

Chemoprevention of azoxymethane/dextran sodium sulfate-induced colon carcinogenesis in mice by yams and its constituent diosgenin

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Colorectal cancer is one of the most common cancers worldwide and prevalent causes of morbidity and mortality. Epidemiological studies have shown that Western-style diet (high in fat and calories and low in fiber and complex carbohydrates) is associated with an increase risk of colorectal cancer, indicating that diet would be the most important exogenous life-style related factor in the etiology of colorectal cancer. It has been estimated that 70% of colorectal cancers could be prevented by nutritional intervention. Moreover recent studies have shown that obesity and related metabolic abnormalities, including hyperglycemia and hyperlipidemia, are associated with an increase risk of colorectal cancer. Yams (*dioscorea*) are perennial trailing rhizome plants of the *Dioscorea* genus (belong to the Dioscoraceae family). The tuber of yam is rich in many nutrients and is consumed as a food in Africa, Asia, Latin America and Oceania. Diosgenin is an aglycone of the steroidal saponin, dioscin, which is present at relatively high concentrations in the tuber of yams and seed of fenugreek. The health benefits of diosgenin have so far been shown in preclinical studies and include its efficacy against hyperglycemia, and hyperlipidemia. It is also reported that diosgenin showed anti-inflammatory and anti-proliferative activities in various cancer cell lines.

In this study, we investigated the effects of diosgenin and several species of freeze-dried yams on the colon carcinogenesis initiated with a single i.p. injection of azoxymethane (AOM; 10 mg/kg bw) and promoted by administration of 1.5% dextran sodium sulfate (DSS) in drinking water for 7 days in male ICR mice. Diosgenin, sanyaku (a traditional chinese medicine, freeze-dried Chinese yam), freeze-dried samples of yamato-imo (Yamato yam), naga-imo (Long yam) and jinenjo (Japanese yam) were given in the diet (20, 100 or 500 mg/kg) to AOM/DSS-treated mice for 17 weeks. Pathological examinations showed that diosgenin and sanyaku significantly suppressed the AOM/DSS-induced colon cancer at all doses, but other yams were less effective. GC-MS analyses revealed that diosgenin was contained in sanyaku (0.0064% wt/wt) but not in other yams. These results suggest that diosgenin may be a possible chemopreventive agent present in yam. Microarray and quantitative RT-PCR analyses revealed that diosgenin administration altered expressions of hepatic genes associated with lipid metabolism. In particular the expression of lipoprotein lipase was 12-fold increased by diosgenin and could contribute to lowering the serum triglyceride levels. Our results imply that diosgenin and “sanyaku” could be used as a potent chemopreventive agent against colon carcinogenesis in humans.