

## REPORT

## Natural Prevention: I3C and Cancer

By Terri Mitchell



Lung, colon, breast and prostate are the leading cancers in America.<sup>1</sup> According to the latest government figures, from 1950 to 2000, lung cancer deaths rose 378% in people aged 65 to 74. The 5-year survival rate for lung cancer is only 15%.<sup>2</sup> What's really shocking, however, is the estimated number of cases of breast and prostate cancer are projected to exceed those of lung cancer. Clearly, new ways of preventing and treating these common cancers are needed.

Indole-3-carbinol (I3C) is a phyto (plant) compound from cruciferous vegetables such as cabbage and brussels sprouts. It has been proven effective against several types of cancer, including colon. Numerous studies have been done in cells, rodents and humans.

They show that I3C has multiple actions against the development of cancer, and cancer itself.

Studies on lung cancer indicate that I3C is powerful against DNA damage caused by cigarette smoke. Nitrosamines found in smoke are a major cause of lung cancer. In a study done at New York University Medical Center, 13 female smokers took 400 mg of I3C for five days, and researchers measured the effects on a nitrosamine known as NNK. Results showed that I3C partially neutralized it.<sup>3</sup> Studies in rodents confirm that I3C prevents NNK and other nitrosamines from causing DNA damage. It works by changing the way they're metabolized.

Diet plays a major role in the development of cancer. In Korea, the incidence of lung, colon, breast and prostate cancers is much lower than in North America. Korean researchers looked into the possible connection between the consumption of cruciferous vegetables and colon cancer. Cabbage and radish are eaten frequently in this Asian country, and they contain I3C. The research was conducted in rodents on both an inherited type of colon cancer, and one that was environmentally-induced by a chemical. The results show that I3C has a significant effect against precancerous conditions. I3C reduced the incidence of polyps in the genetically susceptible mice 24%. Another precancerous condition known as "aberrant crypt foci" also responded to I3C treatment. The number of foci was reduced approximately 60% in the mice that were treated with the chemical.<sup>4</sup> The optimal amount of I3C was not huge-it was a standard dose that can be taken orally (approximately 6 mg per kg of body weight per day). In fact, increasing the dose reduced effectiveness-an effect that has been shown in other studies as well.



Other important research was recently published in the medical journal, Cancer Letters. Researchers in India report that I3C can reverse chemotherapy resistance.<sup>5</sup> Multidrug resistance can develop after treatment with drugs used to treat cancer. When resistance develops, cancer cells no longer respond to treatment. The cause has been traced to a protein called P-glycoprotein (P-gp). Some cancers begin manufacturing P-gp once they are treated with cancer-killing drugs. The P-gp protein causes chemotherapy to be ejected from the cancer cells. While cancer cells use it to their benefit, the P-gp protein is not unique to this type of cell. Normal liver and kidney cells use P-gp to detoxify-it's a normal protein being used in abnormally high amounts by cancer cells.

There are drugs that can reverse multidrug resistance caused by P-gp, but they have serious side effects. Since I3C shares some of the same biochemical characteristics as the beneficial drugs, researchers were anxious to know if it could also reverse multidrug resistance, and whether it would have the same serious side effects.

I3C was given by injection to mice treated with vincristine and vinblastine. The results were excellent. I3C worked slightly better than

Study Casts Doubt on DIM



## Claim

Claims and counter-claims are part-and-parcel of the supplement industry, as lay people and scientists alike strive to get at the truth. One of the claims that surfaced in the past few years is the assertion that I3C's anti-estrogen action is entirely due to one of its metabolites, DIM (diindolylmethane).

The study was done to compare the effects of known estrogen-blockers tamoxifen and I3C on fertility. Because of the claim that I3C's estrogen-blocking effects are due to DIM, it was used in the study as well. When the results came in, both I3C and tamoxifen were shown to block estrogen (in different ways). DIM didn't work at all. The researchers concluded that "DIM exerted no significant effects on any of the endpoints studied, even at the highest dose, indicating that the antiestrogenic effects of I3C are not mediated by this metabolite of I3C."

DIM is a derivative of I3C that

the drug, verapamil, at eliminating the P-gp protein. And the good news was there were no adverse side effects.

Another potential cancer-related action for I3C has been discovered. Researchers in India report that injections of I3C 48 hours prior to treatment with a chemotherapeutic drug known as cyclophosphamide protects bone marrow against toxicity.<sup>6</sup> The research was conducted in mice using three different doses of I3C. In this case, the highest dose (1000 mg/kg of body weight) gave the greatest protection (52% decrease of DNA damage). It is important to stress that in this study, I3C was injected, not given orally, which probably allowed it to be tolerated in a higher dose. In studies where it is administered orally, lower doses usually work better.

I3C is well-known for its ability to modulate cancer-promoting hormones, including estrogen.<sup>7-10</sup> It works by altering the way such hormones are metabolized. By turning metabolism towards less powerful metabolites, I3C helps reduce levels of "strong," cancer-promoting hormones in the body. This helps reduce the potential for the development of hormone-related cancers.<sup>11</sup>

Another way I3C helps prevent cancer is by blocking carcinogens. One cancer-causing agent is aflatoxin, a toxin from mold that causes liver cancer. The mold that creates aflatoxin grows on peanuts, corn and other grains (look for "certified aflatoxin-free" organic products to avoid possible contamination). Several studies have been done on I3C and aflatoxin. They show that dietary amounts of I3C block aflatoxin's effects in the liver, and stop it from causing cancer.<sup>12,13</sup> But the importance of taking I3C, and not one of its derivatives such as DIM (diindolylmethane), was highlighted in a study from Oregon State University.<sup>14</sup> DIM is one of the plant chemicals that I3C converts to in the stomach, and it's available separately as a supplement. It appears that DIM is the factor responsible for modulating certain enzymes in the liver (cytochrome p450) that help detoxify carcinogenic chemicals.<sup>15</sup> But DIM is only one of dozens of factors derived from I3C in the stomach that have anti-cancer effects. After researchers tracked what happens to I3C after it is taken orally by rats for a week, they concluded that its aflatoxin-blocking action is caused by a combination of different I3C derivatives, not any single factor. As a bonus, they also discovered a new I3C derivative.

forms when I3C is broken down by stomach acid. It represents about 10% of the total phyto-compounds that a person gets when they take I3C. There are many others, with two new ones recently discovered. Until a clear-cut advantage for DIM over the other 90% of I3C's derivative phyto-compounds is proven (and it may eventually be in certain types of cancer), I3C is the more prudent choice.

Gao X, et al. Endocrine disruption by indole-3-carbinol and tamoxifen: blockage of ovulation. *Toxicol Appl Pharmacol* 2002 183:179-88.

## References

1. Louisiana, the District of Columbia, Mississippi, and Kentucky are the states with the highest rate of cancer. New Mexico, California, Colorado and Utah have the lowest. Age-adjusted rates, National Vital Statistics Report, Vol. 50, No. 15, Sept. 16, 2002.
2. National Cancer Institute, SEER Cancer Statistics Review 1975-2000.
3. Taioli E, et al. Effects of indole-3-carbinol on the metabolism of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in smokers. *Cancer Epidem Biomarkers Prev* 1997 6:517-22.
4. Kim DJ, et al. Chemoprevention of colon cancer by Korean food plant components. *Mutat Res* 2003 523-24:99-107.
5. Arora A, et al. Modulation of vinca-alkaloid-induced P-glycoprotein expression by indole-3-carbinol. *Cancer Lett* 2003 189:167-73.
6. Agrawal RC, et al. Prevention of chromosomal aberration in mouse bone marrow by indole-3-carbinol. *Toxicology Lett* 1999 106:137-41.
7. Michnovicz JJ, et al. Changes in levels of urinary estrogen metabolites after oral indole-3-carbinol treatment in humans. *J Nat Cancer Inst* 1997 89:718-23.
8. Yuan F, et al. Anti-estrogenic activities of indole-3-carbinol in cervical cells: implication for prevention fo cervical cancer. *Anticancer Res* 1999 19:1673-80.
9. Jellinck PH, et al. Distinct forms of hepatic androgen 6 beta-hydroxylase induced in the rat by indole-3-carbinol and pregnenolone carbonitrile. *J Steroid Biochem Mol Biol* 1994 51:219-25.
10. Wortelboer HM, et al. Acid reaction products of indole-3-carbinol and their effects on cytochrome P450 and phase II enzymes in rat and monkey hepatocytes. *Biochem Pharmacol* 1992 43:1439-47.
11. Frydoonfar HR, et al. The effect of indole-3-carbinol and sulforaphane on a prostate cancer cell line. *ANZ J Surg* 2003 73:154-6.
12. Dashwood RH, et al. Mechanisms of anti-carcinogenesis by indole-3-carbinol: detailed in vivo DNA binding dose-response studies after dietary administration with aflatoxin B1. *Carcinogenesis* 1988 9:427-32.
13. Manson MM, et al. Chemoprevention of aflatoxin B1-induced carcinogenesis by indole-3-carbinol in rat liverpredicting the outcome using early biomarkers. *Carcinogenesis* 1998 19:1829-36.
14. Stresser DM, et al. Mechanisms of tumor modulation by indole-3-carbinol. Disposition and excretion in male Fischer 344 rats. *Drug Metab Disp* 1995 23:965-75.
15. Renwick AB, et al. Effect of some indole derivatives on xenobiotic metabolism and xenobiotic-induced toxicity in cultured rat liver slices. *Food Chem Toxicol* 1999 37:609-18

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other

treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.