

Studies on the Anticancer Effects of Thiosulfinates from *Allium tuberosum* L.

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KOSEF - 10508

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This study was aimed to elucidate anticancer effects of thiosulfinates (TS) in *Allium tuberosum* L., and to clarify the mechanism using human cancer cells.

At first two thiosulfinates, S-methyl methanthiosulfinate (MTS) and S-methyl 2-propene-1-thiosulfinate (MPTS), were isolated from *Allium tuberosum* L., and each structure was determined using Mass and NMR-spectroscopic methods. Then, their in vitro cytotoxicity against human cancer cells and in vivo antitumor activity were investigated. Their cytotoxic effect was strong in the order of (MPTS), crude TS, and (MTS). These TS induced apoptosis in MCF-7 breast cancer cells. When these TS were administered consecutively into the mice inoculated with Sacoma-180 tumor cells, for 7 days at 10, 30, and 50 mg/kg i.p., significant elongation of life span was observed.

These TS induced cell numbers decrease in a dose- and time-dependent manner in HT-29 colon cancer cells, with cell cycle arrest at the sub-G1 phase, apoptotic cell death, morphological change, internucleosomal DNA fragmentation. The apoptosis induced by TS is associated with the activation of caspase-3, 8, and 9. TS also stimulated Bid cleavage. In addition, TS decreased the expression of Bcl-2, but increased the expression of Bax and AIF, in HT-29 cells. Similar result was obtained in metastatic (DU145) and primary (RC-58T/h/SA#4) malignant tumor cells, derived from human prostate cancer. These results suggest that TS from *Allium tuberosum* L. inhibit the proliferation of human cancer cells via apoptosis, through both caspase-dependent and -independent pathways.