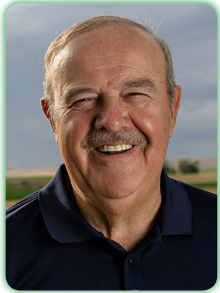


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The Ohio State University, USA

Black raspberries in cancer clinical trials: Past, present and future

Black raspberries (BRB) inhibit a broad range of cancers in preclinical models, including animal models of oral, esophageal, colon, breast and skin cancer. Promising preclinical results have led to clinical evaluations in cancer patients or in patients at increased risk for cancer development. The initial clinical study in humans was a phase I trial in which BRBs were administered to humans at a dose known to be chemopreventive in animal models. The berries were found to be well tolerated however; the uptake of both BRB anthocyanins and ellagic acid into blood was less than 1% of the administered dose. Thus, berries are most effective in tissues where localized absorption is possible. With this in mind, different formulations of BRBS have been evaluated for their effects on preneoplastic lesions or cancers of the human oral cavity, esophagus and colon.

Oral cavity: Topical application of a BRB gel to dysplastic lesions (oral leukoplakia) caused histologic regression that was associated with improved histologic grade and significantly reduced loss of heterozygosity at tumor suppressor gene loci, as well as modulation of genes linked to RNA processing and growth factor recycling.

Esophagus: In patients with Barrett's esophagus, oral consumption of BRBs increased tissue levels of *GST-P1* and decreased urinary 8-isoprostane, a marker of lipid peroxidation and oxidative stress. There was little effect on lesion size.

Colon: In colorectal cancer patients, BRB consumption inhibited cancer cell proliferation, angiogenesis (new blood vessel formation) and caused demethylation of tumor suppressor genes associated with the Wnt signaling pathway. In FAP patients, BRB suppositories inhibited rectal polyp progression and improved plasma cytokine profiles.

Stomach: Because we have found recently that an extract of BRBS inhibits the growth of *Helicobacter pylori*, there is an ongoing trial to evaluate the effects of BRBS on stomach cancer. Common themes across studies support that berries are anti-proliferative, anti-inflammatory reduce oxidative stress and restore tumor suppressive activity.

Biography

Gary Stoner, PhD., is Professor Emeritus in the College of Medicine, Ohio State University. His areas of expertise are chemical carcinogenesis and cancer chemoprevention. His early research was focused on lung cancer and tobacco carcinogenesis. Later he investigated the cancer preventative effects of naturally-occurring isothiocyanates and found them to be potent inhibitors of N-nitrosamine carcinogenesis. He then pioneered a "food-based" approach to cancer prevention using freeze-dried black raspberries. The berries significantly reduce tumorigenesis in the oral cavity, esophagus and colon of rodents and regress premalignant lesions in these same tissues in humans. His laboratory identified multiple mechanisms of cancer prevention by berries. His research is documented in more than 350 peer reviewed publications. He has received numerous awards for his research including the US NIH Merit Award and he is a member of the American Association for the Advancement of Science. He is also a recipient of the Distinguished Alumni Award and an Honorary Doctorate from Montana State University.

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