

4th International Conference and Exhibition on **Nutrition**

October 26-28, 2015 Chicago, Illinois, USA



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Chemoprevention of gastrointestinal tract cancers with berries

Our laboratories have examined the ability of freeze-dried berries to prevent G.I. tract cancers in animals and humans. Most studies have used black raspberries (BRBs), due to their high antioxidant potential and their high content of anthocyanins and fiber. In rodent studies, the consumption of BRB powder, at concentrations of 2.5, 5 and 10% (w/w) of a synthetic diet, results in a 40-70% inhibition of carcinogen-induced cancer in the rat esophagus and colon and the spontaneous development of intestinal tumors in mice. Mechanistically, BRBs inhibit cell proliferation, inflammation and angiogenesis and stimulate apoptosis and differentiation. They protectively modulate genes in multiple signaling pathways such as P13K/Akt, p38/Erk1/2, NFAT, mTor, NF- κ B, COX-2, iNOS, VEGF and caspase 3/7. The most active inhibitory constituents in BRBs are the anthocyanins and fiber. The anthocyanins are metabolized in the bowel to the phenolic compound, protocatechuic acid (PCA), which appears to have significant promise as a chemopreventive agent. Based upon preclinical observations, we conducted a series of pilot clinical trials of BRBs. A Phase I trial showed that BRBs are well tolerated in normal individuals when consumed orally at doses equivalent to those that elicit chemopreventive effects in rodents. The oral administration of BRB powder (45g/day) to 20 patients with Barrett's esophagus for 6 months led to a reduction in parameters of oxidative stress, but minimal effects on the lesion itself. Oral administration of strawberry powder (60g/day) to 37 Chinese patients with esophageal dysplasia led to histologic regression of ~80% of mildly dysplastic lesions and reduced levels of iNOS, COX-2, and phospho-NF- κ B-p65 proteins in the lesions. Treatment of 20 colorectal cancer patients with BRB powder for an average of 3 weeks led to a significant reduction in cell proliferation and demethylation of suppressor genes in the WNT signaling pathway in colorectal tumors. BRBs reduced DNA methylation, in part, by inhibiting DNA methyl transferases 1 and 3. Finally, a trial in 14 patients with familial adenomatous polyposis showed that daily treatment with rectal suppositories made from BRBs for 9 months caused a 36% regression of rectal polyps. In this same cohort, celecoxib produced a 28% regression of rectal polyps. These preliminary trials indicate that berries have significant promise for chemoprevention of esophageal and colon cancer in humans.

Biography

Stoner is Professor of Medicine at the Medical College of Wisconsin (MCW) Division of Hematology and Oncology, specializing in the fields of chemical carcinogenesis and cancer chemoprevention. He serves as Director of the Molecular Carcinogenesis and Chemoprevention Program in the newly developing Cancer Center. Stoner joined MCW after nearly 20 years at the Ohio State University College of Medicine where he held the positions of Lucius Wing Endowed Chair in Cancer Research and Therapy, Associate Director for Basic Research and Director of the Chemoprevention Program in the Cancer Center, and Chair of the Division of Environmental Health Sciences and Associate Dean for Research in the College of Public Health.

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