

How Cruciferous Vegetables And Their Indole-3-Carbinol Content Help Reduce Cancer Risk

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Introduction

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, various flavonoids, soy isoflavones and dietary fiber. One of the more under-appreciated bioactive agents that is strongly associated with reducing risk of many common cancers is the indole-3-carbinol, found exclusively in cruciferous vegetables and in various indole-3-carbinol-containing 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), which can bind to estrogen receptors on reproductive tissue and exert 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, cauliflower, cabbage, Brussels sprouts, kale and bok choy) is associated with reduced risk of cancer in many human epidemiological studies and in animal experiments. Indole-3-carbinol is a member of the class of sulfur-containing chemicals called glucosinolates (previously called thioglucosides). It is formed from parent compounds whenever cruciferous vegetables are crushed or cooked. Indole-3-carbinol and other glucosinolates (e.g., other indoles and isothiocyanates such as sulforaphane) are antioxidants and potent stimulators of Phase I and Phase II detoxification enzymes in the liver and intestinal epithelial cells.



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 Phase II detoxification. Almost 2 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, xenobiotics, hormones and other compounds, including certain carcinogens. The Phase I and Phase II detoxification processes are known to be 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 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 formed by Phase I detoxification are more dangerous to the body than were the original compound. 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). Indole-3-carbinol has been shown to be one of the very few exogenous agents that can speed up both Phase I and Phase II detoxification centers 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 that the ability of cruciferous vegetables to stimulate Phase I and Phase II detoxification, especially their indole-3-carbinol 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 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.



Phytoestrogen Support

Indole-3-carbinol also acts as a phytoestrogen (plant-based estrogens) and in this capacity can bind to estrogen receptors in the body, reducing the ability of stronger estrogens from over stimulating 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 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 are known to primarily stimulate the beta- receptors on breast cells, which in turn encourage a slower, more controlled cell division rate, which is associated with reducing the risk of breast cancer. Further, phytoestrogens also bind to alpha-receptors, but have only 1/1000 to 1/10,000 the estrogen effect as 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 indole-3-carbinol foods is highly associated with the prevention of reproductive organ cancers in women and men.

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, according to modern wisdom. Some women naturally convert more of their estrone hormone to 16-hydroxyestrone, which has been shown to be a biomarker for increased risk of breast cancer, by some researchers. Supplementation with indole-3-carbinol has been shown to alter genetic expression in such a way as to encourage greater activity of the enzyme that converts estrone into 2-hydroxyestrone, which is considered to be protective against breast cancer. Thus, all women may benefit in this regard as the intake of indole-3-carbinol helps to improve the 2-hydroxy to 16-hydroxyestrone ratio. This may be important in men as well from the standpoint of preventing prostate cancer. (18, 19, 20) Thus far, 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.

1. Prevention of Female Reproductive Cancers

In experimental animal testing with mice and rats, indole-3-carbinol and brussels sprouts, respectively, have demonstrated an ability to reduce mammary cancer incidence in animals exposed to carcinogens that are known to promote mammary cancer in these species. As mentioned above in human studies, the ingestion of indole-3-carbinol has been shown to increase the metabolism of estrone hormone to 2-hydroxyestrone rather than the 16-alpha-hydroxyestrone metabolite. 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 in a fashion that favorably influences the 2-hydroxyestrone to 16-alpha-hydroxyestrone ratio, helping to reduce risk of breast cancer. 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 hydroxyestrone ratio to predict, which women were less prone to breast cancer development.

- Breast Cancer

Epidemiological studies and experimental evidence strongly suggests that indole-3-carbinol may reduce breast cancer risk through the above-cited mechanisms. To date there are no human intervention trials that have tested indole-3-carbinol as a preventive or therapeutic agent against breast cancer.

- Cervical Cancer

In a 12-week double-blind study, 8 of 17 patients with early-stage cervical cancer given 200 or 400 mg of indole-3-carbinol per day experienced a complete reversal of their condition. Animal studies have also shown that indole-3-carbinols can help prevent cervical cancer in the presence of various carcinogens.

2. Respiratory Tract Papillomas

Indole-3-carbinol 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.

3. 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). A Seattle study of men living in that city indicated that men consuming three or more servings per week of cruciferous vegetables had a risk of prostate cancer that was 50% lower than men consuming fewer servings of these vegetables, after controlling for other confounding variables. 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. As well, indole-3-carbinol is a powerful stimulator of Phase I detoxification enzymes, and as such it may speed up the detoxification of certain medications, changing their required dosage. However, one challenge study of this kind revealed that indole-3-carbinol intake did not interfere with oral contraceptive medications. Nevertheless, health practitioners and patients should 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:

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

Drug-Nutrient Interactions

1. Antacids and 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.

2. More Rapid Detoxification Of Other Drugs

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



Summary and Conclusion

Despite the lack of extensive human intervention trials, the overall body of evidence strongly suggests that 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 that find their way into our body from food, water and air, it is of great importance to realize that indole-3-carbinol ingestion can help to optimize the body's detoxification processes, reducing the potential damage and carcinogenic effects of many of these exogenous agents. The phytoestrogen effects of indole-3-carbinol have been well studied and appear to account for much of its ability to prevent reproductive cancers in animal. Based upon numerous animal experiments, human epidemiological studies, treatment of cervical cancer patients with indole-3-carbinol supplementation, and studies in humans evaluating the influence of indole-3-carbinol on estrone metabolism, it appears likely that 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. A growing 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.

For more information on this or other related topics, go to Dr. Meschino's website at:

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