

A Nutraceutical Approach to Cancer Prevention and Treatment

Catégorie : Traitement alternatif du cancer

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The relationship *between diet and disease* There is no question the link between diet and the incidence of disease, particularly cancer, has been established. Observational and cohort studies have clearly revealed this. Recently, for the first time, a study by Newark et al(1) designed a diet to mimic the Western diet (reduced calcium, Vit. D, folic acid, methionine and B12, as well as increased fat), which induced colonic tumours in normal mice without using any chemical carcinogens. Knowing that nutrients play such an important role in cancer development, the question researchers are investigating is, what role or effect can nutrients play in cancer prevention and/or treatment? This discussion will review some of the familiar micronutrients as well as a few less familiar compounds and their suggested mechanisms of action in cancer prevention and how they can be applied in treatment. **FOLIC ACID** Folic acid has been proven to reduce the risk of neural tube defects and cardiovascular disease, and now more recently it has been shown to have a role in reducing the risk of colon cancer.(2, 3) The Nurses Health Study(3) results indicated a 75% decrease in risk for women using a multivitamin with folic acids levels greater than 400 mcg, with the greatest effect occurring after 15 years of use. Using multivariate models it was determined that folic acid intake was the principal nutrient associated with risk reduction, and, inversely, studies have shown a higher risk for colon cancer among people with low folic acid intake.(4) Interestingly, the association between folic acid and colon cancer was strongest with supplemental folate vs. dietary folate. This may be due to the high bioavailability of supplemental folate. The mechanism of how folic acid reduces carcinogenesis is still not elucidated, however its role may lay in the methylation of DNA. Hypomethylation of DNA is one of the key events in colon carcinogenesis. An easy way to incorporate the protective effect of folic acid is to utilize a daily multivitamin with greater than 400 mcg as a lifelong preventive strategy. Although the study did try to account for any other variables, it also did address the idea that the combination of nutrients in a multivitamin may contribute to decreased risk, so it would seem prudent to incorporate the same thinking and use a multivitamin as the preferred source of folic acid. **CALCIUM** Calcium has been shown to be a promising chemo preventive agent in colon cancer. A recent large cohort study evaluated the link between calcium intake and colorectal cancer.(5) An inverse relationship was seen with calcium from supplementation and the incidence of colorectal cancer. These results were consistent with two intervention trials, which showed that calcium supplementation of 1200 mg daily was associated with lower incidence of recurrence of adenomatous polyps, the precursor to colon cancer. It was interesting to note the risk reduction was not seen with dietary sources of calcium. Follow-up studies showed that reduced risk may occur at lower intakes (700-1000mg/day). It has been hypothesized that the mechanism by which calcium reduces the risk of colon cancer is by binding secondary bile acids and ionized fatty acids, forming insoluble soaps, reducing their proliferative stimulus on colonic mucosa.(5) Another mechanism may be through the activation of calcium-sensing receptors, which through a range of biological effects decreases growth and promotes the differentiation of transformed colon cells.(6) **TEA EXTRACTS** It has been reported that green tea lowers the risk of many cancers including gastric, pancreatic, and colorectal. This has been attributed to the catechins, particularly (-) epigallocatechin-3-gallate (EGCG). In vitro studies have demonstrated

EGCG can inhibit the growth of human mammary, lung, prostate and colon cancer cells. More recently, Ahn et al. found EGCG possessed inhibitory growth properties in the human papilloma virus 161, associated with cervical carcinoma. In vivo anti-tumour effects were observed when mice were ingesting 35 μ M of EGCG. The mechanism appeared to be mediated by apoptosis and cell cycle arrests and regulation of gene expression. Further studies by Ahn et al. (7) involved patients with atypical squamous cervical lesions (low grade to high grade) who were treated with EGCG in capsule form. The results from this study were exciting in that 35 of the 51 patients using green tea extract showed a positive response compared to the control group where only four of the 39 did. Considering that epidemiological review indicates the development of invasive cervical cancer from intraepithelial neoplasm may take 10 to 15 years, there is an excellent window of time for intervention. The use of green tea may reduce or delay the progression from pre-cancerous lesions to full blown cervical cancer. Another interesting study showed that a constituent in black tea (theaflavin) may play an important role in reducing the conversion of testosterone to DHT via inhibition of the 5 alpha-reductase enzyme. This study found that soy phytochemicals and tea extract synergistically prevented the progression of prostate androgen-sensitive tumours in vivo.(8) Tea extracts may not only prove to be a viable chemo preventive strategy but may also be a potential treatment approach to specific cancers.(7,9)

I3C AND DIM One of the most exciting areas of chemo prevention and possibly treatment involves indole-3-carbinol (I3C) and one of its polymeric products, 3, 3'-diindolylemethane (DIM). Both I3C and DIM come from cruciferous vegetables containing glucobrassicin. (10, 11), showing apoptic effects in human breast and prostate cancer cell lines in vitro. Chen et al showed similar effects in both cervical and endometrial cancer cells. Several studies support the results that I3C and DIM cause growth arrest, increased apoptosis, and decrease the effects of estrogen. Estrogen inhibits apoptosis in breast cancer cells whereas BC and DIM have been shown to induce apoptosis of breast cancer cells in vitro. How I3C and DIM diminish the effects of estrogen on tumour is as suggested: ->I3C and DIM induce enzymes that encourage the conversion of estrone to 2-hydroxyestrone leading to metabolites that are antiproliferative and proapoptotic. ->I3C and DIM up-regulate the tumour suppressor breast cancer 1 gene.(12) It is important to note that some of I3C is converted to DIM in low acidic environments; however, both I3C and DIM appear to have distinct but overlapping effects on the transcription of cell cycle genes in breast cancer. When exposed to breast cancer cells, DIM and I3C induced G1 cell cycle arrest with both estrogen-responsive and non-responsive cells. It was also demonstrated that the combination of tamoxifen and I3C in estrogen-responsive breast cancer cells induced G1 cell cycle arrest more effectively than when treated with either alone.(13)

RESVERATROL Resveratrol has gained attention as the antioxidant in red wine. It has been demonstrated to be an effective scavenger of free radicals and to protect cell membranes from lipid peroxidation. It has also been reported to protect against DNA damage caused by reactive oxygen species (ROS).(14, 15) Its role in chemoprevention may come from its ability to induce specific enzymes that metabolize carcinogenic substances. Scarlattie et al. (16) showed resveratrol can induce growth inhibition and apoptosis in invasive metastatic breast cancer cell line by activating the de novo ceramide synthesis. Current anti-tumour drug therapy focuses on interrupting cell cycles. Resveratrol inhibits cellular events of tumour initiation, promotion, and progression via its anti-cyclooxygenase activity (cox-1).(17) The hypothesized mechanism of action includes inhibition of cytochrome P450 enzymes, antioxidant, anti-inflammatory, cell cycle effects and cell proliferation and apoptosis.(18) In vitro range of biological activity for resveratrol is 5-50 μ M. Wine has 3-20 μ M (.65mg/L-5mg/L). The exciting research with resveratrol is in the treatment of lung carcinoma in vitro where it is reported to inhibit the growth of cancerous cells.(19) The challenge is to demonstrate these effects with in vivo studies and determine a manageable dose that does not necessitate the over-indulgence of wine. Supplementation may prove to be the more practical option. The ability to affect gene expression is exciting and will need to be explored further. It is encouraging that studies,

at least in vitro, show nutrients not only play an important role in cancer prevention but may have a profound effect in treatment. In summary, recommending the use of a comprehensive multivitamin, a calcium supplement, drinking green tea or supplementing with tea extracts, and resveratrol are safe preventative strategies. Anyone with hormonal issues placing them at risk should seriously consider using I3C and DIM as a preventative strategy, or those diagnosed with hormone-sensitive cancers may want to use I3C and DIM to enhance treatment. Regarding treatment for a diagnosed cancer, a patient should discuss complementary strategies with their health-care provider. Some nutraceuticals may be contraindicated with certain forms of chemotherapy (i.e., Folic acid with chemo drug 5-FU) and other treatments such as radiation may rely on the production of reactive oxygen species with which powerful antioxidants could interfere. Most nutraceuticals, however, are safe and their use may be encouraged to not only ease symptoms but enhance treatment. Of course, there are many other nutrients to consider such as vitamin C and Quercetin. We have focused here on a few common and not so common nutrients that are backed by recent exciting research. Note: To view the full list of references accompanying this article, please go to our web site : www.canadianchiropractor.ca