. Although chemical component(s) responsible for tumor cell cytotoxicity remains undefined, crude essential oil prepared from hydrodistillation of *Boswellia sacra* gum resins might be a useful alternative therapeutic agent for treating patients with pancreatic adenocarcinoma, an aggressive cancer with poor prognosis.

