Dynamic Chiropractic

Reducing Cancer Risk With Cruciferous Vegetables and Indole

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There is a growing awareness among health practitioners and the general public about the importance of nutrition and supplementation in the prevention of cancer and other degenerative diseases.

A great deal of this attention has focused on various protective nutrients such as antioxidants, flavonoids, soy isoflavones and dietary fiber. Indole-3-carbinol, found exclusively in cruciferous vegetables and in various supplements, is one of the more underappreciated bioactive agents strongly associated with reducing risk of many common cancers. This important biological agent is known to speed up the detoxification of many potentially harmful chemicals (including carcinogens), provide antioxidant support, block the overproduction of certain hormones linked to increased risk of breast and prostate cancer, and act as a phytoestrogen (plant-based estrogen), which can bind to estrogen receptors on reproductive tissue and exert potent anti-cancer influences.

As such, indole-3-carbinol has been shown to be one of the major anti-cancer substances found in cruciferous vegetables. Frequent consumption of these vegetables (broccoli, bok choy, brussels sprouts, cauliflower, cabbage, and kale) is associated with a reduced risk of cancer in many human epidemiological studies and in animal experiments.[1-8] Indole-3-carbinol is a member of the class of sulfur-containing chemicals called glucosinolates (previously called thioglucosides).[9] It is formed from parent compounds whenever cruciferous vegetables are crushed or cooked.[10,11] Indole-3-carbinol and other glucosinolates (e.g., other indoles and isothiocyanates such as sulforphane) are antioxidants and potent stimulators of Phase I and Phase II detoxification enzymes in the liver and intestinal epithelial cells.[12-14]

Detoxification Support

The liver and epithelial cells of the intestinal tract contain the major detoxification centers of the body, referred to as Phase I and Phase II detoxification. Almost two quarts of blood pass through the liver every minute of our lives. Among other functions, liver cells are capable of detoxifying a large number of end products of metabolism, drugs, xenbiotics, hormones and other compounds, including certain carcinogens. The Phase I and Phase II detoxification processes are vital aspects of preventing the accumulation of toxins in the body and neutralizing and eliminating various cancer-causing agents and procarcinogens.

The Phase I detoxification enzymes can directly neutralize some dangerous chemicals, but they primarily convert most compounds into intermediate end products that must be further acted upon by the Phase II enzyme system. In fact, many of the intermediates that are formed by Phase I detoxification are more dangerous than the original compound. Many of these intermediates are free radicals that cause DNA mutations and other damage, and can deplete the liver of its glutathione stores, if sufficient nutritional support for glutathione synthesis is not available.

Phase II detoxification enzymes conjugate the intermediate end products with various amino acids and other chemicals to neutralize them and make them easier for the body to eliminate (e.g., attaching sulfur makes many compounds more water-soluble and easier to eliminate in the urine). Indole-3-carbinol is one of the very few exogenous agents that can speed up Phase I and Phase II detoxification in the liver and the intestinal epithelial cells. It has even been shown to improve the function of Phase II glutathione-S-transferase detoxification activity, which is an extremely important pathway in the elimination of many dangerous chemicals. Many researchers indicate the ability of cruciferous vegetables to stimulate Phase I and Phase II detoxification, especially their indole-3-carbinol content, is a primary factor in reducing cancer risk in humans.

Animal studies have repeatedly shown that when animals are exposed to or injected with carcinogens, the animals receiving the cruciferous vegetables or the indole-3-carbinol in their food supply have a significantly lower tumor yield and incidence than the animals fed the same diet, but without cruciferous vegetables or indole-3-carbinol fortification.[15-17]

Phytoestrogen Support

Indole-3-carbinol also acts as a phytoestrogen (plant-based estrogen) and can bind to estrogen receptors in the body. It reduces the ability of stronger estrogens to overstimulate reproductive tissues in women and the prostate gland in men. Researchers recently discovered that breast cells, for instance, contain alpha- and beta-estrogen receptors. The body's estrogens (estradiol, estrone and estriol), estrogen-replacement therapy and the estrogen in oral contraceptives primarily stimulate the alpha receptors, which encourage breast cells (and estrogen-dependent breast cancer cells) to rapidly divide and proliferate. As breast cells divide more rapidly, they are more inclined to make genetic mistakes and allow cancerous mutations to express themselves. This is how high exposure to estrogen, hormone-replacement therapy and oral contraceptives are linked to the increased risk of breast cancer.

Conversely, phytoestrogens primarily stimulate the beta receptors on breast cells, which encourage slower, more controlled cell division. This is associated with a reduced risk of breast cancer. Phytoestrogens also bind to alpha receptors, but have only 1/1,000 to 1/10,000 the effect of estradiol and thus compete for binding on these receptors with other more powerful estrogens. In this way phytoestrogens also are capable of toning down the influence of more powerful estrogens on various reproductive tissues. This also helps prevent hyperproliferation of breast cells. Epidemiological studies consistently show a higher ingestion of indole-3-carbinol foods is associated with the prevention of reproductive-organ cancers.[3,4,8]

Indole-3-carbinol also promotes the metabolism of certain endogenous estrogens (estrone) into a safer, less cancer-promoting form (2-OH-estrone), further helping to reduce risk of reproductive organ cancers. Some women naturally convert more of their estrone hormone to 16-hydroxyestrone, which is a biomarker for increased risk of breast cancer. Supplementation with indole-3-carbinol alters genetic expression in such a way as to encourage greater activity of the enzyme that converts estrone into 2-hydroxyestrone, which is protective against breast cancer. Thus, all women may benefit from the intake of indole-3-carbinol helps to improve the 2-hydroxy to 16-hydroxyestrone ratio. This may be important in men from the standpoint of preventing prostate cancer.[18-20] Human studies have used a dose of 300-400 mg per day to demonstrate a significant change in the 2-hydroxy to 16-hydroxyestrone ratio, but a lower dosage may still be effective.[33]

Prevention of Female Reproductive Cancers. In experimental animal testing, indole-3-carbinol and brussels sprouts, respectively, have demonstrated an ability to reduce mammary cancer incidence

in animals exposed to carcinogens known to promote cancer.[21,22] Studies indicate that 16-alpha-hydroxyestrone is associated with an increased risk of breast cancer in humans and conversely, 2-hydroxyestrone is associated with a reduction in breast cancer risk.

Thus, indole-3-carbinol influences the body's enzyme systems to favorably influence the 2-hydroxyestrone to 16-alpha-hydroxyestrone ratio.[20-24] A large prospective study involving 5,000 Italian women and a second study of patients with either benign or malignant breast lesions highlighted the ability of a higher 2/16 hydroxy- estrone ratio to predict which women were less prone to breast cancer development.[33]

Epidemiological studies and experimental evidence strongly suggest indole-3-carbinol may reduce breast cancer risk through the above-cited mechanisms.[25-28] To date, however, there have been no human intervention trials that have tested indole-3-carbinol as a preventive or therapeutic agent against breast cancer.

In a 12-week double-blind study, eight of 17 patients with early-stage cervical cancer who were given 200 or 400 mg of indole-3-carbinol per day experienced a complete reversal of their condition.[29] Various animal studies also have shown that indole-3-carbinols can help prevent cervical cancer in the presence of various carcinogens.[30,31]

Respiratory Tract Papillomas. In a small trial, indole-3-carbinol supplementation either reduced or halted the formation of precancerous lesions (papillomas) in two-thirds of patients (12 of 18) with recurrent lesions in the respiratory tract.[32]

Prostate Cancer. In animal studies, the ingestion of indole-3-carbinol has been shown to inhibit the growth of PC-3-type human prostate cancer cells by arresting their cell-division cycle and by promoting apoptosis (programmed cell death).[8] A study of men living in Seattle indicated those eating three or more servings per week of cruciferous vegetables had a risk of prostate cancer that was 50 percent lower than those consuming fewer servings, after controlling for confounding variables.[33] To date, no human intervention trials have tested indole-3-carbinol as a preventive or therapeutic agent against prostate cancer.

Adverse Side Effects and Toxicity

At doses of 800 mg per day, indole-3-carbinol has caused dizziness and unsteady gait (signs of nervous system toxicity) in humans and in animal studies. Indole-3-carbinol also is a powerful stimulator of Phase I detoxification enzymes and, as such, may speed up the detoxification of certain medications, changing their required dosage. However, one challenge study revealed that indole-3-carbinol intake did not interfere with oral contraceptive medications.[33] Health practitioners and patients should still monitor their response to indole-3-carbinol supplementation, if taken at therapeutic doses concurrently with other drugs. According to animal studies, this appears to be especially true in regards to the following medications:[33]

- Testosterone replacement therapy
- Oral contraceptives
- Hormone replacement therapy
- Anti-seizure medications
- Immune-suppressant and antiviral drugs
- Digoxin

Drug-Nutrient Interactions

Antacids/Heartburn Medications (H-2 antagonist drugs). By reducing stomach acidity, these drugs reduce the absorption of indole-3-carbinol. Therefore, they should not be taken at the same time of day or at the same meal.[33]

More Rapid Detoxification of Other Drugs. As stated previously, indole-3-carbinol may speed up the detoxification of any number of drugs due to its stimulation affect on Phase I detoxification centers. Therefore, patient monitoring is required with indole-3-carbinol supplementation at the therapeutic doses mentioned previously (300-400 mg per day).[33]

Despite the lack of extensive human intervention trials, the overall body of evidence strongly suggests indole-3-carbinol, and possibly other nutrients in cruciferous vegetables, act through various biological means to help defend against certain cancers, particularly reproductive cancers in women and men. Given our high exposure to environmental toxins, additives, pollutants and contaminants from food, water and air, it is of great importance to realize that indole-3-carbinol can optimize the body's detoxification processes. Phytoestrogen effects of indole-3-carbinol have been well-studied and appear to account for much of its ability to prevent reproductive cancers in animals.

Based upon numerous studies, it appears likely indole-3-carbinol may be one of the most important cancer-protective nutrients discovered to date. In my view, health practitioners should encourage patients to consume at least three servings per week of cruciferous vegetables and consider ingesting 30-60 mg of indole-3-carbinol as part of a cancer-prevention and detoxification-booster supplement cocktail. An increasing number of such supplements are now available in the marketplace due to the growing scientific understanding of the important biological activities exhibited by indole-3-carbinol.

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