Dynamic Chiropractic

How Cruciferous Vegetables and their I3C Content Help Reduce Cancer Risk

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There is a growing awareness among health practitioners and the general public about the importance of nutrition and antioxidants, flavonoids, soy isoflavones and dietary fiber.

One of the less appreciated bioactive agents strongly associated with reducing risk of many common cancers is indole-3-carbinol (I3C), found exclusively in cruciferous vegetables (broccoli, cauliflower, cabbage, Brussels sprouts, kale and *bok choy*), and in various supplements. 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 that are linked to increased risk of breast and prostate cancer; and act as a phytoestrogen (plant-based estrogen) that can bind to estrogen receptors on reproductive tissue and exert anti-cancer influences.

I3C has been shown to be one of the major anti-cancer substances found in cruciferous vegetables. Frequent consumption of cruciferous vegetables is associated with reduced risk of cancer in many human epidemiological studies and in animal experiments.[1-8] I3C is a member of the class of sulfurous chemicals called glucosinolates (previously called thioglucosides).[9] It is formed from parent compounds whenever cruciferous vegetables are crushed or cooked.[10,11] I3C and other glucosinolates (e.g., other indoles and isothiocyanates, such as sulforphane) are antioxidants and potent stimulators of phase I and 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 in of the body, referred to as phase I and 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. Phase I and II detoxification is known to be a vital aspect of preventing the accumulation of toxins in the body, and neutralizing and eliminating various cancer-causing agents and procarcinogens.

Phase I detoxification enzymes can directly neutralize some dangerous chemicals, but primarily convert most compounds into intermediate end-products that must be further acted upon by the phase II enzyme system. Many of the intermediates formed by phase I detoxification are more dangerous to the body than were the original compounds. Many of these intermediates are free radicals that are known to 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.

The phase II detoxification enzymes primarily act to conjugate intermediate end-products (formed in phase I detoxification) with various amino acids and other chemicals that neutralize these

intermediates and make them easier for the body to eliminate (e.g., attaching sulfur via sulfation makes many compounds more water-soluble and easier to eliminate in the urine). I3C is one of the very few exogenous agents that can speed phase I and II detoxification centers in the liver and the intestinal epithelial cells, and can improve the function of phase II glutathione-S-transferase detoxification activity, an extremely important pathway in the elimination of many dangerous chemicals.

Many researchers indicate that the ability of cruciferous vegetables to stimulate Phase I and II detoxification, especially their I3C content, is a primary factor in which these nutrients are related to reduced 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 I3C in their food have a significantly lower tumor yield and incidence than those fed the same diet, but without cruciferous vegetables or I3C fortification.[15-17]

Phytoestrogen Support

I3C is a phytoestrogen (plant-based estrogen), and can bind to estrogen receptors in the body, reducing the ability of stronger estrogens from overstimulating reproductive tissues such as the breast; cervix; uterus; and in males, the prostate gland. Researchers have 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 create cancerous mutations. This is how high exposure to estrogen, hormone replacement therapy and oral contraceptives are linked to the increased risk of breast cancer. Conversely, phytoestrogens are known to primarily stimulate the beta receptors on breast cells, which encourages a slower, more controlled cell division rate associated with reducing the risk of breast cancer. Further, phytoestrogens also bind to alpha receptors, but have only .0001 to .00001 the estrogen effect of estradiol, and thus compete for binding on these receptors with other more powerful estrogens. In this way, phytoestrogens are also capable of toning down the estrogenic influence of more powerful estrogens on various reproductive tissues. This effect also helps to prevent hyperproliferation of breast cells. Epidemiological studies consistently show that a higher ingestion of I3C foods is highly associated with the prevention of reproductive organ cancers in women and men.[3,4,8]

I3C 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 (according to modern wisdom). Some women naturally convert more of their estrone hormone to 16-hydroxyestrone (H), considered by some researchers a biomarker for increased risk of breast cancer. Supplementation with I3C has been shown to alter genetic expression in such a way as to encourage greater activity of the enzyme that converts estrone into 2-H, which is considered to be protective against breast cancer. Thus, all women may benefit in this regard as the intake of I3C helps to improve the 2-hydroxy-to-16-H ratio. This may be important in men, as well, 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-H ratio, but a lower dosage may still be effective.[33]

1. Prevention of Female Reproductive Cancers

   In experimental animal testing with mice and rats, I3C and Brussels sprouts each have demonstrated an ability to reduce mammary cancer incidence in animals exposed to carcinogens known to promote mammary cancer in these species.[21-22] As mentioned earlier in human studies, the ingestion of I3C has been shown to increase the metabolism of estrone hormone to 2-H, rather than the 16-alpha-H metabolite.

   Studies indicate that 16-alpha-H is associated with an increased risk of breast cancer in humans and conversely, 2-H is associated with a reduction in breast cancer risk. Thus, I3C influences the body's enzyme systems in a fashion that favorably influences the 2-H-to-16-alpha-H ratio, helping to reduce risk of breast cancer.[20,21,23,24] 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 two-to-16-H ratio to predict which women were less prone to breast cancer development.[33]

   1. Breast Cancer

      Epidemiological studies and experimental evidence strongly suggests that I3C may reduce breast cancer risk through the above-cited mechanisms.[25-28] To date, there are no human intervention trials that have tested I3C as a preventive or therapeutic agent against breast cancer.

   2. Cervical Cancer

      In a 12-week, double-blind study, eight of 17 patients with early-stage cervical cancer given 200 or 400 mg of I3C per day experienced a complete reversal of their conditions.[29] Animal studies have also shown that I3C can help prevent cervical cancer in the presence of various carcinogens.[30-31]

2. Respiratory Tract Papillomas

   I3C supplementation reduced or halted the formation of papillomas (precancerous lesions) in 12 out of 18 patients with recurrent respiratory tract papillomas in a small trial.[32]

3. Prostate Cancer

   In animal studies, the ingestion of I3C 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 Seattle study of male residents indicated that men consuming three or more servings per week of cruciferous vegetables had a 50-percent lower risk of prostate cancer than men consuming fewer servings, after controlling for other confounding variables.[33] To date, no human intervention trials have tested I3C as a preventive or therapeutic agent against prostate cancer.

Adverse Side Effects and Toxicity

At doses of 800 mg per day, I3C has caused dizziness and unsteady gait (signs of nervous system toxicity) in humans and in animal studies. It is also a powerful stimulator of phase I detoxification enzymes, and may speed up the detoxification of certain medications, changing their required dosage. However, one challenge study revealed that I3C intake did not interfere with oral

contraceptive medications.[33] Nevertheless, health practitioners and patients should monitor their responses to I3C supplementation if taken at therapeutic doses concurrently with other drugs. According to animal studies, this appears to be especially true:[33]

- testosterone replacement therapy;
- oral contraceptives;
- hormone replacement therapy;
- anti-seizure medications;
- immune-suppressant and antiviral drugs; and
- digoxin

Drug-Nutrient Interactions

1. Antacids and Heartburn Medications (H-2 antagonist drugs)

   These drugs reduce the absorption of I3C by reducing stomach acidity, and should not be taken at the same time of day or at the same meal.[33]
2. More Rapid Detoxification of Other Drugs

   As stated earlier, I3C may speed up the detoxification of any number of drugs, due to its stimulation effect of phase I detoxification centers. Patient monitoring is required with I3C supplementation at the therapeutic doses mentioned previously (300-400 mg per day).[33]

Summary and Conclusion

Despite the lack of extensive human intervention trials, the overall body of evidence strongly suggests that I3C (and possibly other nutrients in cruciferous vegetables) acts 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 that find their way into our body from food, water and air, it is of great importance to realize that I3C ingestion can help to optimize the body's detoxification, reducing the potential damage and carcinogenic effects of many of these exogenous agents.

The phytoestrogen effects of I3C have been well studied, and appear to account for much of its ability to prevent reproductive cancers in animals. Based upon numerous animal experiments, human epidemiological studies, treatment of cervical cancer patients with I3C supplementation, and studies in humans evaluating the influence of I3C on estrone metabolism, it appears likely that I3C 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 I3C as part of a cancer-prevention-and-detoxification-booster- supplement cocktail. A growing number of such supplements are now available in the marketplace because of the growing scientific understanding of the important biological activities exhibited by I3C.

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