

Indole-3-Carbinol and Its Advantages Over DIM

Indole-3-carbinol (I3C) is a naturally occurring compound found in cruciferous vegetables and is also considered a primary contributor in the health benefits these foods provide because it has been associated with activities such as chemoprevention and endocrine balance.¹⁻⁴ As we eat a serving of a crucifer such as broccoli or cauliflower, the I3C in the food is released during chewing and transported to the stomach. Once in the stomach, it is converted to many active compounds, one of which is diindolylmethane (DIM).^{5,6} The conversion of I3C to its many active compounds requires the natural acidic environment of the stomach, and the majority of people make enough stomach acid for this conversion. Individuals who do not have enough stomach acid should be provided with an appropriate supplement to support production of stomach acid, since they will not only have problems with I3C conversion but also with digestion of many other important nutrients like proteins, vitamin B₁₂, and folate.

Supplementation with I3C may have benefits over DIM for several reasons. The most important one is that the majority of the published literature and clinical trials on the important health benefits of cruciferous vegetables has been on I3C, while very little data exists to support DIM as having all of the same activities. Studies in human clinical trials have shown that at doses of 300 to 500 mg per day, I3C can influence estrogen metabolism and promote

formation of 2-hydroxyestrone (2-OH-estrone), which is considered the protective estrogen.⁷⁻⁹ As an example of its influence on estrogen metabolism, early clinical trial data suggest that in doses of 200 and 400 mg per day, I3C may support remission in cervical intraepithelial neoplasia.¹⁰ The estrogen metabolism data for I3C are compelling enough that the National Cancer Institute has nominated I3C for testing as a preventative for breast cancer.¹¹

It is known that I3C can form the spectrum of active compounds associated with the endocrine balancing and chemopreventative effects of crucifers, but there is no conclusive evidence that DIM can mimic all the activities of I3C. Most likely, it cannot. For instance, along with the ability to induce production of 2-OH-estrone, I3C has been shown to induce both phase I and phase II detoxification activities, regulate cell-cycle progression, suppress activation of invasion-promoting molecules associated with breast cancer cell metastasis, affect transcription of the estrogen receptors in human cells, and reverse the activation of multidrug resistance in cancer cells.¹²⁻¹⁵ Many of these activities can be related to the multiple actives produced after ingestion of I3C. For instance, in addition to DIM,¹⁶ two other compounds produced from I3C have been shown to influence estrogen metabolism. These include indolo[3,2-b]carbazole (ICZ), which exhibits antiestrogenic activity and

supports phase I detoxification activities; and hexahydrocycloindole (HNTI), which binds the estrogen receptor and shows chemical structure similarities to tamoxifen.^{17,18}

Supplementation with I3C is taking the natural approach and Mother Nature's wise lead, which is also consistent with the functional approach as opposed to the drug-model of "one compound for one specific activity." We know that cruciferous vegetable intake is safe and that we should increase our intake of these foods for health support. I3C has substantial clinical data on its efficacy and safety, and has been shown to provide a wide spectrum of active functional compounds.^{19,20} Although a single compound like DIM may have some of the necessary activities, it may also imbalance the system. For example, we know that I3C can induce both phase I and phase II detoxification activities; however, we don't know whether DIM can also induce both activities or just induces phase I detoxification. We also know that compounds derived from I3C are responsible for a variety of effects, such as suppression of cell growth and proliferation, but it is not clear that DIM can support these activities on its own. As an analogy, we may standardize an herbal extract to one specific active, but we still want the whole spectrum of compounds generally found in that herbal remedy for therapeutic use.

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