



## Clinical Applications

- Helps Maintain a Ratio Higher 2/16 of Hydroxy Estrogen\*
- Supports Healthy Balance of Testosterone and Estrogen\*
- Provides Antioxidant Cell Protection\*
- Promotes Healthy Inflammatory Response\*

*DIM provides 100 mg of diindolymethane (DIM), a compound classified as a "plant indole." Plant indoles are also called glucosinolates, which are found in cruciferous vegetables such as broccoli, cabbage, and cauliflower, and they are among the nutrients responsible for the widely recognized healthful properties of these foods, including the support of a healthy estrogen balance.\**

All Absolute Health Formulas Meet or Exceed cGMP Quality Standards

## Discussion

**Diindolymethane (DIM)** is derived from the primary plant indole found in cruciferous vegetables, known as indole-3-carbinol (I3C). Mastication, cooking, and other actions activate the enzyme myrosinase to convert I3C to DIM. Stomach acid additionally contributes to the formation of DIM, which is a more stable compound than I3C.<sup>1,2</sup> Research identifies beneficial actions of DIM on estrogen metabolism and associated conditions.

**Estrogen Metabolism** Estrogen balance plays an important role in health, and disturbances of this hormone are associated with polycystic ovary syndrome, endometriosis, osteoporosis, Alzheimer's disease, autoimmune disorders, male hypogonadism, schizophrenia, and breast, ovarian, and other estrogen-related cancers. Estrogen is involved in glucose homeostasis, lipid homeostasis, bone metabolism, brain function, follicular growth, skeletal growth, and ovulation. Estrogen biosynthesis involves the aromatization of androgen into estrogen.<sup>3,4</sup>

The main circulating estrogen is 17 beta-estradiol (E2), which is produced in the ovaries as a circulating hormone. In postmenopausal females and those without ovaries, E2 is synthesized in extragonadal sites to act locally as a paracrine, with the aromatization of androgens to estrogens playing a more significant role. Estrogen metabolism involves hydroxylation at the A-ring or D-ring by cytochrome P450 isoforms. This may occur on the C2 or C4 position in the A-ring or in the 16-alpha position in the D-ring, producing the metabolites 2-hydroxy estrone/estradiol, 4-hydroxy estrone/estradiol, and 2-hydroxy estrone/estradiol.<sup>5-11</sup>

The specific cytochrome P450 enzyme promotes which metabolite is produced. For example, CYP1B1 converts E2 to 16 alpha-hydroxy estradiol, whereas CYP1A1 converts it to 2-hydroxyestradiol. Both enzymes can also convert E1 and E2 into 4-hydroxy metabolites. The different metabolites have different functions in the body, and a balance is required for optimal health. The 16-alpha hydroxy estrone has a high capacity to bind to estrogen receptors and produce estrogenic effects, and 2-hydroxyestrone has little to no affinity for the estrogen receptor. The 4-hydroxy estrogens have the potential to cause DNA damage, generate mutations, and create oxidative damage. The lower affinity and subsequent decrease of bioavailable estrogens may be why the two-pathway metabolites relate to a lower risk of breast cancer. However, the ratio of metabolites and the clearance of estrogens may matter more than the level of the individual metabolites.<sup>6-11</sup>

Higher levels of 4-hydroxy estrogens and 16-alpha-hydroxy estrogens are associated with a higher risk of breast cancer.<sup>7</sup> High levels of 4-hydroxy estrogens are also associated with endometriosis.<sup>12</sup> A high 2:16 ratio (with 2 hydroxy to 16 hydroxy estrogens) is associated with reduced inflammation and a lower risk of breast cancer.<sup>8,13</sup> Upon activation, estrogen receptors trigger pathways for cell growth, proliferation, and inflammation in addition to pre-malignant pathology. These estrogen metabolites may stimulate the synthesis of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF- $\alpha$ ). They may also impact other conditions, including autoimmune diseases. Studies have found that higher levels of estrogen, including the hydroxylated metabolites, were significantly increased in the synovial fluid of patients with rheumatoid arthritis (RA).<sup>13-15</sup> One study found that the 2:16 ratio in patients with RA and systemic lupus erythematosus (SLE) was more than 20 times lower than healthy subjects due to significantly lower levels of 2-hydroxy estrogens. These results were independent of steroid use and sex.<sup>16</sup>

**DIM and Estrogen Metabolism** Certain compounds, such as DIM, can influence estrogen metabolism to determine which metabolite is synthesized, pushing the pathways toward the more harmful or beneficial metabolites.<sup>6,17</sup> DIM supports the synthesis of 2-hydroxyestrone, which in turn supports an increase of the 2:16 ratio without elevating the 4-hydroxy estrogens. This is likely due to its impact on cytochromes P450 (CYP) enzymes, supporting the expression of CYP1A1 over the other enzymes.<sup>1,18</sup> This positive impact on estrogen metabolism may also support conditions associated with higher levels of the more harmful estrogen metabolites.

\*These statements have not been evaluated by the Food and Drug Administration.  
This product is not intended to diagnose, treat, cure, or prevent any disease.



# Supplement Facts

Serving Size 1 softgel

Amount Per Serving	% Daily Value
Diindolylmethane (DIM)	100 mg *

\* Daily Value not established.

**Other Ingredients:** Medium chain triglycerides, softgel ingredients (bovine gelatin, glycerine, purified water, annatto [color]), quillaja extract, tocotrienols. DIM120-7

WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under the age of 6. KEEP OUT OF REACH OF CHILDREN. In case of accidental overdose, call a doctor or poison control center immediately.

## Directions

Take one softgel per day with a meal, or as directed by your healthcare provider.

## Does Not Contain

Free of the following common allergens: lactose, starch, milk/casein, eggs, fish, shellfish, tree nuts, peanuts, wheat/gluten, corn, yeast, and soybeans or other fillers that can cause digestive intolerance. Contains no artificial colors, flavors, or preservatives.



## References

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