



## AUSTRALIAN MENOPAUSE CENTRE

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### **DIM Information**

#### **DIINDOLYLMETHANE (DIM)**

Diindolylmethane, or DIM for short, is a plant indole—a plant compound with health-promoting properties. DIM and other plant indoles are found in all cruciferous vegetables. Cruciferous vegetables include cabbage, broccoli, brussels sprouts, and cauliflower. These plant indoles such as DIM affect estrogen metabolism in ways that might help prevent breast cancer, by modifying the rate of synthesis of estrone metabolites. It is also popular as an antioxidant.

DIM provides benefits in two ways:

- 1) The indole group binds to chemical carcinogens and activates enzymes which, in turn detoxify these harmful chemicals.
- 2) Acts as a catalyst to direct estradiol down a benign pathway to 2-hydroxyestrone thus decreasing levels of the carcinogenic 16-alpha hydroxyestrone, “bad estrogen” and also reducing the conversion of estrogens to Estrone.

There are 3 estrone metabolites

- 2-hydroxy-estrone which is shown to be beneficial
- 4-hydroxy-estrone which is shown to be carcinogenic
- 16-alpha-hydroxyestrone is implicated in cancer promotion

#### **WHAT DOES DIM DO?**

DIM shows great potential in preventing cancer, especially hormone-related cancers such as those of the breast and prostate. Researchers have been able to show that these plant indoles have powerful and diverse ways of stopping 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-hydroxyestrone).

A summary of recent studies shows that plant indoles such as DIM:

- Increase the conversion of estradiol to “weaker” (2-hydroxyestrone) estrogen, which is thought to reduce the incidence of breast cancer.
- Works in estrogen receptor negative breast cancer cells.
- Provides antioxidant protection
- Protects against the environmental toxin, dioxin



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### DIINDOLYLMETHANE & ESTROGEN BALANCE

Diindolylmethane (DIM) is the most active cruciferous derived substance for promoting beneficial, estrogen metabolism in both women and men. DIM is actually formed in vivo (in the body) from its precursor indole, Indole-3-carbinol (I3C), after the enzymatic release of I3C from parent glucosinolates found in all cruciferous vegetables.

The supplemental use of DIM began with early experiments which demonstrated that animal diets with added diindolylmethane, like diets with added cruciferous vegetables, appeared to prevent chemically induced cancer. Pure diindolylmethane was first used in 1987 as a dietary supplement in animals, shown to be non-toxic, and to prevent breast cancer caused by the well known human carcinogen, dimethylbenz-anthracene. Similarly, the initiation pathway to chemically induced colon cancer was inhibited with the diindolylmethane precursor, I3C.

The mechanisms by which DIM prevents cancer in animals has subsequently been shown to involve a **reduction in activity of the estrogen receptor system, promotion of beneficial estrogen metabolism, and support for selective apoptosis, or “programmed cell death” which removes damaged cells.**

Supplemental use of DIM in humans is effective in adjusting the pathways of estrogen metabolism to favour the production of 2-hydroxyestrogen metabolites. These shifts in estrogen metabolites were significant and showed an approximate 75% increase in production of 2-hydroxyestrone and a 50% decrease in 16-hydroxyestrone. An increased proportion of 2-hydroxy metabolites is correlated to protection from breast cancer.

Additional case-control studies have also documented that low levels of 2-hydroxy metabolites are associated with breast cancer in women, breast cancer in men, familial risk of breast cancer, uterine cancer, cervical cancer, and systemic lupus erythematosus. An increase in the rate of breast cancer has now been associated with lupus. Many established risk factors for breast cancer including obesity, high fat diets, and diets deficient in omega-3-fatty acids have also been correlated with low 2-hydroxy metabolite production.

Diindolylmethane is highly stable, requires no conversion in the stomach, and is the most active cruciferous indole in promoting beneficial estrogen metabolism. DIM enhances the protective mechanism of apoptosis, or programmed cell death, promoting beneficial elimination of damaged cells. The combination of these effects on cell behaviour, sets DIM apart from all other dietary substances and gives diindolylmethane a unique capability to promote beneficial actions of the estrogens.

Active apoptosis is central to preventing the initiation and promotion of breast, colon, and other cancers. Since these effects are specific to rapidly dividing cells, diindolylmethane does not prevent the beneficial effects of estrogen in supporting the health of the central nervous and skeletal systems.

In a nutshell, DIM is thought to create a safer cellular environment for estrogen.



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### THE IMPORTANCE OF DIINDOLYLMETHANE SUPPLEMENTATION FOR PRE AND POSTMENOPAUSAL WOMEN

In premenopausal women, the first age-related hormonal imbalance involves a decreased production of progesterone. This reduction in progesterone output during the second half or luteal phase of the menstrual cycle can cause irregular periods and contribute to premenstrual mood disorders.

**The “good estrogen” metabolites, 2-hydroxy and 2-methoxy estrogen are notable in that they stimulate increased progesterone production from ovarian cells.** By promoting this 2-hydroxy production, supplementation with DIM can help support progesterone production and maintain progesterone levels throughout the perimenopause. This balancing effect can benefit disorders associated with estrogen-progesterone imbalance including chronic, recurring breast pain, fibrocystic disease, and endometriosis.

### THE IMPORTANCE OF HEALTHY ESTROGEN METABOLISM IN MEN’S HEALTH

Recent work shows that estradiol, the active form of estrogen, provokes increases in prostate specific antigen (PSA) production in human prostate tissue. Increased PSA production was specifically inhibited by 2-methoxyestradiol, the beneficial estrogen metabolite whose production is promoted by DIM.

Environmental estrogens, high fat diets and pesticide residues in food all serve as additional sources of elevated estrogen exposure (often referred to as xenoestrogens - "foreign estrogens"). In addition, high fat diets, especially those rich in animal fats or omega-6 fatty acids can shift the metabolic pathways of estrogen towards the 16-hydroxy metabolites. These “bad estrogens” are associated with higher rates of benign breast disease, and cancer in both women and men.

Alternatively, diets rich in omega-3 fatty acids from fish or supplemented with diindolylmethane produce more of the “good estrogens” identified as the 2-hydroxy metabolites of estradiol and estrone. The use of cruciferous indoles in test animals has been shown to be associated with the prevention of spontaneous, estrogen related cancers of the breast and uterus.

When tested in animals, DIM is unique in its effectiveness to favorably shift estrogen metabolism and decrease the over activity of the estrogen receptor system. The supplemental use of DIM allows women to promote and maintain a safer metabolism of estrogen.

#### FAQs

#### **“Q: What can DIM achieve for Women by optimising estrogen metabolism?:**

“Breast tenderness, endometriosis, and uterine cervical dysplasia have been shown to improve with DIM supplementation. The use of both DIM and progesterone is recommended for women in their forties who have evidence of progesterone deficiency, such as irregular menstrual periods. DIM can help support natural progesterone production.”



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### **“Q: How does DIM impact on testosterone levels in women?”**

“It has been shown that testosterone supports physiologic responses in sexual arousal. In studies of mood and depression, testosterone alone or with estrogen was most effective in reducing depression. **DIM** promotes a consistent rise in the levels of ‘good’ estrogen metabolites. Even a small increase in the concentration of ‘good’ estrogen metabolites results in higher levels of free testosterone. Even tiny increases in amounts of free testosterone are capable of influencing mood and behavior since the brain possesses a multitude of hormone receptors that can be influenced by testosterone.”

### **“Q: DIM for Men—how can it be of benefit and what is “optimum” hormone balance for men?”:**

“DIM helps to eliminate active estrogen from the male body by promoting its conversion into the ‘good’ estrogen metabolites. These metabolites then free up testosterone by bumping it off the testosterone-binding proteins.

Optimum hormone balance for men is defined by strong testosterone activity and the lowest possible level of unmetabolised estrogen.”

### **“Q: What role does supplemental DIM play in an aging-intervention plan for men?”**

“Supplemental DIM reduces the effects of unmetabolised estrogen and promotes testosterone action. It does this by maximizing the testosterone-to-estrogen ratio in the body, thus increasing the activity of testosterone. By increasing the activity of testosterone, DIM can improve mood, fight depression, and support memory. DIM also can be used to help address many of the unwanted side effects of estrogen in men—particularly those that occur with the age-related accumulation of estrogen. DIM can now be used to reduce the risk of prostate enlargement and promote a healthy prostate. Optimum testosterone-to-estrogen hormonal balance achieved with the use of DIM can help to preserve a youthful urinary tract and prevent age-related prostate enlargement.”

### **“Q: What about the other cruciferous indole, indole-3-carbinol (I3C)?”**

Though used by some people as a dietary supplement, it turns out the I3C is not active in your body until it is converted into DIM. DIM is formed as I3C combines with itself, that is, two molecules of I3C combine to form DIM (a chemical process called dimerisation). This occurs only if just the right amount of stomach acid is present. The usual dose of DIM for women is 100 to 200 mg per day taken with food. The usual dose range of DIM for men is 200 to 400 mg per day taken with food.”

### **“Q: Are there any reported side effects associated with supplemental DIM?”**

“Some people taking DIM have noticed a darkening of their urine to a brownish color. This has been seen when DIM is taken by someone who drinks little water throughout the day. This is a normal, harmless occurrence and is not associated with any abnormalities in kidney function or health status.”