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Good Science, Good Medicine, Good Grief Indole-3-Carbinol and Breast Cancer

By: James L. Holly, MD

"Daughters eat your vegetables!" This has been the admonition of mothers and grandmothers to daughters and granddaughters for centuries. And, as we are finding out, such "common sense" advice has sound scientific support. Who would have ever believed that Popeye had it right? We now know that spinach may be the richest source of antioxidants in the human diet. It contributes tremendously to the maintenance of good health, and it has been recommended by a cartoon character for decades!

One of the greatest fears of women is breast cancer. And, it turns out that "eating your vegetables" may be, along with a regular self-examination, among the most important actions a woman can take to protect herself against this dreaded illness. Yet, while the admonition to "eat your vegetables" is sound, can a woman substitute a "pill" -- a supplement containing extracts of the potential "anti-cancer" substances in vegetables -- for the vegetables themselves? The answer is "maybe," "probably not," and/or "we don't know for sure."

Good Science

The "active ingredient" in vegetables which has been associated with protection against breast cancer is **Indole-3-Carbinol**. It is touted by some supplement manufacturers as "the single most effective way to reduce the risk of breast cancer. Every healthy, non-pregnant woman over 30 years should be on this compound, to give her the best possible protection against breast cancer. There is no risk. There is no downside. And the cost is minimal." That's the claim. What is the science?

Indole-3-Carbinol (I3C) is the phytonutrient that occurs naturally in certain cruciferous vegetables, like broccoli, cabbage, cauliflower, Brussels Sprouts and kale. I3C has been proven to affect estrogen metabolism in ways that might help prevent breast cancer. I3C provides benefits in two important ways:

1. The indole group of sulfur compounds binds to chemical carcinogens and active enzymes that, in turn, detoxify the carcinogens.
2. I3C has been shown to act as a catalyst to pull estradiol down a benign pathway to 2-hydroxy estrone thus decreasing levels of the carcinogenic 16-alpha hydroxy estrone.

Evidence

In 1991, researchers proved that I3C significantly reduced the incidence and, in fact, the number of tumors in female mice prone to developing breast cancer. In human studies, levels of a carcinogenic estrogen declined and levels of a benign estrogen increased. Most important, there was a marked decrease in the level of the estrogen metabolite associated with breast and endometrial cancer (16-alpha hydroxy estrone).

An impressive and consistent body of studies since 1966 has made it clear that increased 16 α -hydroxylation of estradiol is associated with breast cancer and risk for breast cancer in both mice and humans. There are three down-stream products of metabolism (metabolites) of estradiol:

1. 16-alpha hydroxy estrone,
2. 4-hydroxy estrone, and
3. 2-hydroxy estrone.

It is the 16-alpha hydroxy estrone that has been shown to be carcinogenic, in animal studies and in vitro studies. The 16-alpha hydroxy estrone is sometimes called "strong" estrogen. The "weak," or benign estrogen is the 2-hydroxy estrone. Indole-3-Carbinol catalyzes the reaction of estradiol to 2-hydroxy estrone. Therefore, there is an increase in 2-hydroxy estrone and a decrease in 16-alpha hydroxy estrone, resulting in a commensurate lowering of the risk of breast cancer.

The results of a 1996 placebo controlled double-blind study of 57 healthy, adult women at increased risk for breast cancer, suggests that Indole-3-Carbinol is an extremely promising agent for prevention of breast cancer. A 1997 study noted that I3C not only stopped 54-61% of the human cancer cells from growing, but actually provoked the cells to self-destruct.

Animal Studies of I3C Are Mixed

Feeding indole-3-carbinol or broccoli extracts rich in indole-3-carbinol has dramatically reduced the frequency, size, and number of tumors in laboratory rats exposed to a carcinogen. It appears to be especially protective against breast and cervical cancer because of a number of actions, including an ability to increase the breakdown of estrogen. However, while most animal studies report protective effects, a few indicate that indole-3-carbinol may actually promote cancer formation in certain situations, depending upon the chemical initiator of cancer, method of exposure, and species of animal studied.

Until there is further research and more human clinical data to determine if indole-3-carbinol actually inhibits rather than stimulates cancer formation, some researchers have recommended proceeding with caution when using isolated indole-3-carbinol as a dietary supplement. The areas where its use has currently been documented in humans are only preliminary, but the results are promising.

Indole-3-carbinol reduced or halted the formation of papillomas (precancerous lesions) in 12 out of 18 patients with recurrent respiratory tract papillomas. In addition, in a small double-blind trial, supplementation with 200 or 400 mg of indole-3-carbinol per day for 12 weeks reversed early-stage cervical cancer in 8 of 17 women. Preliminary studies have also shown indole-3-carbinol has significantly increased the conversion of estrogen from cancer-producing forms to nontoxic breakdown products.

Good Medicine?

The real question is: can Indole-3-Carbinol be taken in a pill rather than in dietary consumption of vegetables? The following on-going discussion between advocates of I3C and those who, while not opposed to its use, are cautious about the scientific support for the claims made by those advocates, addresses the important elements of this question.

One supplement industry "watch dog" organization was asked what the best Indole-3-Carbinol supplement product is. Their response was, "Short answer, none." They continued, "(this is) primarily because the indoles compounds are very unstable and are very difficult (almost impossible) to put into a supplement form that remains stable (and active) for more than a few days." The response continued:

"Longer answer: Many of the 'indole' compounds are touted as anti-cancer agents (which they very well might be) because they can alter estrogen metabolism toward what we might call a more 'favorable' profile. There are a great number of these dietary indoles, which we get primarily from cruciferous vegetables such as cauliflower and broccoli - but **the problem isn't so much whether they 'work' or not (they do) - but more about whether they are stable in the form of a dietary supplement (which they typically are not).** (emphasis added)

"The chemical structure of the indoles is such that they break down extremely rapidly when they are isolated (as they need to be for manufacture into a supplement form). They also break down very quickly when cooked (so broccoli and cauliflower that are 'less-cooked' are better sources of indoles than those that are 'more-cooked').

"Many people who ask us about indole supplements are concerned about prostate enlargement, and in these cases, we feel that the best choice is saw palmetto (320mg/day). Saw palmetto has a terrific effect in slowing the conversion of testosterone into DHT (which, as you know, is a powerful growth stimulant for prostate tissue).

"Saw palmetto will keep the testosterone from being converted into DHT - but then you'll need to do something to keep that testosterone from being converted directly into estrogen - and the best solution for that is to exercise on a regular basis and eat your (fresh) cruciferous veggies a few times per week."

Good Medicine: Contrary Opinion

Another organization which recommends Indole-3-Carbinol supplements -- and which sells one -- responded to the above comments: "Relating to Indole-3-Carbinol -- ...there are currently 337 literature references to the use of Indole-3-Carbinol and different experimental settings...In the epidemiologic studies, they have demonstrated results with orally bioavailable capsule form of Indole-3-Carbinol, and describe their results and effects as such. I would think if this supplement were not stable enough for a distribution, that the literature would not be so rich in describing its affects. I would think that patients in studies and laboratories would still have to acquire Indole-3-Carbinol, and it would have to maintain some dependable stability

for them to generate repeatable results."

Response to the response

The supplement watchdogs responded:

"There are also many publications showing that the indoles breakdown quite rapidly - the majority of the articles to which (the above comment refers) are vegetable-consumption studies where the foods are prepared and eaten within a very short time.

"Within the small fraction of the published reports investigating supplement-forms of the indoles given to humans, there are both positive and negative findings - and the positive findings tend to be for sponsored studies (make the capsules, feed them to people in a short period of time) rather than for investigative studies (test a product 'off-the-shelf' to see if it works as claimed).

"As you probably gathered from our original reply, we are not against the idea of indoles as a beneficial part of the diet (they are wonderfully beneficial compounds), but we are skeptical (based on the published results) that putting these compounds into a capsule is the best way to go."

Good Grief

Whose right? Actually, they both may be. Here is what we know:

1. Eating vegetables is healthy for everyone. Eating the cruciferous vegetables, particularly broccoli, cauliflower, cabbage, Brussels Sprouts and Kale is particularly healthy. A diet rich in these vegetables will contribute to general health and specifically to a decreased probability of breast cancer.
2. The more these vegetables are cooked, the less nutrient value they have. That is true of many foods.
3. Indole-3-Carbinol (I3C) appears to have beneficial effects on preventing breast cancer. It is certain that I3C beneficially affects the metabolism of estrogen.
4. The jury is still out on I3C supplements. They probably help and they certainly do not appear to do any harm.
5. More studies are needed before a final answer can be given to our original question: "can a woman substitute a 'pill' -- a supplement containing extracts of the potential "anti-cancer" substances in vegetables -- for the vegetables themselves?"
6. Interestingly, we come down to the same conclusion in this analysis as in all, the best way to retain and/or to regain your health is exercise and eating vegetables. Boring advice maybe, but there will never be a pill which can substitute for self-discipline in eating and consistent exercise.

Remember, it is your life and it is your health.