Letter to the Editor

Cancer Prevention Research

Hexane Fraction of American Ginseng Suppresses Colitis and Colon Cancer—Letter

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Studies by Poudyal and colleagues (1) reported that a hexane solvent fraction of American ginseng (AG) suppressed mouse colitis and associated colon cancer in a dextran sulfate sodium mouse model, posed via anti-inflammatory and proapoptotic mechanisms. Because these authors were unaware of our carcinogenesis studies on Panax ginseng (2, 3), we thought that these findings would be useful and informative.

Ginseng is a popular herbal remedy, used in eastern Asian cultures for thousands of years. Chronic high-dose ginseng (~15 g/d and higher) was reported in 1979 to cause "ginseng abuse syndrome" (4), with stimulation, well-being, increased cognition; diarrhea, skin eruptions, sleeplessness, nervousness; yet adverse effects from ginseng commercial products with recommended dosages (~500 mg ginsenosides/capsule) are less prominent and scientifically based (5). However, because chronic effects were not well characterized, because of significant human exposures, and because information on toxicity was unavailable, Panax ginseng was studied for toxic and carcinogenic potential by U.S. National Toxicology Program (2, 3).

Male and female F344/N rats and B6C3F1 mice received extracts of ginseng root by gavage for 2 weeks (short-term toxicity), 3 months (longer term toxicity and dose finding), or 2 years (toxicity and carcinogenicity). Genetic toxicology studies were conducted in *Salmonella typhimurium*, *Escherichia coli*, and mouse peripheral blood erythrocytes, whereas 3-month reproductive toxicity was assessed in rats and mice.

Ginseng was not mutagenic in 2 independent bacterial mutagenicity assays, with or without exogenous metabolic activation. Strains included *S. typhimurium* TA97, TA98, TA100, TA102, TA104, TA1535, and *E. coli* strain WP2uvrA/pKM101. No significant increases in micronucleated erythrocytes in peripheral blood of B6C3F1 mice exposed for 3 months to 1,000 to 5,000 mg/kg ginseng via gavage. Also, on the basis of sperm motility, vaginal cytology, reproductive organ weights, histopathology of 3-month study animals, no ginseng toxicity to reproductive systems was observed in rats or mice.

In 16- and 90-day studies, no chemical-related gross or microscopic findings were attributed to ginseng. For 2-year bioassays, groups of 50 male and 50 female rats and mice received ginseng in sterile water by gavage at 0; 1,250; 2,500; or 5,000 mg/kg body weight, 5 d/wk. Body weights and survivals were comparable among groups. Gross and microscopic histopathology on approximately 40 tissues/organs revealed no nonneoplastic or neoplastic lesions in any sex species group attributable to ginseng. A single finding considered related to ginseng was a decrease in mammary gland fibroadenomas in 5,000 mg/kg female rats (32 of 50 vs. 30 of 50, 30 of 50, 16 of 50; $P < 0.01$). Accordingly, under our long-term experimental conditions, Panax ginseng was considered non-genotoxic, -toxic, and -carcinogenic.

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