AOR CODE: AOR04250

Premium

I-3-C

Protection from Estrogen Related Diseases
A phytonutrient found in broccoli

Reduces the formation of harmful estrogens

An effective dose of I-3-C per capsule

Gluten Free   Vegan   Non-GMO   Cellular

Health Menstrual Cycle/PMS

AOR Code       Variant
AOR04250       60 VEGI-CAPS

Details
Indole-3-carbinol (I-3-C) is a phytonutrient found in Brassica vegetables such as broccoli, kale and cabbage, and is one of the key health-promoting compounds in these foods. Many studies have had phenomenal success using I-3-C to shift the balance of metabolic enzymes that process estrogens thereby reducing the formation of "bad" estrogens and increasing the formation of "good" estrogens. Human studies in women taking I-3-C have shown a favourable shift in estrogen metabolism, and I-3-C has been shown to be protective against estrogen dominance. Estrogen dominance has been linked to fibroids, breast tenderness, premenstrual syndrome, endometriosis and other women's health concerns.

Women who are concerned with safer estrogen metabolism, who have a family history or increased risk of estrogen-dependent cancers, or those that have a higher ratio of bad to good estrogens can benefit from this product. I-3-C may also be a beneficial supplement for those who want to reap some of the benefits of Brassica vegetables but have difficulty eating them raw.

Label Info

Discussion
I-3-C helps to promote healthy estrogen metabolism and balance.

Product Variation
Product Code       Size
Supplements Facts

Serving Size: 1 Capsule

<table>
<thead>
<tr>
<th>Amount</th>
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<tr>
<td>Indole-3-Carbinol (I3C)</td>
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Non-medical ingredients:
microcrystalline cellulose, sodium stearyl fumarate. Capsule: hypromellose.

Guarantees

AOR™ guarantees that all ingredients have been declared on the label. Contains no wheat, gluten, corn, nuts, peanuts, sesame seeds, sulphites, mustard, soy, dairy, eggs, fish, shellfish or any animal byproduct.

Adult Dosage

Take 1 capsule one to two times daily with/without food, or as directed by a qualified health care practitioner.

Cautions

Consult a health care practitioner prior to use to exclude the diagnosis of a serious cause of hormonal imbalance, if you are taking any medications or natural health products, if you are attempting to conceive, if you have a liver disorder, or symptoms of low estrogen (such as joint pain, mood changes, changes in libido, hot flashes, night sweats, vaginal dryness or irregular menstruations). Discontinue use and consult a health care practitioner if you develop liver-related symptoms (e.g. abdominal pain, jaundice) or symptoms of low estrogen. Do not use if you are pregnant or breastfeeding.

NOTE: I-3-C can have a strong, characteristic smell that may be unpleasant to some people. This effect is harmless and not indicative of loss of potency.

Source

Pharmaceutical synthesis

Main Application

Estrogen metabolism

Women's health

Disclaimer
The information and product descriptions appearing on this website are for information purposes only, and are not intended to provide or replace medical advice to individuals from a qualified health care professional. Consult with your physician if you have any health concerns, and before initiating any new diet, exercise, supplement, or other lifestyle changes.

**Research**

**Background**

**Indole-3-carbinol, or I3C**, is a phytonutrient found in Brassica vegetables – relatives of the mustard plant, like broccoli, cabbage, and Brussles sprouts. Interestingly, other common detoxifiers such as d-glucarate and sulforaphane are also found alongside I-3-C in the same foods.

**“Good” vs “Bad” Estrogens**

The key risk factor in the development of most women’s reproductive cancers – and the point for I3C to play a role in risk reduction - is exposure to estrogen. “Estrogen” is actually not one substance, but a family of hormones that stimulate the growth and development of women’s reproductive systems. And in fact, the effect of estrogens on women’s health is as much a product of which estrogens and estrogen metabolites a woman is exposed to, as it is of how much estrogen her body makes.

The estrogen metabolite 16 alpha-hydroxyestrone (16OHE) is considered a “bad” estrogen. On the other hand, “good” estrogens also exist, in the form of 2-hydroxyestrone (2OHE), along with 2-methoxyestradiol. These estrogen metabolites are either harmless, and may actually have protective effects.

**Enter I3C**

This is where I3C comes into the picture. Following up on extensive animal experimentation, the intriguing finding of several human studies has been that, by shifting the balance of metabolic enzymes that process estrogens in the body, I3C reduces the formation of “bad” estrogens, and increases the formation of “good” ones.

**I3C vs DIM: Myth or Fact**

Recently, there has been some controversy about the relative advantages of I3C compared with one of its condensation products, DIM (diindolylmethane). Research suggests that both compounds are safe and effective, and provide beneficial estrogen balancing effects. I3C is naturally broken down by the body to produce DIM, thereby providing the benefits of both molecules. Years of detailed analysis of the role of estrogen metabolites in women’s health, extensive animal experiments, and now a successful controlled trial in human women all provide support for I3C’s ability to provide an effective natural support for safer estrogen metabolism, and thus for women’s health.

**Research**

**Human Research**
Knowing the role of “bad” estrogen in women’s health and I3C’s ability to change estradiol metabolism from “bad” to “good,” a series of experiments have been conducted using I3C. Favorable results ultimately led up to a prospective, randomized, double-blind, placebo-controlled trial of I3C in women.

Dr. Bell and her colleagues from Louisiana State University Medical Center recruited thirty women having had unfavourable biopsies. For twelve weeks, one third of these women received 200 mg of I3C; a second group got 400 mg; the remaining women were given a placebo. The women’s 2OHE:16OHE ratios were tested to see what effect the I3C would have on their metabolism of estrogen. There was a dose-dependent increase in the ratio of “good” to bad” estrogens in the two I3C groups, and no effect in the placebo group.

Market Trends

I3C and DIM are both well-known supplements for ameliorating estrogen metabolism and reducing the risk of women’s cancers. I-3-C is converted into DIM when consumed. Although DIM is both safe and effective, most of the clinical studies have been done on I-3-C.

AOR Advantage

When consumed, I-3-C is converted into DIM. I-3-C is the natural form of the compound found in Bassica vegetables like broccoli. AOR’s I-3-C provides an effective dose of this natural ingredient.

References


Abstract

Evaluation of chronic dietary exposure to indole-3-carbinol and absorption-enhanced 3,3\'-diindolylmethane in Sprague-Dawley rats.


Leibelt DA, Hedstrom OR, Fischer KA, Pereira CB, Williams DE.

Indole-3-carbinol (I3C) and 3,3\'-diindolylmethane (DIM) are naturally occurring dietary components found in cruciferous vegetables. In the stomach, I3C forms condensation products including DIM. I3C and DIM are marketed as dietary supplements, but little is known about the safety of long-term exposure. Rats were fed either control diet, 1 or 10x the current human dose of absorption-enhanced DIM [BioResponse DIM® (Indolplex®)] or 5-7x the maximal recommended dose of I3C. Experimental diets were fed continuously for 3 or 12 months or 2 months followed by control diet for 1 month. Results at 3 or 12 months were similar in most respects. No significant differences between groups were found in blood chemistry. A general decrease in serum enzyme levels in male rats was observed, perhaps indicative of a protective effect. Males fed I3C exhibited higher serum levels of 25-hydroxy-vitamin D3 (25OH-D3). There were no observable differences grossly or histologically between groups, although a high number of hyaline casts were found throughout the kidneys of all animals. In both sexes total hepatic CYP levels were significantly induced by I3C, but not by either dose of DIM. Induction of CYP1A1 and CYP1A2 in liver and CYP1A1 in colon was detected for both sexes fed I3C and the high dose of DIM. CYP3A2 was induced in females fed I3C or the high dose of DIM; males were induced with I3C, but not DIM. No induction of CYP1B1 in the colon was observed in either sex. Long-term exposure to DIM produced no observable toxicity, and comparison to I3C
indicates that DIM is a markedly less efficacious inducer of CYP in the rat at doses relevant to human supplementation.

**Effects of treatment of rats with indole-3-carbinol or 3,3?-diindolylmethane on the hepatic P450-dependent metabolism of estrogen and tamoxifen.**

*Cancer Epidemiol Biomarkers Prev. 2003 Oct; 11 Suppl:1215(AbsD111).*

Malejka-Giganti D, Parkin DR, Ritter CL, Bliss RL.

..... This effect is presumably mediated through modification by I3C of cytochrome P450 (CYP) complement and activities leading to estrogen detoxification. In our previous study, treatment of female Sprague-Dawley rats by oral gavage with I3C at 5, 25 and 250 mg/kg body weight (bwt) in ethanol:olive oil (1:4) for 4 to 10 days yielded dose-dependent increases in the hepatic P450 level, CYP1A1, 1A2 and 2B1/2 probe activities, and in the rates of microsomal oxidations of 17 b-estradiol (E2) to 2-hydroxy (OH)- E2, 2-OH-estrone (E1), 6a-OH-E2, 6b-OH-E2, estriol and 15a-OH-E2, and of E1 to 2-OH-E1, 2-OH-E2, 6(a b)-OH-E1 and 6a-OH-E2. The 4-day treatment with the highest dose of I3C produced the largest increases in the rates of E2 or E1 metabolism, whereas the lowest dose had no effect. Since the action if I3C is, in part, ascribed to its acid-condensation product 3,3?- diindolylmethane (DIM), we examined the effects of a 4-day oral treatment of rats with DIM at 8.4 and 42 mg/kg bwt (or at an assumed 2 and 10%, respectively, conversion of I3C at 250mg/kg bwt). DIM at 42 but not at 8.4 mg/kg bwt effected only small increases of the hepatic CYP1A1 and 2B1/2 activities. By contrast to I3C, DIM effected significant decreases in the rates of metabolism of E2 to 4-OH-E2, 4- OH-E1, 6a-OH-E2 and 6(a b)-OH-E1 (by 34,36,70 and 60%, respectively), and E1 to 6(a b)-OH-E1 (by 40%), indicating that it inhibits CYP(s) catalyzing the formation of the potentially adverse estrogen metabolites. The differences between I3C and DIM in eliciting CYP-mediated responses suggest that DIM alone is not a key player in the mechanism of action of I3C [emphasis added]. We also examined whether the I3C-or DIM-effected changes in CYP-catalyzed reactions affect hepatic metabolism of tamoxifen (TAM), an antiestrogen for breast cancer prevention. After treatment with I3C or DIM at the above dose levels, the rates of formation of the microsomal metabolites of TAM: a-OH-TAM, 4-OH-TAM and TAM-N-oxide remained unchanged, and that of N-desmethyl-TAM increased ~3-fold only after I3C at 250mg/kg bwt. The data suggest that oral intake of I3C or DIM at lower dose levels will not alter CYP-mediated metabolism of TAM, and hence, its therapeutic efficacy.

**Increased estrogen 2-hydroxylation in obese women using oral indole-3-carbinol.**

*Int J Obes Relat Metab Disord 1998 Mar;22(3):227-9*

Michnovicz JJ.

**OBJECTIVE:** To investigate whether the dietary phytochemical, indole-3-carbinol (13C), influences the level of estradiol 2-hydroxylation in obese women.

**DESIGN:** A clinical intervention study involving the ingestion of purified 13C, 400 mg, for two months.

**SUBJECTS:** Five healthy, overweight, premenopausal women (age: 35-47 y, body mass index (BMI):
Two estrogen metabolites, 2-hydroxyestrone (2OHE1) and estriol (E3), were measured by radioimmunoassay in untimed overnight urine samples, before and after ingestion of 13C.

The ratio of urinary estrogens, 2OHE1/E3, was significantly increased in obese women following 13C, reflecting induction of 2-hydroxylation in these women.

Obese premenopausal women experience increased estrogen 2-hydroxylation in response to the dietary agent, 13C, similar to non-obese women. This response to 13C may result in a hormonal milieu....

Changes in levels of urinary estrogen metabolites after oral indole-3-carbinol treatment in humans.


Michnovicz JJ, Adlercreutz H, Bradlow HL.

The oxidative metabolism of estrogens in humans is mediated primarily by cytochrome P450, many isoenzymes of which are inducible by dietary and pharmacologic agents. One major pathway, 2-hydroxylation, is induced by dietary indole-3-carbinol (I3C), which is present in cruciferous vegetables (e.g., cabbage and broccoli).

Because the pool of available estrogen substrates for all pathways is limited, we hypothesized that increased 2-hydroxylation of estrogens would lead to decreased activity in competing metabolic pathways.

Urine samples were collected from subjects before and after oral ingestion of I3C (6-7 mg/kg per day). In the first study, seven men received I3C for 1 week; in the second study, 10 women received I3C for 2 months. A profile of 13 estrogens was measured in each sample by gaschromatography-mass spectrometry.

In both men and women, I3C significantly increased the urinary excretion of C-2 estrogens. The urinary concentrations of nearly all other estrogen metabolites, including levels of estradiol, estrone, estriol, and 16alpha-hydroxyestrone, were lower after I3C treatment.

These findings support the hypothesis that I3C-induced estrogen 2-hydroxylation results in decreased concentrations of several metabolites known to activate the estrogen receptor. This effect may lower estrogenic stimulation in women....

Long-term responses of women to indole-3-carbinol or a high fiber diet.
We test the hypothesis that the estrogen metabolite ratio 2-OH-estrone:estriol can be raised via dietary indole-3-carbinol (I3C) and that this higher ratio can be sustained over a 3-month test period. We also explore the possible role of pure fiber on estradiol metabolism. Using a randomized clinical trial with three arms, each containing 20 subjects, arm 1 received 400 mg/day of I3C daily for 3 months, arm 2 received 20 g of alpha-cellulose daily for the same time period as a source of added fiber, and arm 3 received a placebo dose. Blood levels of a variety of biochemical parameters were measured. The urinary 2-OH-estrone:estriol estrogen metabolite ratio was measured monthly at the same time of the menstrual cycle. While no changes were observed in the control and alpha-cellulose-treated arms, a substantial mean increase in the ratio was observed in the I3C-treated arm at month 1; that increase was maintained over the 3-month time period. Three of the 20 subjects in this I3C-treated group differed from the others in that no significant change in the metabolite ratio was observed at any time point. The results suggest that I3C can serve to increase the 2-OH-estrone:estriol metabolite ratio in a sustained manner without detectable side effects and that some individuals may be resistant to such change.

Altered estrogen metabolism and excretion in humans following consumption of indole-3-carbinol.


Michnovicz JJ, Bradlow HL.

.....Indole-3-carbinol (I3C), obtained from cruciferous vegetables (e.g., cabbage, broccoli, etc.), is a known inducer of oxidative P-450 metabolism in animals. We investigated the effects in humans of short-term oral exposure to this compound (6-7 mg/kg/day over 7 days). We used an in vivo radiometric test, which provided a highly specific and reproducible measure of estradiol 2-hydroxylation before and after exposure to I3C. In a group of 12 healthy volunteers, the average extent of reaction increased by approximately 50% during this short exposure (p less than 0.01), affecting men and women equally. We also measured the urinary excretion of two key estrogen metabolites, 2-hydroxyestrone (2OHE1) and estriol (E3). We found that the excretion of 2OHE1 relative to that of E3 was significantly increased by I3C, further confirming the ongoing induction of 2-hydroxylation. These results indicate that I3C predictably alters endogenous estrogen metabolism toward increased catechol estrogen production.....