

Anti-Inflammatory Herb Combination: A Promising Strategy for Preventing Colon and Other Cancer

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Evidence suggests that 70 percent to 90 percent of colon cancer cases are caused by faulty nutrition and other factors associated with lifestyle. Colon cancer continues to be the second leading cause of cancer death in North America, with about 140,000 new cases diagnosed each year in the United States. Despite recent advances in medicine, mortality remains unacceptably high. It is noteworthy, however, that periodic colonoscopy assessment after age 50 (or earlier in individuals with a strong family history) is associated with a 15 percent to 33 percent reduction in risk of colon cancer death. Thus, early detection of colon cancer via colonoscopy screening in high-risk individuals and those over 50 years of age is a prudent primary prevention step.

With respect to preventing colon cancer development, dietary modifications linked to reduced colon cancer incidence include consuming a low-animal-fat diet with minimum intake of trans and hydrogenated fats; consuming more fiber, fruits and vegetables, especially cruciferous vegetables, as well as allium-containing foods (garlic and onions) and omega-3 fats; minimizing alcohol consumption; and attaining optimal levels of folic acid, calcium, vitamin D, selenium, antioxidants and several other micronutrients. It also is best to minimize intake of barbequed foods (charring of such foods results in the formation of highly carcinogenic chemical compounds), and sodium nitrite, which is found in many processed foods.

Cell Membrane Receptors and Cancer

In recent years, cancer researchers have discovered that an important part of the puzzle in colon cancer development involves the expression of certain cell membrane receptors and their stimulation by various chemical agents (ligands). Stimulation of various cell membrane receptors by specific ligands produces profound effects on cellular proliferation, cell growth, cell differentiation and apoptosis (programmed cell death). As an example, the binding of vitamin D to the vitamin D receptor on the cell membrane triggers a series of reactions (known as signal transduction) that ultimately promotes the induction of intracellular messengers, which slows the rate of cell division and promotes cell maturation; two outcomes linked to the reduction of cancer development.

On the other hand, the over-expression of epidermal growth factor receptors (EGFR) and other members of the tyrosine kinase family frequently are indicated in epithelial cancers, including colon cancer. The epidermal growth factor (EGF) family of receptor tyrosine kinases consists of four receptors: EGF-R (ErbB1), ErbB2 (Neu), ErbB3, and ErbB4.

In response to these discoveries, pharmaceutical companies have produced a number of drugs that inhibit the activation of specific receptors of the EGFR series (EGFR inhibitor drugs). However, in general, these drugs have had limited success because cancer cells usually possess more than one type of EGFR receptor. As such, researchers conclude that what is needed to help prevent colon cancer, as well as to help treat colon cancer, is a broad-spectrum EGFR receptor inhibitor that

inhibits signal transduction for all EGFR cell membrane receptors (pan-erb signal transduction inhibitors). To this end, there is a naturally-occurring pan-erb signal transduction inhibitor that is showing promise in experimental and animal studies; it is known as EGFR Related Protein. This protein occurs naturally, meaning its use as a targeted therapeutic agent is unlikely to produce toxic side effects.

Curcumin: A Natural Pan-erb Signal Transduction Inhibitor

With respect to natural medicine, it is well documented that curcumin, the active ingredient in the spice turmeric, also acts as a powerful inhibitor of EGFR receptors. Experimental studies, animal studies and a recent phase I clinical trial, have shown that curcumin inhibits the growth of colon cancer cells and reduces tumor incidence in high-risk human subjects. Curcumin inhibits the EGFR receptor, which in turn inhibits the propagation of metabolic reactions (e.g., decreased synthesis of the tumor promoting messenger NF-kB), leading to inhibition of cell replication of cancer cells and preneoplastic cells.

Curcumin also exerts anti-inflammatory effects on cells by inhibiting synthesis of pro-inflammatory prostaglandins. Inhibiting pro-inflammatory prostaglandins also has been shown to reduce the risk of colon cancer, as demonstrated by studies linking the effects of aspirin and other nonsteroidal anti-inflammatory drugs to reduced incidence of the disease. However, unlike aspirin, curcumin does not cause gastrointestinal erosion leading to ulceration and bleeding disorders. As such, daily supplementation with curcumin may be viewed as part of a chemoprevention strategy to help reduce risk of colon cancer development.

Prostaglandin series-2 and its metabolites have been shown to contribute to the cancer processes through one or more of several mechanisms, including increased proliferation, apoptosis, enhanced carcinogen metabolism or modulation of the immune system. Along with curcumin, other anti-inflammatory herbs that block the activity of cyclooxygenase and/or lipoxygenase (6- and/or 12-lipoxygenase), inhibiting synthesis of prostaglandin series-2 and its metabolites (related eicosanoids of the PG-2 series) have shown promise as agents to reduce risk of cancer, including colon cancer. In my view, the most important herbs in this regard include white willow extract, ginger and boswellia.

Many holistic health practitioners have recognized the value of these herbs as nontoxic, anti-inflammatory supplements that are useful in the management of inflammatory musculoskeletal conditions (e.g., arthritis, tendonitis, fascitis, bursitis). However, similar to curcumin, each of these herbs also demonstrates anti-cancer properties.

The main ingredients in ginger that have an anti-inflammatory effect, in addition to anti-tumor and antiproliferative properties against tumor cells, are 6-gingerol and 6-paradol, which are found in the oleoresin fraction in ginger. Other constituents of ginger, 8-paradol and 8-shogaol, demonstrate a significant inhibitory effect on the cyclooxygenase enzyme system, which in turn reduces the synthesis of prostaglandin series-2 metabolites. As such, ginger supplements should be standardized to contain 5 percent gingerols.

Gummy exudates of the herb boswellia traditionally have been used as anti-arthritic and anti-cancer medications. Boswellic acid and its acetates, when isolated from these gummy exudates, were found to be inhibitors of topoisomerases and to be non-redox, noncompetitive specific inhibitors of 5-lipoxygenase (5-LOX). All of these properties are key factors in preventing and controlling cancer. Experimental evidence has shown that boswellic acid acetates isolated from *Boswellia carterri Birdw* inhibit cell growth and induce apoptosis (programmed cell death) in prostate cancer cells by inhibition of 5-lipoxygenase. Other studies have shown that boswellic

constituents exhibited potent cytotoxic activities against three types of human neuroblastoma cells.

White willow bark contains salicin. The role of salicylates in inflammation and pain management is well documented in medicine. Salicin is a potent inhibitor of cyclooxygenase and thus reduces synthesis of prostaglandin series-2 and its metabolites. Ingestion of acetylsalicylic acid (aspirin) is highly associated with reduced risk of colon cancer in human epidemiological studies. However, unlike aspirin, salicylic acid from white willow bark does not cause intestinal erosion or bleeding and does not impair platelet coagulation to an appreciable degree. As such, white willow bark extract has a much higher safety profile than synthetic aspirin. To be effective, white willow bark extract should be standardized to contain 15 percent salicin.

Summary

A strong body of evidence indicates that an important aspect of cancer prevention involves containment of prostaglandin series-2 synthesis and inhibition of cell membrane receptors associated with the receptor tyrosine kinase family (EGFR, ErB-2, ErB-3 and ErB-4). Curcumin, derived from the spice turmeric, has shown significant anti-tumor properties against colon cancer. Curcumin has been shown to inhibit the receptor tyrosine kinase family and decreases synthesis of prostaglandin series-2.

The anti-inflammatory herbs ginger, boswellia and white willow bark extract also have been shown to inhibit prostaglandin series-2 synthesis, as well as other pro-inflammatory mediators; and experimental evidence suggests their active constituents possess important anti-tumor properties. As such, health practitioners may wish to encourage their patients to ingest an herbal combination supplement product each day containing curcumin, ginger, white willow bark extract and boswellia, as an additional part of a wellness and cancer prevention program. Such supplementation may have important applications, especially in regards to colon cancer, the second leading cause of cancer death.

A suggested combination formula would include taking two capsules per day of the following supplement, to derive sufficient dosages of the active ingredients in these herbs for chemoprevention purposes. Slightly higher dosages would be required to manage moderate to severe inflammatory conditions. I now take this combination myself as part of my cancer prevention campaign.

Curcumin	200 mg
Boswellia (standardized to 70 percent boswellic acids)	200 mg
White willow extract (std to 15 percent salicin content)	33 mg
Ginger root extract (std to 5 percent gingerols content)	50 mg

Resources

1. Reddy S, Rishi AK, Xu H, et al. Mechanisms of curcumin-and EGF-receptor related protein (ERRP)- dependent growth inhibition on colon cancer cells. *Am J Clin Nutr* 2006;55(2):185-194.
2. Ciardiello F, Caputo R, Bianco R. Antitumor effect and potentiation of cytotoxic drugs activity in human cancer cells by ZD-1839 (Iressa), an epidermal growth factor Receptor-selective tyrosine kinase inhibitor. *Clinical Cancer Research*, May 2000;6:2053-2063.
3. Ciardiello F and Tortora G. Interactions between the epidermal growth factor receptor and type I protein kinase A: biological significance and therapeutic implications. *Clinical Cancer Research* 1998;4:821-828.

4. Al-Achi. "Anti-Inflammatory Herbs." *U.S. Pharmacist* online ([url=http://www.uspharmacist.com]http://www.uspharmacist.com[url]); posted March 15, 2004.
5. McCarty M.F. Targeting multiple signaling pathways as a strategy for managing prostate cancer: multifocal signal modulation therapy. *Integrative Cancer Therapies* 2004;3(4):349-380.
6. Wells A. EGF receptor. *Int J Biochem Cell Biol* 1999;31:637-643.

JANUARY 2007