



Innovative
by nature

BIO DIM[®] I-3-C Complex

Hormonal Health Made Simple*

Be Strong[™]

*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.

Dear Practitioner,

When it comes to cell and hormonal health, you can never be too careful. Science looks to microenvironments to explain the world for a reason—the constituents of our bodies that are invisible to us and operate without our immediate knowledge are also the most important.

Patients may remain unaware of just how important cell and hormonal health are, and how greatly both affect our daily actions, until it is too late for adaptation or repair. That's why it's important for you to bring the issue to light and offer simple solutions for overall health.

Balance is a beautiful thing.

While estrogen is responsible for many worldly miracles, studies on the effects of certain estrogen compounds (like those caused by metabolism of xenoestrogens) indicate that we can also look to estrogen for information on apoptosis.

DIM I-3-C offers comprehensive support for hormonal balance and normal apoptosis through addressing estrogen metabolism within the body, which can contribute to bone health and mood balance. A combination of indole-3-carbinol, patented DIMPRO (a blend of diindolylmethane with phosphatidylcholine and vitamin E), calcium glucarate, HMRLignans, vitamins E and D3 and trans-resveratrol provides a wide spectrum of support for cellular health, from antioxidant support to proper elimination of foreign elements.**

Begin the process of bringing balance into your patients' lives today. Help them understand the value of cellular and hormonal health and they should start down the path to understanding their cells' environments while they have the opportunity.

To your practice and your patients' good health,

*Dom Orlandi
President
DaVinci Laboratories*

*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.

Introduction

Because hormonal balance is so important, many patients look to hormone replacement therapies in times of production of excess estrogenic compounds to ensure that normal metabolism occurs. When one hormone, progesterone, is deficient and another, estrogen, is dominant, we consider this an imbalance that may cause or be caused by a negative shift in estrogen metabolism. When estrogen metabolism is imbalanced, metabolites that are more estrogenic are produced and not properly eliminated.

Estrogen is commonly associated with women, but the activity and metabolism of estrogenic compounds occur in all human bodies. The current consensus on estrogen is that its compounds have a wide range of physiological effects.

Estrogenic Compound Research:

Studies generally cite urinary 2-hydroxyestrone (2-OHE1), 16alpha-hydroxyestrone (16alpha-OHE1) and 2-OHE1 to 16 alpha-OHE1 ratios as the expression necessary for research.

A 2000 study published in *Epidemiology* confirmed that the maintenance of hormonal balance is an important factor in reproductive cell health: "Results of this prospective study support the hypothesis that the estrogen metabolism pathway favoring 2-hydroxylation over 16-hydroxylation is associated with" reduced risks of reproductive cellular health concerns in women. (Muti et al., 2000)

This information isn't as pervasive as it needs to be in order for patients to understand the effects of excess or deficient estrogen on their own. There is no shortage, however, of people that would be affected by the information:

- According to a 1998 report by the Center for Disease Control, "93 percent of estrogen-deficient women with osteoporosis as defined by bone material density were unaware of this condition." ("Osteoporosis Among Estrogen-Deficient Women — United States, 1988–1994", 1998)
- In the United States alone, hip fractures result in approximately 300,000 hospital visits and roughly \$9 billion in direct medical costs annually. "Most of these fractures result from osteoporosis among women who experience accelerated bone loss after natural or surgically induced menopause," which can cause a shift in estrogen metabolism. ("Osteoporosis Among Estrogen-Deficient Women — United States, 1988–1994", 1998)

Enter Healthy Alternatives

Because so many people are unaware of the potentially harmful effects of hormone imbalance, it is important that healthcare practitioners speak up. Recommendations from individual doctors are one of the main causes of changes in behaviors.

Even with knowledge of potential issues, many patients will still seek drug therapy instead of a lifestyle change. In fact, the 2008 National Ambulatory Medical Care Survey data show us that 74 percent of physician's office visits involve mention of medication and the National Center for Health Statistic's 2007-2008 report notes that over the last 10 years, the percentage of Americans who took at least one prescription drug in the past month increased from 39 to 45 percent, while the use of three or more drugs increased from 12 to 18 percent. This increase is fueled by the large marketing budgets of the pharmaceutical industry.

*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.

Spending for prescription drugs in the United States was \$234.1 billion in 2008, which was more than double what was spent in 1999. Aside from the excessive burden of the cost of health care in the United States, this type of trend has far-reaching consequences, not the least of which is the concern that the remedy may present more issues than the ailment. (Gu et al., 2010)

The Difference Your Patients Are Seeking

Even as prescription drug use continues to rise, there is a growing movement toward natural, alternative and non-prescription solutions for every day health.

The National Center for Health Statistics confirms that in 2007, almost 4 out of 10 adults (38.3%) had used some type of complementary and alternative medicine (CAM) in the past 12 months.

The 2007 National Health Interview Survey (NHIS) alerts us to the fact that Americans spent \$33.9 billion out of pocket on visits and purchases of CAM products, classes and materials.

The list of most common conditions prompting CAM use includes several conditions potentially influenced by estrogen, such as headaches, stress, sleep issues and deep tissue aches.

What's Next?

Increased clinical research tells us that there are a variety of supplements to support a beneficial shift in estrogen metabolism.* ***DIM I-3-C is at the leading edge of this movement because of its unique combination of ingredients, which includes both indole-3-carbinol and diindolylmethane, both of which are backed by years of extensive research.***

Of course, we recognize that a variety of lifestyle changes may be helpful. At DaVinci® Laboratories, we recommend creating a total wellness package to support your patients' overall health with regard to hormonal balance. The best hope for compliance is a patient's own positive perception of his or her results.

Discover DIM I-3-C's formula to support overall cellular health and normal apoptosis through supporting hormone balance, and find out what you need to know to decide if DIM-I-3-C is the right formula for your patients.*

DIM- An Overview

Diindolylmethane, a phytoestrogen found in cruciferous vegetables like broccoli and cauliflower, is a compound formed during glucobrassicin breakdown (which occurs during digestion due to the catalytic reaction that occurs when the cell wall ruptures and the myrosinase enzyme is released). DIM is a lipophilic oil-soluble compound whose absorption is promoted by the presence of lipophilic compounds like vitamin E. * (BioResponse patented DIM is a blend of diindolylmethane, vitamin E and another lipophilic compound, phosphatidylcholine.) Shown below, DIM has been researched extensively in recent years to determine its relationship to cell division and targeted proteins that commonly affect apoptosis and cellular health.

What does the research show?

Research on estrogen metabolism has shown that hormone balance may have a large effect on reproductive cellular health. The subsequent research on the ingredients in DIM I-3-C is focused on their support of cellular health, apoptosis and hormone balance for this reason.*

Research on DIM has been largely focused on its support of estrogen metabolism and balance.*

*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.

Indole-3-Carbinol: An Overview

Indole-3-Carbinol is similarly contained within cruciferous vegetables and produced by glucobrassicin breakdown, but DIM is a product of I3C, meaning the same catalyst and subsequent reaction are not required for I3C to enter the body.

I3C targets certain proteins in the body and supports a shift in estrogen metabolism toward less estrogenic compounds.* Research is largely focused on its potential antioxidant properties.

What does the research show?

Because DIM is a product of Indole-3-Carbinol, they are often included in the same studies, especially those that focus on apoptosis. See the question & answer section or the sidebar of page 6 for more information on our decision to include both ingredients.

The 2001 publication of research from the North Shore-Long Island Jewish Research Institute showed new benefits of I3C. Researchers asked whether I3C and its major product diindolylmethane (DIM) could induce apoptosis and whether this effect could be observed in vivo. Resulting “data confirm the proapoptotic action of I3C on transformed cells in vitro, extend the observations to cervical cells and to DIM and show for the first time that dietary I3C results in increased apoptosis in target tissues in vivo.” (Chen, Qi, Auburn, & Carter, 2001)

A 1991 study highlighted the demonstrated effects of I-3-C, with researchers concluding that a “protective effect may be mediated in part by the increased 2-hydroxylation and consequent inactivation of endogenous estrogens.” (Bradlow, Michnovicz, Telang, & Osborne, 1991, p.1571-74)

The potential of I-3-C as a dietary supplement is astounding. This compound supports a beneficial shift in estrogen metabolism, which supports hormonal balance as well as weight management and other hormone-influenced activities of the body, like normal mood balance.*

Calcium Glucarate: An Overview

Calcium glucarate is a perfect addition to DaVinci's DIM I-3-C formula because of its supportive effects on apoptosis.* A naturally occurring compound, glucaric, is combined with calcium to create this compound which supports detoxification processes within the glucuronidation pathway and, consequently, hormonal balance by supporting proper excretion of excess hormones from the body.* This process is especially important for those exposed to high levels of xenoestrogens like those found in insecticides, lubricants, adhesives, paints and personal care products like shampoos and lotions. It is important to also note that calcium-d-glucarate contains vitamin D, essential for the proper absorption and utilization of calcium, and a supporter of bone health.*

*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

Amount Per Serving

Vitamin D3 (as Cholecalciferol)	1000 IU
Vitamin E (as d-alpha Tocopheryl Succinate)	50 IU
Calcium (as Ca D-Glucarate)	50 mg
Indole-3-Carbinol	200 mg
DIM® (a proprietary enhanced bioavailability complex of starch, diindolylmethane, Vitamin E as d-alpha tocopheryl succinate, phosphatidylcholine, silica)	100 mg
Green Tea (<i>Camellia sinensis</i>) Leaf Extract	250 mg
yielding EGCG	175 mg
HMRlignan™ (a Norway Spruce (<i>Picea abies</i>) Standardized Lignan Extract)	30 mg
Trans-Resveratrol (from <i>Polygonum cuspidatum</i> Root Extract)	50 mg

Suggested Use

As a dietary supplement, take 2 capsules daily, or as directed by your healthcare practitioner.

Warning: If you are pregnant or nursing, consult your healthcare practitioner before taking this product.

What does the research show?

Obviously, working under the premise that estrogenic compounds produced within or absorbed into the body can result in estrogen dominance, any nutrient that supports the detoxification pathways of the body or supports free radical neutralization and elimination will be supportive of cellular health and hormonal balance.*

In a study titled “A comparative study of antioxidative activity of calcium-D-glucarate, sodium-D-gluconate and D-glucono-1,4-lactone in a human blood platelet model,” it was determined that “sources of large amounts of tested derivatives have beneficial effects on platelets under oxidative stress,” showing that calcium-d-glucarate can function as a free-radical fighter.* (Saluk-Juszczak, 2010)

HMR/lignan™: An Overview

HMR/lignan™ is another important addition to DaVinci’s DIM I-3-C. HMR/lignan™ is a lignan (a phytoestrogen that acts as a free-radical fighter) derived from Norwegian Spruce. Lignans are important for their free radical scavenging supportive properties.* In binding to estrogen receptors, these compounds may support the body’s ability to interfere with abnormal proliferation.*

What does the research show?

Lignan 7-hydroxymatairesinol (also known as HMR/lignan™) is a precursor of the mammalian lignan enterolactone (EL). One study “investigated the estrogenicity of HMR and of EL in comparison to estradiol (E2), by measuring their effects on growth and apoptotic markers in the human estrogen-sensitive cell line MCF-7.” The results indicate that “dietary supplementation with HMR may result in a mild estrogenic activity,” along with free-radical fighting activity, meaning HMR can play a supportive role in normal apoptosis.* (Consentino et al., 2007, p. 140-147)

Trans-Resveratrol: An Overview

Resveratrol is a phytoalexin generally known for its presence in red wine—of course, this association actually comes from the fact that resveratrol is found in certain fruits (grapes) used for wine-making. It is well known that resveratrol offers free-radical fighting support.* Still, researchers often cite resveratrol’s low bioavailability as an inhibitory factor in its ability to support bodily processes, hence DIM I-3-C’s inclusion of trans-resveratrol, a compound wherein the molecules face away from one another.

What does the research show?

Trans-resveratrol is the active form of resveratrol, a natural polyphenol with powerful free-radical fighting activity that supports the body’s ability to protect its cells against dangerous free radicals that can contribute to prostate problems.* Studies with resveratrol indicate that this polyphenol may interfere with the activity of aromatase, an enzyme that converts testosterone to estrogen.*

In a 2005 study of two rat groups, researchers investigated trans-resveratrol because one of the known “mechanisms by which it exerts its action is through modulating the estrogen response systems. Because estrogen is involved in male reproductive biology, we investigated the effect of trans-resveratrol on testis and spermatogenesis,” with the following results: “Sperm counts were significantly greater in the resveratrol-treated rats (24.8 +/- 3.30 x 10(7)) than in the control group (14.1 +/- 0.80 x 10(7)), but sperm quality did not differ. Serum concentrations of gonadotrophins and testosterone were significantly higher in the resveratrol-treated group,” indicating a beneficial shift in estrogen metabolism. (Juan et al., 2005, p. 757-60)

*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.

Vitamin E:

Vitamin E is an important ingredient in DIM I-3-C, but as there exists a plethora of research on the vitamin, highlighting its main purpose in this formula will allow your patients to better understand its supportive properties.* Vitamin E is a powerful antioxidant that helps protect cells.* Defective cells are believed to result from oxidative damage to DNA caused by free radicals. Antioxidants such as vitamin E help protect against the damaging effects of free radicals.* Most important, perhaps, is the fact that DIM is a lipophilic oil-soluble compound, and vitamin E is also a lipophilic compound that supports DIM's absorption.*

DIM I-3-C: An Uncommon Response To A Common Concern

DaVinci® Laboratories' DIM I-3-C is unparalleled in its comprehensive nature, making it the most advanced formula on the market today for optimal support of hormonal balance and normal apoptosis.* The BioResponse DIM in DaVinci's formula is a proprietary blend of diindolylmethane, vitamin E and phosphatidylcholine and is the only DIM currently used in clinical studies. This microencapsulated, absorbable and patented DIM is an especially significant addition to DIM I-3-C because lipophilic compounds support optimal bioavailability and absorption of DIM.*

This comprehensive formula has been designed to support hormonal balance through addressing factors like detoxification pathways, enzyme inhibition and platelet aggression, as well as to support the body's ability to regulate mood.* As I-3-C has been shown to support a shift in estrogen metabolism towards less estrogenic metabolites, DIM I-3-C supports a beneficial shift in estrogen sensitivities.* The formula is designed to provide support for the health of the breast, prostate, cervix and other reproductive organs.*

Hormones make the world go 'round.

So it makes sense that those looking for support for their bodies' cellular health are searching for a supplement to address hormonal balance. DIM-I-3-C offers free-radical fighting support, as well, making it a formula in which your patients can trust.*

BIO DIM I-3-C Complex Q & A

Why did you include . . .

Q. Both DIM and I-3-C? What is the difference?

A. DIM is a product of I-3-C and a catalyst enzyme in the human stomach. While I-3-C is highly reactive and soluble, DIM is highly stable but insoluble. Including both nutrients in this formula supports the conversion process so as to not interfere with nutrient delivery. It is generally accepted that DIM can act as a complement to I-3-C, supporting its activity.*

Q. Vitamin D3?

A. Vitamin D3 is essential for the formation, growth and repair of bones and is also supportive of calcium absorption and immune function.* In this formula, it is also meant to support cellular differentiation and supports apoptosis.*

Q. Green tea extract?

A. Green Tea Extract comes from the tea plant, *Camellia sinensis*, which is an excellent source of potent polyphenols/bioflavonoids with powerful free-radical fighting properties to support free radical neutralization.* Research has identified the polyphenol epigallocatechin-3-gallate (EGCG) as the most active agent in green tea.* EGCG also supports thermogenesis and weight management.*

For more information on resources, please see the document entitled "Resources on Estrogen Metabolism."

*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.

About DaVinci[®] Laboratories

For over 45 years, DaVinci[®] Laboratories has developed and produced leading edge, high quality supplements exclusively for health care professionals.

In 1972, Guido and Maria Orlandi founded FoodScience Corporation on a passion for discovering natural alternatives for human and animal health solutions. Our flagship product, N,N-Dimethylglycine (DMG), led the charge.

Today, a high level of innovation and evidence-based science form a strong foundation of our product development process. Research and Development team members work closely with our Scientific Review Boards to help ensure these values lead the careful creation of every one of our formulas.

The Orlandi family's original commitment to finding the best natural alternative health solutions stuck with the family through the years. Guido's son, Dom, and Dom's wife, Claudia, moved the company forward based on these foundational principles. Today, two members of the Orlandi family play integral roles in management. Guido's grandson, Dom, is president and Claudia manages the family trust which owns our company.

Over 45 years of experience in product development now allows our company to provide custom formulation and private labeling options for our customers who, like Guido Orlandi, are wholly committed to health, science and innovation.

References

- Bradlow, H.L., Michnovicz, J., Telang, N.T., Osborne, M.P. (1991) Effects of dietary indole-3-carbinol on estradiol metabolism and spontaneous mammary tumors in mice. *Carcinogenesis*, 12(9): 1571-4. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/1893517>
- Centers for Disease Control and Prevention (1988). Osteoporosis Among Estrogen-Deficient Women -- United States, 1988-1994. *Morbidity and Mortality Weekly Report*, 47(45); 969-973. Retrieved from <https://www.cdc.gov/mmwr/preview/mmwrhtml/00055690.htm>
- Cosentino, M. et al. (2007) Estrogenic activity of 7-hydroxymatairesinol potassium acetate from Norway spruce (*Picea abies*) knots and of its active metabolite enterolactone in MCF-7 cells. *Pharmacological Research*, 56(2) 2007, Pages 140-147. Retrieved from <http://www.sciencedirect.com/science/article/pii/S1043661807000990>
- Da-Zhi Chen, Mei Qi, Karen J. Auburn, Timothy H. Carter; Indole-3-Carbinol and Diindolylmethane Induce Apoptosis of Human Cervical Cancer Cells and in Murine HPV16-Transgenic Preneoplastic Cervical Epithelium, *The Journal of Nutrition*, Volume 131, Issue 12, 1 December 2001, Pages 3294–3302, <https://doi.org/10.1093/jn/131.12.3294>
- Gu Q, Dillon CF, Burt VL. Prescription drug use continues to increase: U.S. prescription drug data for 2007–2008. NCHS data brief, no 42. Hyattsville, MD: National Center for Health Statistics. 2010.
- Joanna Saluk-Juszczak (2010) A comparative study of antioxidative activity of calcium-D-glucarate, sodium-D-gluconate and D-glucono-1,4-lactone in a human blood platelet model, *Platelets*, 21:8, 632-640. Retrieved from <https://www.tandfonline.com/doi/abs/10.3109/09537104.2010.512210>
- M. Emília Juan, Eulalia González-Pons, Thais Munuera, Joan Ballester, Joan E. Rodríguez-Gil, Joana M. Planas; trans-Resveratrol, a Natural Antioxidant from Grapes, Increases Sperm Output in Healthy Rats, *The Journal of Nutrition*, Volume 135, Issue 4, 1 April 2005, Pages 757–760, <https://doi.org/10.1093/jn/135.4.757>
- Muti, P., Bradlow, H., Micheli, A., Krogh, V., Freudenheim, J., Schünemann, H., . . . Berrino, F. (2000). Estrogen Metabolism and Risk of Breast Cancer: A Prospective Study of the 2:16-Hydroxyestrone Ratio in Premenopausal and Postmenopausal Women. *Epidemiology*, 11(6), 635-640. Retrieved from <http://www.jstor.org/stable/3703815>
- National Center for Complementary and Integrative Health. (2017). The Use of Complementary and Alternative Medicine in the United States. Retrieved from https://nccih.nih.gov/research/statistics/2007/camsurvey_fs1.htm
- National Center for Health Statistics. (2007). Health, United States, 2007, p 336. Hyattsville, MD: 2007. Retrieved from <https://www.cdc.gov/nchs/data/hus/07.pdf>
- National Center for Health Statistics (2008). National Ambulatory Medical Care Survey: 2008 Summary Tables. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2008_namcs_web_tables.pdf