Indole-3-Carbinol (http://www.mskcc.org/mskcc/html/69263.cfm)

Scientific Name

Indole-3-Methanol
TOP

Common Name

I3C, 1H-Indole-3-methanol, indole-3-methanol, 3-(Hydroxymethyl)indole, 3-indolylcarbinol, indolylmethanol
TOP

Brand Name

I3C Plus (Health Products Distributors)
TOP

Clinical Summary

Indole-3-Carbinol (I3C) is a specific compound found in cruciferous vegetables including broccoli, cabbage and cauliflower. Because diets high in these vegetables retard cancer growth in animals, I3C is thought to be a good candidate for cancer prevention. I3C is known to stimulate detoxification enzymes in the gut and liver [6]. Several studies demonstrate that it can cause cell cycle arrest [3] [8] and apoptosis [4] [13] [14] [15]in cancer cell lines. Data from clinical trials show that I3C is effective in treatment of precancerous cervical dysplasia [2]and vulvar intraepithelial neoplasia [16].
I3C is generally well tolerated when taken orally. Certain studies suggest I3C may promote tumor growth in animals that have been exposed to carcinogens [5], but the potential risk has never been documented in humans. Because it may induce cytochrome P450s [17], I3C may interact with several medications.
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Food Sources

Broccoli, brussel sprouts, cabbage, cauliflower, collards, kale, kohlrabi, mustard greens, rapeseed, rutabaga, turnip
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Purported uses

- Cancer prevention
- Detoxification
- Viral infections

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Mechanism of Action

I3C is a naturally occurring compound found in cruciferous vegetables that is known to stimulate detoxifying enzymes in the gut and liver [6]. Many studies indicate its potential value as a chemopreventive agent for breast cancer through its estrogen receptor (ER) modulating effect [7]. I3C also down-regulates the expression of the estrogen-responsive genes pS2 and cathepsin-D and up-regulates BRAC1 [12]. Other in vitro studies show that I3C inhibits the expression of cycline-dependent kinase-6 and induces a G1 cell cycle arrest independent of ER signaling [8]. Diidolylmethane (DIM), a metabolite of I3C, can induce apoptosis by modulating the expression of the Bax/Bcl-2. [14] There is evidence to support the fact that I3C has a different mechanism of action than tamoxifen and that these two substances can be used synergistically [3]. One randomized clinical trial suggests that I3C can increase the 2-OH-estrone:estriol metabolite ratio [10]. This is thought to decrease the risk of ER-sensitive breast cancer and cervical cancer. I3C can cause apoptosis of prostate cancer cells in vitro by inhibition of Akt activation [4]. It also holds promise in preventing cancer with a papillomavirus component [11]. I3C induces cytochrome P450 1 family, which may lead to potential drug interactions [17]. There is some evidence from animal studies that increases in cytochrome P450 1A1 activity also metabolizes some environmental procarcinogens to their carcinogenic form, but this has not been confirmed in humans.

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Pharmacokinetics

No published data regarding the pharmacokinetics of I3C in humans currently exists. Animal studies shows that I3C itself is not active. Gastric acid converts I3C to active metabolites diindoylmethane and indolylcarbazole, which are further metabolized in the liver. Most metabolites are excreted through the feces.
(6)

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Warnings

Preliminary evidence suggests that I3C might promote tumor growth in animals exposed to carcinogens.
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Adverse Reactions

I3C is usually well tolerated when taken orally.
Reported: Some patients can experience skin rash.
(6) (7)

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Herb-Drug Interactions

Theoretically, I3C induces cytochrome P450 1 family and reduces serum concentration of medications metabolized by this enzyme.

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Lab Interactions

In rare cases, small increases in ALT have been known to occur.
(6) (7)

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Literature Summary and Critique

Bell MC, et al. Placebo-controlled trial of indole-3-carbinol in the treatment of CIN. *Gynecol Oncol* 2000;78:123-9.
A double-blind placebo-controlled study of indole-3-Carbinol. Thirty women with biopsy-proven cervical intraepithelial neoplasia (CIN) received placebo, 200 or 400 mg/day of I3C for 12 weeks. None of the patients in the placebo arm had complete regression of CIN, whereas 4 of 8 (p=0.023) from the 200 mg/day arm and 4 of 9 (p=0.032) from the 400 mg/day arm had complete regression after 12 weeks. The ratio of 2-hydroxyestrone to 16-alpha-hydroxyestrone changed in a dose-dependent fashion. The results of this study show promise for the use of I3C as a nonsurgical option for the treatment of CIN, although the data needs to be confirmed in a large multicenter trial.
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