

## DIM 200 plus CDG 100

### TECHNICAL SUMMARY

Protocol For Life Balance® DIM 200 plus CDG 100 promotes healthy hormone metabolism by supporting your body's normal detoxification processes.\* The featured ingredient, diindolylmethane (DIM), is a phytochemical that's a metabolite of certain compounds found in cruciferous vegetables such as broccoli, Brussels sprouts, and cabbage. We've also included calcium D-glucarate (CDG) to support the glucuronidation process, an important mechanism of detoxification, aiding in the elimination of certain environmental toxins from the body.\*

#### Structure formula:

- DIM: diindolylmethane. (Figure 1) DIM is one of the metabolites of Indolyl-3-carbinol, a compound naturally present in cruciferous vegetables.
- Calcium D-glucarate: Calcium D-glucarate is the calcium salt of D-glucaric acid. (Figure 2) D-glucaric acid is naturally present in small quantities in fruits and vegetables (for reference, one orange, the most abundant fruit source, has around 5 mg glucaric acid).

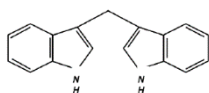


Figure 1: DIM

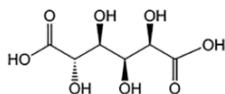


Figure 2: D-glucaric acid

#### Chemical name:

- DIM: 3,3-diindolylmethane
- Calcium D-glucarate: (2S,3S,4S,5R)-2,3,4,5-tetrahydroxyhexanedioic acid

**Allergen and Additive Disclosure:** Not manufactured with yeast, wheat, gluten, soy, corn, milk, egg, fish, shellfish, or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens. This product is not considered vegetarian/vegan as sodium copper chlorophyllin is isolated from the excreta of silk worms.

**Delivery Form:** Vegetable capsules

### ROLE AS NUTRIENT/FUNCTION

- DIM is a multi-functional compound. In laboratory experiments it was shown to support the liver CYP detoxification system.\* It was also studied for its ability to regulate different stages of the division cell cycle of cell lines isolated from breast, cervix, thyroid, colon, ovarian, and thyroid tissues.\* Many other DIM functions have been described at the cellular and molecular levels in laboratory settings, including but not limited to regulation of oxidative stress, of enzymatic systems, of transcription factors, of autophagy and apoptosis processes.\* More research is needed to confirm how these properties translate into clinical benefits.

## Supplement Facts

Serving Size 1 Veg Capsule

	Amount Per Serving	% Daily Value
Calcium (from Calcium D-Glucarate)	12 mg	1%
DIM (3,3'-Diindolylmethane)	200 mg	†
Calcium D-Glucarate (Tetrahydrate Form)	100 mg	†
Sodium Copper Chlorophyllin (Chlorophyll)	20 mg	†

† Daily Value not established.

Other ingredients: Hypromellose (cellulose capsule), Microcrystalline Cellulose, Stearic Acid (vegetable source) and Silicon Dioxide

- **Diindolylmethane plus Calcium D-Glucarate**
- **Promotes Healthy Hormone Metabolism\***

**SUGGESTED USAGE:** Take 1 capsule daily with a meal, or as directed by your healthcare practitioner.

- In order to understand the mechanism of action of calcium D-glucarate, a short overview of one aspect of the body's detoxification system is detailed below.

In the liver, part of the normal phase II detoxification process consists of transferring glucuronic acid to potentially harmful xenobiotics and steroid hormones. This process allows for rapid elimination of these conjugated compounds through urine and bile.

Beta-glucuronidase is an enzyme naturally present in the small intestine, the general circulation, and all tissues. It is able to deconjugate xenobiotics and steroid hormones. Thus, deconjugation allows these compounds to be reabsorbed in the intestinal tract and to recirculate in the body as "free" deconjugated (aglycone) compounds.

The body normally maintains a balance between conjugation (in the liver) and deconjugation (via beta-glucuronidase). However, in certain circumstances†, levels of beta-glucuronidase are elevated, which offsets the natural balance towards more deconjugation, and in turn can lead to an increased presence of free steroid hormones and xenobiotics.

When beta-glucuronidase levels are high, calcium D-glucarate supplementation may be useful. Indeed, calcium D-glucarate is metabolized into D-glucaro-1,4-lactone (see Naturokinetics section for more details about the metabolism of calcium D-glucarate), which is known to decrease beta-glucuronidase activity.\* By reducing the

\* Some epidemiological data suggest that older men with higher BMI and certain dietary patterns have higher beta-glucuronidase levels. Beta-glucuronidase levels are increased in the blood of individuals submitted to high levels of certain environmental toxins. Some bacteria, as part of the normal GI microbiota, produce different amounts of beta-glucuronidase. Finally, in some animal models, higher beta-glucuronidase levels are observed in situations of localized alteration of cell multiplication.

activity of beta-glucuronidase, D-glucaro-1,4-lactone may help to rebalance the conjugation/deconjugation detoxification system of the body towards conjugation and thereby promote normal, healthy elimination of steroid hormones and everyday xenobiotics.\*

## NATUROKINETICS®

**Liberation:** This product dissolves within 60 minutes using a standard USP water dissolution test.

**Absorption:** The crystalline form of DIM has low solubility in water and fat that hinder its absorption in the digestive track. However, in a study using a physiologically based pharmacokinetic model in mice, DIM is rapidly absorbed with a maximum concentration reached 0.5 to 1 hour after ingestion.

In animal models, D-glucaric acid and D-glucaro-1,4-lactone are absorbed in the intestine.

**Distribution:** In a study using a physiologically based pharmacokinetic model in mice, DIM was found in the liver, heart, kidney, lung, blood, and brain. Both D-glucaric acid and D-glucaro-1,4-lactone are endogenously produced in the body. The body distribution of these compounds after oral ingestion of calcium D-glucarate has not been evaluated.

**Metabolism:** No known metabolites of DIM have been yet identified in humans.

In the acid environment of the stomach, calcium D-glucarate is metabolized into D-glucaric acid, which is further metabolized into D-glucaro-1,4-lactone and D-glucaro-6,3-lactone.

**Elimination:** DIM is excreted intact in urine.

D-glucaric acid is eliminated in urine. D-glucaro-1,4-lactone is eliminated in urine and, to a lesser extent, in bile.

## CLINICAL VALIDATION

- In a phase I, dose-ranging, clinical study on healthy individuals receiving from 1.5 to 9.0 g/d calcium D-glucarate for six weeks, blood levels of D-glucaric acid and beta-glucuronidase were measured at baseline and every two weeks. Researchers observed a consistent reduction of beta-glucuronidase levels as well as increased D-glucaric acid levels.
- There is currently no published clinical study using crystalline DIM. However, studies using other forms of DIM suggest that this compound may have a clinically relevant impact on estrogen metabolism.

## SAFETY INFORMATION

**Tolerability:** DIM intake has been associated with mild GI disturbance in a subset of volunteers participating in a clinical study using a proprietary, enhanced-bioavailability DIM product. Because this product features a crystalline form of DIM, reported adverse events may differ.

No unusual toxicity was encountered in a phase I dose escalation study at up to 9.0 g/d, and calcium D-glucarate was well-tolerated, even at the highest dose.

**Contraindications:** None known. Due to the potential interference with hormonal metabolism this product is not recommended for pregnant/nursing women.

## INTERACTIONS

### Drug Interactions:

Preliminary evidence suggests that DIM can increase the activity of CYP1A2 and CYP3A4.

Calcium D-glucarate may affect the metabolism of any medication metabolized through phase II glucuronidation in the liver.

Because both DIM and calcium D-glucarate interact with liver xenobiotic detoxification processes, healthcare practitioners should take this effect into consideration when recommending this product to individuals taking medications metabolized by the liver.

### Supplement Interactions:

Because both DIM and calcium D-glucarate interact with liver xenobiotic detoxification processes, healthcare practitioners should take this effect into consideration when recommending this product to individuals taking other supplements metabolized by the liver.

**Interaction with Lab Tests:** None known.

## STORAGE

Store in a cool, dry environment in a tightly sealed container. Protect from extended exposure to light, moisture, and air.