

## For improvement of recurrent breast pain. Helps in reducing pain associated with cyclical mastalgia.

RxBalance™ Breast-Plex contains BioResponse DIM®, which is formed by acid-catalyzed dimerization of indole-3-carbinol. It appears to support the activity of specific enzymes that improve estrogen metabolism. Scientific research shows that diindolylmethane (DIM) increases the level of "good" estrogens (2-hydroxy estrogen) while reducing the level of "bad" estrogens (16-hydroxy estrogen). In its pure, crystalline state, diindolylmethane is insoluble in water and fats, making it poorly absorbed by the human body. RxBalance™ Breast-Plex uses BioResponse DIM®, the only patented absorption-enhanced formulation for diindolylmethane. BioResponse DIM® combines vitamin E and phosphatidylcholine with DIM, then microencapsulates the combination to deliver enhanced bioavailability.

### Ingredients: Medicinal

Each capsule contains:

BioResponse DIM®	120 mg
providing:	
3,3'-Diindolylmethane	30 mg
Vitamin E (d-alpha tocopheryl succinate)	7.37 mg AT/11 IU
Phosphatidylcholine ( <i>Glycine max</i> seed)	5 mg

### Ingredients: Non-medicinal

Cellulose, corn starch, silicon dioxide, stearic acid, hypromellose.

This product does not contain dairy, egg, gluten, shellfish, sulfites, animal derivatives or artificial colours, flavours or preservatives.

### Recommended Use

For symptomatic improvement of cyclical mastalgia (recurrent breast pain). Helps in the reduction and management of cyclical mastalgia symptoms in premenopausal women. Helps in reducing pain associated with cyclical mastalgia.

### Recommended Dose

Adults take 2 capsules daily for three months. For prolonged use, consult a health care practitioner.

### Risk Information

Do not use if you are pregnant or breastfeeding. Consult a health care practitioner prior to use if you are trying to conceive or if you have a liver disorder and/or a predisposition to cancer. Harmless changes in urine colour may occur with the use of this product.

### Interactions with Drugs/Supplements

Consult a health care practitioner prior to use if you are taking prescription medication.

### Dosage Form Description

Clear, hard gelatin capsule with an off-white to beige coloured fill. Colour variance is normal.

### Packaging

Available in bottles of 60 vegetable capsules.

### Stability

Shelf life of 3 years when stored in a cool, dry place.

### Ingredient Description

Diindolylmethane (DIM) is an indole plant nutrient found in cruciferous vegetables, such as broccoli, cabbage, Brussels sprouts, and cauliflower. Unlike other plant nutrients, such as soy isoflavones, DIM has been shown to have unique and distinct hormonal benefits, including its ability to favourably modify estrogen metabolism in the direction of greater 2-hydroxy estrogen production.<sup>1</sup> BioResponse DIM® is a microencapsulated preparation that contains DIM, vitamin E, and phosphatidylcholine, co-dried to enhance DIM availability. Vitamin E (d-alpha tocopheryl succinate) is a potent antioxidant that protects the body from free radical damage, and phosphatidylcholine plays a role in regulating the absorption of certain lipids and lipid-soluble vitamins.



## Reason for Combination

Supplemental use of DIM can be effective in adjusting the pathways of estrogen metabolism to favour the production of 2-hydroxy estrogen metabolites. An increased proportion of 2-hydroxy metabolites is correlated with protection from familial risk of breast cancer, uterine cancer, cervical cancer, and systemic lupus erythematosus. Low 2-hydroxy estrogen production is also associated with mid-life weight gain, cyclical mastalgia, obesity, and elevated systolic blood pressure in otherwise healthy post-menopausal women. DIM, at low doses, also promotes healthy estrogen metabolism and prostate health in men, and is a rational dietary intervention for estrogen's role in male "Andropause".

## Research Synopsis

1. An intervention study investigated the efficacy and safety of absorbable diindolylmethane (BioResponse DIM®) in alleviating symptoms of cyclical mastalgia (recurrent breast pain). Otherwise healthy premenopausal women with cyclical mastalgia were given absorbable diindolylmethane (DIM) or placebo for consecutive three-month periods in a randomized, double-blind, crossover study. Breast symptoms were monitored using daily entries in a "breast pain diary" as the assessment tool. Urine and blood samples were collected to confirm safety and the impact of absorbable DIM on estrogen metabolism. Results showed clinical improvement with absorbable DIM, but not with the placebo. A statistically significant reduction in duration of breast pain, severity of pain, swelling, and soreness accompanied absorbable DIM use, based on comparison of visual analog pain scores from treatment and placebo periods. In addition, absorbable DIM was shown to increase the ratio of 2-hydroxy to 16-hydroxy estrone metabolites in urine. Supplementation with absorbable DIM was found to be an effective intervention for cyclical mastalgia. The researchers concluded that its use as a dietary supplement deserves further investigation in conditions where modifying estrogen metabolism may be of benefit.<sup>1</sup>
2. Dietary indoles, present in *Brassica* plants such as cabbage, broccoli, and Brussels sprouts have been shown to provide potential protection against hormone-dependent cancers. 3,3'-Diindolylmethane (DIM) is under study as one of the main protective indole metabolites. Postmenopausal women aged 50 to 70 years from Marin County, California, with a history of early-stage breast cancer were screened for interest and eligibility in this pilot study on the effect of absorbable DIM (BioResponse DIM®) supplements on urinary hormone metabolites. The treatment group received daily DIM (108 mg DIM/day) supplements for 30 days, and the control group received a placebo capsule daily for 30 days. Urinary metabolite analysis included 2-hydroxy estrone (2-OHE1), 16- $\alpha$ -hydroxyestrone (16- $\alpha$ -OHE1), DIM, estrone (E1), estradiol (E2), estriol (E3), 6- $\beta$ -hydroxycortisol (6- $\beta$ -OHC), and cortisol in the first morning urine sample before intervention and 31 days after intervention. DIM-treated subjects, relative to placebo, showed a significant increase in levels of 2-OHE1, DIM, and cortisol, and a nonsignificant increase of 47% in the 2-OHE1/16- $\alpha$ -OHE1 ratio from 1.46 to 2.14. In this pilot study, DIM increased the 2-hydroxylation of estrogen urinary metabolites.<sup>5</sup>
3. A study published in *Molecular Pharmacology* in 2006 showed that DIM shows promising cancer-protective activities, especially against mammary neoplasia in animal models. The researchers had observed previously that DIM induced a G(1) cell-cycle arrest and strong induction of cell-cycle inhibitor p21 expression and promoter activity in both estrogen-responsive and estrogen-independent breast cancer cell lines. They also showed that DIM up-regulates the expression of interferon-gamma (IFN-gamma) in human MCF-7 breast cancer cells, which may contribute to the anticancer effects of DIM because IFN-gamma plays an important role in preventing

the development of primary and transplanted tumours. In the 2006 study, the researchers observed that DIM activated the IFN-gamma signaling pathway in human breast cancer cells. DIM activated the expression of the IFN-gamma receptor (IFNGRI) and IFN-gamma-responsive genes p56- and p69-oligoadenylate synthase (OAS). In cotreatments with IFN-gamma, DIM produced an additive activation of endogenous p69-OAS and of an OAS-Luc reporter and a synergistic activation of a GAS-Luc reporter. DIM synergistically augmented the IFN-gamma-induced phosphorylation of signal transducer and activator of transcription factor 1, further evidence of DIM activation of the IFN-gamma pathway. DIM and IFN-gamma produced an additive inhibition of cell proliferation and a synergistic increase in levels of major histocompatibility complex class-1 (MHC-1) expression, accompanied by increased levels of mRNAs of MHC-1-associated proteins and transporters. These results reveal novel immune activating and potentiating activities of DIM in human tumour cells that may contribute to the established effectiveness of this dietary indole against various tumour types.<sup>4</sup>

4. A study in mice led by researchers at the University of California, Berkeley, showed that DIM is effective in augmenting the immune response. Specifically, DIM led to a jump in levels of four types of cytokines: interleukin-6, granulocyte colony-stimulating factor, interleukin-12, and interferon-gamma. Compared with a control sample, DIM doubled the number lymphocytes. The researchers concluded that DIM is a potent stimulator of immune function, which might contribute to the cancer-inhibitory effects of this indole.<sup>5</sup>

## References

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BioResponse DIM® is a patented, enhanced bioavailability, oral delivery system for diindolylmethane (U.S. patent # 6,086,915) and for breast health (U.S. patent #6,689,387) licensed from BioResponse, L.L.C., Boulder, Colorado.

PRODUCT CODE: 403 285 - 60 Vegetable capsules

**RX BALANCE**

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Not for use if you are pregnant or breastfeeding. For pregnant or breastfeeding women, consult your doctor. Each capsule contains 1.0 mg of 3,3'-diindolylmethane. Ingredients: 3,3'-diindolylmethane, Phosphatidylcholine, Vitamin E, Lecithin, Stearic acid, Magnesium stearate, Cellulose, Hydroxypropyl methylcellulose, Polyethylene glycol, Croscarmellose, Polyvinylpyrrolidone, and Purified Water. Contains 60 capsules. © 2010 RX Balance, L.L.C. All rights reserved.

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