Grape Seed Extract Inhibits In vitro and In vivo Growth of Human Colorectal Carcinoma Cells

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Purpose: Accumulating evidences suggest the beneficial effects of fruit-and-vegetable consumption in lowering the risk of various cancers, including colorectal cancer.

Herein, we investigated the in vitro and in vivo anticancer effects and associated mechanisms of grape seed extract (GSE), a rich source of proanthocyanidins, against colorectal cancer.

Experimental Design: Effects of GSE were examined on human colorectal cancer HT29 and LoVo cells in culture for proliferation, cell cycle progression, and apoptosis. The in vivo effect of oral GSE was examined on HT29 tumor xenograft growth in athymic nude mice.

Xenografts were analyzed by immunohistochemistry for proliferation and apoptosis. The molecular changes associated with the biological effects of GSE were analyzed by Western blot analysis.

Results: GSE (25-100 μg/mL) causes a significant dose- and time-dependent inhibition of cell growth with concomitant increase in cell death. GSE induced G1 phase cell cycle arrest along with a marked increase in Cip1/p21 protein level and a decrease in G1 phase–associated cyclins and cyclin-dependent kinases.

GSE-induced cell death was apoptotic and accompanied by caspase-3 activation. GSE feeding to mice at 200 mg/kg dose showed time-dependent inhibition of tumor growth without any toxicity and accounted for 44% decrease in tumor volume per mouse after 8 weeks of treatment.

GSE inhibited cell proliferation but increased apoptotic cell death in tumors. GSE-treated tumors also showed enhanced Cip1/p21 protein levels and poly(ADP-ribose) polymerase cleavage.

Conclusions: GSE may be an effective chemopreventive agent against colorectal cancer, and that growth inhibitory and apoptotic effects of GSE against colorectal cancer could be mediated via an up-regulation of Cip1/p21.

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Ann's NOTE: This study was done in animals and in cell culture. Added June 2023 – Funding was and is a BIG ISSUE in studies of natural substances or protocols. Much of research is funded by Big Pharma and they have told us and myself that they have NO INTEREST in what they cannot patent. That's not changed in all our years doing this work. ADVOCATE for change.