DIM-Evail™

Highly Absorbable Diindolylmethane softgels

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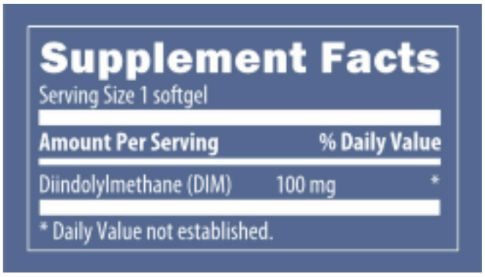
Plant indoles, also called glucosinolates, found in cruciferous vegetables provide health benefits to humans. Cruciferous vegetables are known for their cancer protection. Two such indoles provided by cruciferous vegetables are I3C (Indole-3-Carbinol) and DIM (Diindolylmethane). DIM is not naturally present in these plants. It gets released with the help of enzymes upon crushing of the broccoli, cauliflower, cabbage or brussel sprouts or during human digestion.[1,3] Stomach acid, or HCl, can also aid the joining of two indole 3 carbinols to make diindolylmethane. Lack of HCl will hinder one's ability to make DIM from I3C.[2]



Other Ingredients: Medium chain triglycderides, vitamin E, sunflower lecithin; gelatin, purified water, glycerine, turmeric (softgel ingredients).

Basically, DIM is two molecules of I3C combined together. I3C in a capsule is not shelf stable because it is sensitive to light, heat and moisture. I3C is irritating to the stomach and research tells us that it can have very negative side effects in doses over 300mg daily such as dizziness and unsteady gait which may be due to nervous system toxicity. One study shows evidence that 90% of orally consumed I3C converts to other compounds. It may be these other compounds that cause these side effects. One compound I3C converts to is ICZ, or indolocarbazole. This compound causes DNA damage.[4] DIM studies show no toxicity when given triple the dose in humans.

The Designs for Health Evail™ Process

Due to its crystalline structure, absorption of DIM is minimal when given orally. For this reason, DIM-Evail™ is manufactured utilising the new Designs for Health Evail™ process, which is an all-natural formulation that improves the absorption of DIM. This process uses a proprietary blend of MCT oils, non-soy derived lecithin, and vitamin E, without the use of potentially harmful surfactants.

What Actions Does DIM Have on the Body that Make it Beneficial to our Health?

It has been suggested that a low level of the 2-hydroxyestrone metabolites (2-OHE) and a high level of 16 alphahydroxyestrone (16 alpha-OHE1) is associated with an enhanced risk of breast cancer. DIM increases 2 hydroxyestrone and therefore improves the 2/16 hydroxyestrone ratio, making it very protective for women at high risk for this condition.[6]

Research by Bradlow says that DIM also reduces availability of 4-androstenedione for aromatisation to estrone.7 He concludes that DIM is more potent than I3C at protecting against mammary carcinoma due to decreased formation of 16 alpha-hydroxyestrone from estrone.[6]

Doesn't Research Support the Use of I3C for Cancer Prevention Such as Breast Cancer?

There are positive studies on supplementation of I3C because they are looking at limited parameters such as improvement in the 2/16 hydroxyestrone ratio. When we take a broader look, however, I3C raises 4-hydroxyestrogen with the potential of aggravating cancers such as breast, endometrial and prostate cancer. I3C increases 4-hydroxyestrogen production in animals and in humans.8 DIM does not. 4-hydroxyestrogens and CYP1B1, the only CYP source of 4-hydroxyestrogen, have both been implicated in the causation of prostate and breast cancer in humans. 4-hydroxyestrogens and CYP1B1 are also implicated in the causation and growth of uterine fibroid tumours and endometriosis.

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Researchers from the Department of Pathology, Sasaki Institute, Tokyo, Japan concluded the following: "These results suggest that induction of the CYP1 family in the liver and sequential modulation of estrogen metabolism to increase 4HE might play a crucial role in promoting the effects of dietary I3C on endometrial adenocarcinoma development."[8]

What About Toxicity Studies?

In acute toxicity studies in mice, "DIM produced no observable 24-hr acute toxicity up to 4 g/kg body weight, except for a slight decrease in haematocrit. However, I-3-C exhibited a dose-dependent toxicity above 100 mg/kg body weight, including a decrease in hepatic reduced glutathione after 2 hr and severe neurological toxicity, and the release of liver enzymes to the plasma at 24 hr."[9]

Bottom Line: Supplementation of DIM should be recommended over supplementation of I3C for safety purposes.

DIM is a More Potent Antioxidant Than I3C

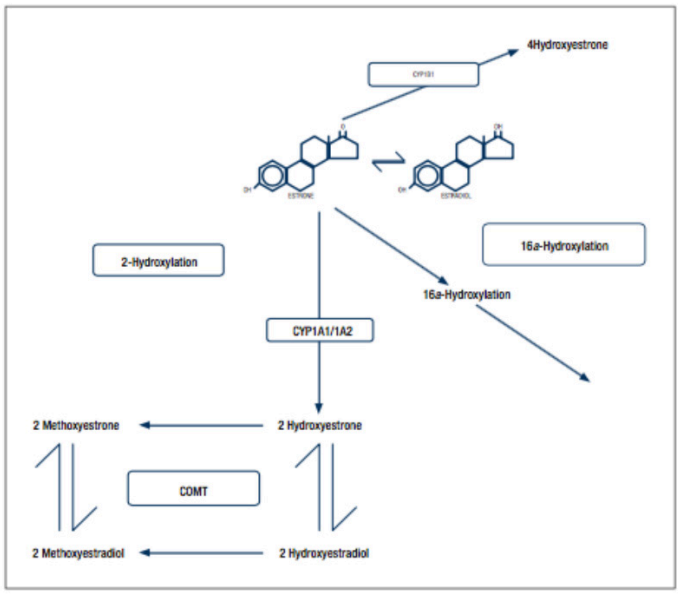
When tested side by side with I3C, DIM was shown to be a more potent antioxidant with greater activity than vitamin E because of its hydrogen (electron) donating ability.

Should We Just Eat Cruciferous Vegetables?

Eating two pounds of cruciferous vegetables like raw cabbage or broccoli can ultimately supply, via I3C conversion into DIM, about 20-30mg of DIM. Therefore, supplementation is ideal along with consuming cruciferous vegetables.

What Does DIM Do?

Research clearly shows that 4-hydroxyestrogen and 16 hydroxyestrogen are not favourable when elevated. Many doctors are now performing clinical tests on their patients to screen for risk of breast cancer. Low risk for breast cancer is marked by a high 2/16 ratio (2 hydroxy to 16 hydroxyestrogen). It is clearly established by research that DIM raises the 2/16 ratio without elevating 4 hydroxyestrogen. DIMhelps men too because it is an aromatase inhibitor. DIM helps to block the conversion of testosterone to estrogen.10 Regarding dosing, I3C needs to be given at 3-4 times the dosage of DIM to provide the same positive benefits. (Note: 300-400mg I3C as compared to 60-100mg DIM). I3C in low doses, like the amounts found in cruciferous vegetables is safe. I3C ingested at higher doses needed to shift estrogen ratios may be problematic.



Pathways to hydroxylated estrone metabolites

Can DIM be Taken with Medications?

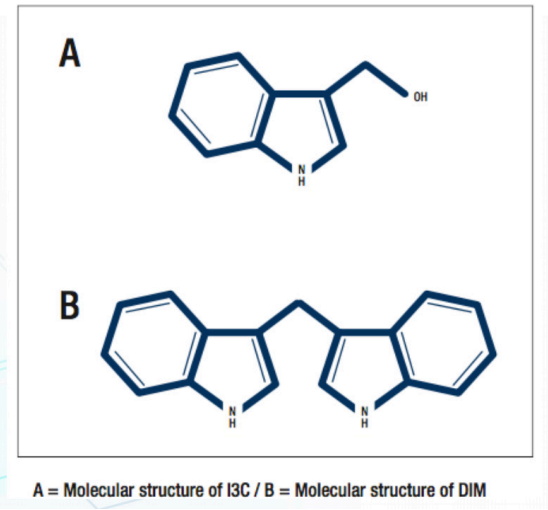
DIM is safe when taken with Tamoxifen, birth control pills and other herbs such as St. John's Wort that affect cytochrome p450 enzymes. Because of its effects on CYP enzymes, I3C, however, should not be taken with any of these. I3C blocks ovulation, can interfere with birth control pills and may alter the effects of many herbs such as St John's Wort and could lead to Tamoxifen toxicity if taken simultaneously. Researchers in Minneapolis found that DIM does not affect the metabolism of Tamoxifen. I3C on the other hand, converts Tamoxifen into N-desmethylTamoxifen 3 fold, which itself gets transformed into a genotoxic metabolite.[13]

Research titled Endocrine Disruption by I3C and Tamoxifen: Blockage of Ovulation may be disturbing to some. This is a quote from the Gao ovulation study: "In the current study, I3C disrupted ovulation already at doses that did not elicit systemic toxicity as indicated by a lack of reduced body weight gain, which was then observed at higher doses." Gao asserts that "I3C appears to have TCDD-like inhibitory effects on ovulation."14 TCDD is a strong dioxin chemical. Researchers in Denmark state "Indolo[3,2-b]carbazole (ICZ), which is formed in the acidic environment of the stomach after intake of I3C, has a similar structure to, and shares biological effects with, the well-known tumour promoter 2,3,7, 8- tetrachlorodibenzo-p-dioxin (TCDD)." This is the conclusion of their study: "Further studies are needed in order to clarify the anti- carcinogenic/carcinogenic effects of I3C and ICZ before high doses of I3C may be recommended as a dietary supplement." They feel that ICZ's tumour promoting activity is due to its activation of the Ah receptor and stimulation of certain cytochrome p450 enzymes mainly Cyp1a1, Cyp1a2 and Cyp1b1.[15]

DIM's proven safety means that DIM can be used by women wishing to get pregnant but should be discontinued during pregnancy and lactation. There are no known contraindications for DIM supplementation.

Should Men Take DIM?

Men who wish to prevent prostate cancer and men with a family history of prostate cancer should take DIM. Research published in the British Journal of Cancer, 2004 states," Prostate cancer mortality results from metastases to the bones and lymph nodes and progression from androgen-dependent to androgen-independent disease. Although androgen ablation was found to be effective in treating androgendependent prostate cancer, no effective life-prolonging therapy is available for androgenindependent cancer." Results of this study suggest that DIM induces apoptosis in PC3 cells, through the mitochondrial pathway suggesting that DIM is hopeful as a therapeutic strategy for the treatment of androgen-independent prostate cancer.11



A = Molecular structure of I3C / B = Molecular structure of DIM

According to UC Berkeley researchers, "DIM exhibits potent anti-proliferative and anti-androgenic properties in androgen-dependent human prostate cancer cells. DIM suppresses cell proliferation of LNCaP cells and inhibits dihydrotestosterone (DHT) stimulation of DNA synthesis." DIM is a strong competitive inhibitor of DHT binding to the androgen receptor. This study is titled: Plant-derived 3,3_-Diindolylmethane Is a Strong Androgen Antagonist in Human Prostate Cancer Cells.[10] An in vivo study in rats showed that DIM cut in half testosterone 16 alpha and 2 alpha-hydroxylation.[12]

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