Constitutional Health`s

DWDx3™:
Clinical, Scientific Studies & Research Report
1. Botanicals that work to support healthy glucose levels directly*
2. Nutrients to support insulin sensitivity*
3. Healthy nerve innervation support from fat-soluble B1 and the bioactive form of B6*

**DWDx3**, like all products in our Benefits Line, is formulated to deliver more. With the branded ingredients Glucevia®️, GlucodOX®️ and BenfoPure®, **DWDx3™️** provides a balanced approach to energy balance.*

The fruit and seeds of *Fraxinus excelsior* L. (commonly known as the Ash), have long been used, just like Ash bark and leaves, for medicinal purposes. In recent years, researchers have found its properties are supportive of metabolic health. In one human study, researchers concluded that “The administration of an extract from Fraxinus excelsior L. seeds/fruits in combination with a moderate hypocaloric diet may be beneficial in metabolic disturbances linked to impaired glucose tolerance, obesity, insulin resistance and inflammatory status, specifically in older adults” (Zulet et al., 2014.)

**Glucevia®️**, which supports healthy glucose levels, is just one of the clinically relevant, researched botanical extracts in the Benefits Line that reflects the Constitutional Health commitment to formulation.*

A combination of a *Commiphora mukul* (guggul) extract and a medium-chain triglyceride (MCT) oil composed of C8 and C10 fatty acids, **GlucodOX®️** is a well-researched ingredient to support healthy lipid and glucose metabolism. The research on guggulsterones is clear: the mechanisms that control GlucodOX’s action may support normal insulin sensitivity, cholesterol levels within normal ranges, regulate pre-adipocyte to adipocyte transformation balance, and support healthy glucose transport based on AMPK activity stimulation* (“GlucodOX™ - Natural metabolic support*,” 2013).

**GlucodOX®️ supports:**
- Blood glucose levels within normal ranges*
- Enhanced cellular energy*
- Balanced fat cell formation and storage*
**Vitamin B1**, or thiamin, is known for its support of normal nerve health and function.* A required cofactor in the production of certain enzymes (such as those involved in glucose metabolism pathways), thiamin is critical for healthy metabolic function. **BenfoPure** is a benfotiamine formulation, an analog of thiamin. As a lipid-soluble compound, it is both more ready for use and more active than traditional forms of thiamin. Benfotiamine supports normal intracellular glucose levels, and normal rates of AGE formation.* It also supports the healthy stimulation of the enzyme transketolase, which helps to convert toxic compounds into less harmful compounds.*

To create a protocol for healthy blood sugar support and metabolic health, consider trying these other Constitutional Health products with **DWDx3**:

- Metabolic Multi™ or Daily Best™ Ultra
- Right Whey
- Omega 3 HP-D
- or
- Berberine Force
- Adrenal Benefits

*View the Clinician’s Protocol Guide to learn more.*

**DWDx3** also contains **B6, R-Alpha Lipoic Acid and Chromium**.

Supplementing with chromium can help the body to build lean muscle mass, maintain glucose and cholesterol levels within normal ranges, and metabolize fat more efficiently.*

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**SUPPLEMENT FACTS**

**Serving Size 3 Capsules**

<table>
<thead>
<tr>
<th>Servings Per Container 30</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Vitamin B6 (as Pyridoxal-5-Phosphate)</td>
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</tr>
<tr>
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</tr>
<tr>
<td>BenfoPure® Benfotiamine</td>
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</table>

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

**Caution:** Discontinue use 2 weeks prior to surgery.

**Suggested Use:** As a dietary supplement, take 3 capsules daily, or as directed by your healthcare practitioner.

**Glucovia®**

Glucovia® is a registered trademark of Naturex.

**GlucoDox®** is a registered trademark of Dharma Biomedical LLC.
METABOLIC HEALTH WITH DWDx3™

BALANCE IS ESSENTIAL

Metabolic health is an intricate puzzle dependent on the balance of our energy system. Think of energy production and use as an equation. When the equation is balanced, we see overall metabolic health result. Insulin sensitivity, nourishment, hormonal health and glycation levels are invaluable components of the equation.

As metabolic health remains a topic of extreme importance and relevance for your patients, understanding the above factors can help you develop the best lifestyle recommendations for every individual's needs.

This paper will discuss glycation, liver health and hormonal health — and their respective impacts on insulin sensitivity — as well as nutritional factors that may help support multiple areas of metabolic health.*

FACTORS ASSOCIATED WITH NORMAL METABOLISM:

A waistline that measures less than 35 inches for women, and 40 inches for men
Normal triglyceride levels
Normal HDL cholesterol levels
Normal blood pressure
Normal fasting blood sugar levels

GLYCATION

Glycation occurs when a protein or lipid molecule binds with a sugar molecule like glucose or fructose without the necessary moderating action of an enzyme. When an enzyme is present, glycosylation (a process necessary for molecular function) occurs; without it, glycation results, forming rogue molecules called advanced glycation endproducts. These endproducts (AGEs), are connected to a number of biological processes, such as the antioxidant system and the formation of reactive oxygen species (Tan et al., 2006).

Additionally, high levels of AGEs can deplete levels of nitric oxide, thereby creating vascular damage and setting the stage for heart concerns. In short, endogenous glycation is one of the major molecular processes that causes an accrual of damage.

It has been shown that lower levels of AGEs support nerve, eye and kidney health, three common metabolic systems. In addition, oral AGEs have been shown to promote insulin resistance by depleting antioxidant defenses of AGE receptor-1 and sirtuin-1. It is widely suspected that glucose, via glycation, is the primary damaging molecule in the aging body (Suji & Sivakami, 2004).
GLYCATION AND INSULIN SENSITIVITY

It’s important to discuss glycation when we examine the body’s metabolic health because AGEs may contribute to insulin resistance by a variety of mechanisms, including:

Generation of tumor necrosis factor (TNF)
Direct modification of the insulin molecule
Oxidative stress
Impairment of mitochondrial function

AGE receptor interaction perpetuates both AGE formation and cellular stress. It does so by inducing inflammation, oxidative stress, and a reduction in the expression and activity of the enzyme glyoxalase I. Glyoxalase 1 detoxifies the AGE precursor, methylglyoxal.

The glycation-promoting mechanisms may further stimulate AGE production and reduce insulin responsiveness by targeting tissue stresses (Song & Schmidt, 2012). Therefore, any consideration of support for normal rates of AGE formation may be beneficial in addressing overall insulin sensitivity.

GLYCATION AND NERVE HEALTH

Glycation end products can disrupt function in many tissues, including nerves (Brownlee, 2001; Feldman, 2012; Morales-Vidal, Morgan, McCoyd, & Hornik, 2012).

According to a 2008 study in Current Pharmaceutical Design, “Although the precise mechanisms underlying diabetic neuropathy remain unclear, there is evidence that hyperglycemia-induced formation of advanced glycation end products (AGEs) is related to diabetic neuropathy; AGE-modified peripheral nerve myelin is susceptible to phagocytosis by macrophages and contributes to segmental demyelination; modification of major axonal cytoskeletal proteins such as tubulin, neurofilament, and actin by AGES results in axonal atrophy/degeneration and impaired axonal transport; and glycation of extracellular matrix protein laminin leads to impaired regenerative activity in diabetic neuropathy” (Sugimoto, Yasujima, & Yagihashi).

Another possible mechanism is binding: AGEs can trigger a cytokine response by binding to nerve cell surfaces (Vincent, Callaghan, Smith, & Feldman, 2011).
LIVER HEALTH

Given the emergence of understanding surrounding the glycemic index, high glycemic foods have earned a negative status with regard to health. In 2007, researchers from Children's Hospital Boston demonstrated a clear relationship (in mice) between consuming carbohydrates with a high glycemic index and the development of fatty liver.

According to Scribner, Pawlak and Ludwig, “A diet high in RAC causes accumulation of fat in liver, adipose tissue, and plasma in mice. Therefore, a low glycemic index diet may help prevent or treat NAFLD in humans” (Scribner, Pawlak, & Ludwig, 2007). It appears that the primary mechanism behind the damage caused by a high-glycemic diet is actually increased insulin production. The study also found higher plasma levels of insulin in mice fed the high-glycemic diet compared to those fed the low-glycemic diet (Cutler, 2007).

These results reveal the causal nature of the diet's impact on insulin, and remind us that healthy nourishment is an important factor in metabolic health. Further, these results bring to light the value of the liver in the conversation about insulin and metabolic health.

The liver both stores and manufactures (depending on need) the body's glucose and helps keep circulating levels steady. The signal to release or store comes from insulin or glucagon respectively. When the body is taking sugar in (during mealtime), glucose should be stored as glycogen. When the body needs to produce glucose (overnight, for example), the liver can either convert glycogen to glucose or produce glucose from fat byproducts, waste products and/or amino acids (Nolte Kennedy, Bedrich, White Gray, Kroon, & Demetsky, 2015).

The liver, whose function is so greatly affected by refined carbohydrate consumption, is also the site for much of the estrogen metabolism that occurs in the human body. The deep connections between the liver and the endocrine system tell us that metabolic health and insulin sensitivity support regimens should include support for healthy liver function — and for hormonal balance, as well.

HORMONAL BALANCE

Insulin's status as a hormone tells us how important the endocrine system is to healthy insulin sensitivity. Beyond insulin there exists an intricate web of hormones directly linked to metabolism, insulin sensitivity and peripheral nerve function.

Glucagon, which is released between meals and overnight, helps maintain sugar balance by signaling the liver to break down its stores. After a meal when the liver no longer needs to make sugar (the food sugar is introduced), glucagon levels drop. In people with metabolic challenges, glucagon levels rise.
after a meal. GLP-1 (glucagon-like peptide-1), GIP (glucose-dependent insulinotropic polypeptide) and amylin, three other hormones, help regulate mealtime insulin. These hormones participate in decreasing glucagon levels, thereby decreasing the liver’s mealtime sugar production, preventing levels from skyrocketing (Nolte Kennedy, Bedrich, White Gray, Kroon, & Demetsky, 2015).

Three other hormones still, epinephrine, cortisol and growth hormone, also help maintain blood sugar levels. Simply put, these “stress” hormones make blood sugar rise.

Epinephrine (adrenaline) does this through acting directly on the liver and through promoting fat nutrient breakdown. Those nutrients travel to the liver for conversion. Cortisol, also secreted from the adrenal gland, is incredibly important in our discussion of metabolism. It enhances glucose production by the liver and contributes to fat and muscle cell resistance to insulin. In a healthy body, cortisol works to counterbalance insulin action. In a stressed condition, it may become elevated to the point that insulin resistance could develop as a result.

Growth hormone comes from a different gland - the pituitary. Like cortisol, it acts as a counterbalance to insulin’s effect. And, as is also true of cortisol, elevated levels of growth hormone may cause resistance to insulin’s action.

Still another hormone, thyroid hormone, may also play a role in metabolic health through regulation of insulin’s effect on adipose tissue (Arner, Bolinder, Wennlund, & Ostman, 1984).

**NUTRIENTS TO SUPPORT METABOLIC HEALTH**

**DWDx3™** represents a three-pronged approach to metabolic support:

- Botanicals to support healthy glucose levels*
- Nutrients to support normal insulin sensitivity*
- B vitamins to support healthy nerve innervation*

**Glucevia**, the fruit and seeds of *Fraxinus excelsior* L. (commonly known as the Ash), has long been used, just like Ash Bark and leaves, for medicinal purposes. In recent years, researchers have found its properties are supportive of metabolic health. In one human study, researchers concluded that “The administration of an extract from Fraxinus excelsior L. seeds/fruits in combination with a moderate hypocaloric diet may be beneficial in metabolic disturbances linked to impaired glucose tolerance, obesity and insulin resistance, specifically in older adults” (Zulet et al., 2014).
Another study published in 2015 found that, after seven months of administration, Glucevia supported insulin sensitivity while reducing fatty liver in diabetic mice. The liver of supplemented mice presented 54% fewer fat droplets than the control group. This demonstrates that non-alcoholic steatosis in the liver was markedly reduced in treated mice thanks to Glucevia (“New study suggests preventive effect of Glucevia on liver damage,” 2 GlucodOX®, a combination of a Commiphora mukul (guggul) extract and a medium-chain triglyceride (MCT) oil composed of C8 and C10 fatty acids, is a well-researched ingredient to support healthy lipid and glucose metabolism.

In one study, four groups of rats were treated with C. mukul gum resin ethanolic extract (CMEE) for 60 days. The “diabetic rats showed increased level of enzymatic activities aspartate aminotransaminase (AST), alanine aminotransaminase (ALT) in liver and kidney and oxidative markers like lipid peroxidation (LPO) and protein oxidation (PO) in pancreas and heart. Antioxidant enzyme activities were significantly decreased in the pancreas and heart compared to control group. Administration of CMEE (200 mg/kg bw) to diabetic rats for 60 days significantly reversed the above parameters towards normalcy,” leading the researchers to conclude that the plant may be of use as an adjuvant therapy to support oxidative and glucose balance (Ramesh et al., 2012).

GlucodOX’s action may support normal insulin sensitivity, cholesterol levels within normal ranges, regulate pre-adipoctye to adipocyte transformation balance, and support healthy glucose transport based on AMPK activity stimulation* (“GlucodOX™ - Natural metabolic support*,” 2013).

Benfotiamine is a fat-soluble form of vitamin B1 that also supports glucose balance and addresses glycation through helping to protect the body’s tissues from AGEs. Vitamin B1, or thiamin is known for its support of normal nerve health and function.* A required cofactor in the production of certain enzymes (such as those involved in glucose metabolism pathways), thiamin is critical for healthy metabolic function. BenfoPure is a benfotiamine formulation, an analog of thiamin.

As a lipid-soluble compound, it is both more ready for use and more active than traditional forms of thiamin. Benfotiamine is absorbed through the intestinal mucosa, then converted to its biologically active form, thiamin. Researchers have found that peak plasma concentrations of this form are at least five times greater after oral benfotiamine administration than the concentrations observed when water-soluble thiamine salts were administered (“Benfotiamine,” 2006).

Relative to glucose metabolism, benfotiamine supports healthy transketolase activity, thereby blocking certain molecular pathways that may lead to hyperglycemic concerns.* Further, it supports the health of pathways that address the formation of AGEs.* Benfotiamine also supports eye health through supporting normal, healthy activation of NF-B in the diabetic retina.* Through supporting normal cell replication rates and healthy apoptosis, benfotiamine can also support the healthy of endothelial cells* (“Benfotiamine,” 2006).
**SUPPLEMENT FACTS**

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*Daily Value not established.

Other ingredients: microcrystalline cellulose, hypromellose (capsule), vegetarian leucine.

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**R-alpha lipoic acid** supports both normal macronutrient metabolism and insulin utilization and offers free radical scavenging support to address glycation.* Importantly, it helps support and restore healthy intracellular glutathione levels.* The Linus Pauling Institute writes: “R-LA is the isomer that is synthesized by plants and animals and functions as a cofactor for mitochondrial enzymes in its protein-bound form. Direct comparisons of the bioavailability of oral LA and R-LA supplements have not been published. After oral dosing with LA, peak plasma concentrations of R-LA were found to be 40%-50% higher than S-LA, suggesting R-LA is better absorbed than S-LA” (“Lipoic Acid | Linus Pauling Institute | Oregon State University,” n.d.).

**Chromium** at a relevant dose is key to any glucose support product.* When insulin binds to its receptor, chromium assists in the message and is then excreted from the cell, a process which appears to occur in a glucose-dependent manner, meaning that higher sugar means greater insulin binding, which means greater loss of chromium. The idea that chromium may be an appropriate support agent for people who experience glucose concerns is supported by findings that blood chromium levels are lower in people with metabolic challenges than in those without (“Scientific review: the role of chromium in insulin resistance,” 2004). Supplementing with Chromium can help the body to build lean muscle mass, maintain glucose and cholesterol levels within normal ranges, and metabolize fat more efficiently.*
REFERENCES


GlucodOX™ is a proprietary oleo-gum-resin extract derived from the trunk of the Commiphora mukul tree and formulated in a medium-chain triglyceride (MCT) base, which is composed of C8 and C10 fatty acids for improved absorption. The tree grows in northeast Africa, India, and the Arabian Peninsula and supplies a resin collected from the bark of the growing tree. The oleo-gum-resin known also as guggul has been used for thousands of years in Asia as a natural antiseptic and wound-healing agent and to treat hypercholesterolemia, atherosclerosis, rheumatism, and obesity. The natural product utilizes mukul’s rich aromatic compounds, including volatile oil, resin, and gums. GlucodOX™ is standardized by high-performance liquid chromatography to 2.0% of the active compound guggulsterones, which have beneficial effects for supporting normal lipid metabolism, glucose metabolism, and cellular energy. GlucodOX™ is made from a unique optimized supercritical CO₂ extraction using a co-solvent of ethanol that recovers active constituents that are then dissolved in MCT oil for enhanced efficacy and bioavailability.

Multiple mechanisms of action

The mechanisms of action of GlucodOX™ vary for its different bioactive effects. For glucose control, GlucodOX™ increases cellular glucose, a measure of improved insulin sensitivity (Claudel, 2005). For supporting cholesterol levels already within the normal range, GlucodOX™ works to inhibit the natural production of cholesterol through the enzyme HMG-CoA reductase, a mechanism that highly effective statin drugs are based on (Izzat, 2000; Urizar, 2002). For healthy weight control and fat metabolism, it reduces transformation of preadipocytes to adipocytes (fat cells) and storage of triglycerides (fats) (Yang, 2008; Rizzo, 2006).

Energizing effects

In addition, GlucodOX™ may have other beneficial health effects. Energizing action was found by its ability to stimulate AMPK, (5’ adenosine monophosphate-activated protein kinase) the master energy sensor and regulator in the body that has been described as a nutrient/energy sensor involved in supporting energy levels in cells throughout the body, and in helping with formation of new mitochondria (cellular-energy-producing units) (Lage 2008, Long 2006, Steinberg 2009). AMPK is directly or indirectly involved in the regulation of many other fundamental processes including lipid, carbohydrate, and protein metabolism, cell growth and apoptosis (programmed cell death), and stress response pathways. A comparison between GlucodOX™ and a leading competitor’s guggulsterone extract, Gugulipid®, found that GlucodOX™ had significantly better effects on modulation of AMPK activity than Gugulipid® at every dose. GlucodOX™ enhanced AMPK activity by 123% compared with 56.5% by Gugulipid® at 50 µg/mL (see Fig. 1).
**Joint support**

An anti-inflammatory effect for osteoarthritis of the knee is another physiological benefit. Preclinical and clinical investigations of guggul have shown reduction of pain, stiffness, and improved function. A study used 500 mg of guggul extract three times a day along with food, measuring the WOMAC total score as a primary outcome measure, with visual analog scale (VAS) and a 6-minute walk test used as secondary measure. There was a significant improvement of the primary and secondary outcome measures. For the WOMAC total score, participants were significantly improved ($p < 0.0001$) after taking the supplement for 1 month and continued into the 2-month period and after follow-up. The secondary measures of pain in the VAS format demonstrated participant improvement ($p < 0.05$) up to the 2-month assessment ($p < 0.001$). (Singh, 2003).

**Cholesterol lowering and other cardio benefits**

Clinical studies prove the efficacy of the guggulsterone active compounds in GlucodOX™. The effects of a 50-mg dose of guggulipid twice daily for 24 weeks were evaluated for the management of hypercholesterolemia in 61 patients in a randomized, double-blind study. Guggulipid decreased the total cholesterol level by 11.7%, the low-density lipoprotein cholesterol (LDL) by 12.5%, triglycerides by 12.0%, and the total cholesterol/high-density lipoprotein (HDL) cholesterol ratio by 11.1% compared with placebo group. Lipid peroxides, which are related to vascular damage from free radicals and progression of cardiovascular disease, declined 33.3% in the guggulipid group compared with the placebo group (Singh, 1994).

**Cardio health physiology**

There are multiple mechanisms of action for the cardiovascular benefits of guggulsterone. It has been established as an antagonist at farnesoid x receptor, a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis, which have hypolipidemic effects. Guggulsterone upregulates the bile salt export pump, an efflux transporter responsible for removal of cholesterol metabolites through excretion of bile acids from the liver. Guggulsterone has been found to potently inhibit the activation of nuclear factor-κB, an important regulator of inflammatory responses, explaining its anti-inflammatory effect (Deng, 2007). GlucodOX™ also inhibits a principle enzyme involved in cholesterol biosynthesis known as HMG-CoA reductase, the same mechanism by which statin drugs work, though guggul is not known to have the adverse effects of statins such as muscle and liver damage. GlucodOX™ inhibited HMG-CoA reductase as potently as Pravastatin, a leading statin drug, at only 0.02 mcg, half the concentration of 0.04 mcg of the latter (see Fig. 2).
GlucodOX™ is about twice as potent an inhibitor of HMG-CoA reductase as Gugulipid®.

**Fig. 2: Inhibition of HMG-CoA reductase activity (%) by GUTC7 (GlucodOX) and GL (Gugulipid)**

**Fig. 3: Inhibition of adipocyte differentiation by GUTC7 (GlucodOX) and GL (Gugulipid) in 3T3-L1 adipocytes**

Inhibiting adipocyte differentiation helps reduce fat cell synthesis and subsequent storage and growth of fat tissue. GlucodOX™ inhibited adipocyte differentiation almost twice as effectively as a regular guggulsterone extract over a wide range of concentrations, from 60 µg/mL to 100 µg/mL.

**Anti-obesity effect**

A form of guggul known as guggulsterone phosphate salt compound was tested on body composition and mood states in overweight adults. In a double-masked, randomized, placebo-controlled study, 20 overweight subjects received guggulsterones (750 mg) and phosphate (1,650 mg) daily and were instructed to follow the American Heart Association Step One diet and a 3-day-per-week circuit exercise program. Body weight significantly decreased 3.2%, ($p < 0.05$) in the experimental group, and fat mass significantly decreased 20.6% in the experimental compared with 8.6% in the control groups ($p < 0.01$). In addition, mood and fatigue indices improved significantly in the experimental group (63.7%, $p <0.01$) (Antonio, 1999).

**References**

Naturally improve glucose regulation

Market opportunities

Sugar consumption has increased dramatically over the last two centuries. In 1822, Americans consumed the amount of sugar found in a 12-ounce soda every 5 days, but today consume this same amount every 7 hours. While sugars and their derivatives are essential to human nutrition and help to maintain physiological functions, it has been widely demonstrated that excess sugar in our diet is unhealthy and that elevated blood sugar levels can lead to health issues. Managing blood glucose levels is therefore recommended by health authorities worldwide. With Glucemia™, Naturex offers you an opportunity to provide a new and natural solution to people who want to maintain healthy blood glucose levels.

Glucemia™: a new discovery

Naturex has developed Glucemia™, an innovative extract from the seeds/fruits of Fraxinus excelsior. Fraxinus is a tree native to parts of Europe and Asia and is usually referred to as "common ash" or "European ash." The effect of Fraxinus on blood sugar control had not been widely explored until Naturex conducted clinical trials to demonstrate its benefits. Historically, Fraxinus was largely limited to the Mediterranean Basin, where local populations traditionally used it in food and infusions, and for its hypoglycemic effect.

Premium characteristics

- Innovative ingredient
- Proprietary extraction
- Specifically selected seeds/fruits
- Patented application and composition
- Unique profile in Nuzhenide and GI3

Glucemia™ is the only available extract derived exclusively from the seeds/fruits of Fraxinus excelsior. Proof of its efficacy is based on several years of in-depth scientific research and on well-established use in Mediterranean countries. Using a gentle and traditional extraction process, Naturex was the first to develop a unique patented extract standardized to 10% Nuzhenide and GI3. Thanks to these active components, the ability of Glucemia™ to help balance blood sugar levels has been demonstrated in vitro, in vivo, and in clinical studies.

Scientific evidence

1,000 mg of Glucemia™ per day helps to safely balance blood sugar levels:
- reduces post-prandial blood glucose by acting on the rate of absorption of glucose into the liver and muscle cells (2,3)
- has an effect on the liver and improves liver health on a long-term basis (4,5)
- is safe and does not cause any adverse effects (6)

Glucemia™ immediately reduces the incremental glucose Area Under the Curve (AUC) by 8.8% in healthy volunteers. A dose of 1,000 mg of Glucemia™ has an immediate effect on postprandial blood glucose concentration (7).

Healthy, volunteers received 1,000 mg of Glucemia™ per day for 3 weeks. Incremental glucose AUC was significantly reduced by 28.2% versus baseline. These results demonstrate that a daily dose of Glucemia™ helps to manage glycemia on a long-term basis (8).

Mechanism of action may involve liver metabolism of glucose

Pre-clinical in vivo studies show that Glucemia™ significantly reduces fatty liver in diabetic or obese animals.
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Pre-clinical in vivo studies show that Glucevia™ significantly reduces fatty liver in diabetic or obese animals. Glucose regulation in the long term with no side effects

1. Ibarra et al. (2011) Phytomedicine, 18: 479-485
3. Gomez et al, pending
5. US Patent 8,293,292,B2 Extract of Fraxinus excelsior seeds and therapeutic applications
6. Zulet et al, pending

The claims have not been evaluated by regulatory authorities. This product is not intended to diagnose, treat, cure, or prevent any disease.
Glucevia™ significantly reduces post-prandial blood glucose both immediately and following long term administration. Glucevia™ and its patented active compounds, Nuzhenide and GI3, increase the rate of absorption of glucose into the liver and muscle cells and protect the liver on a long-term basis.

Unlike synthetic drugs for glucose control, Glucevia™ is safe and does not cause any adverse side effects. Glucevia™ helps to balance blood glucose levels and supports healthy liver function.

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<th>Commercial name</th>
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<td>Complete name</td>
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<td>Appearance</td>
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<td>Glucose management</td>
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<td>Claims</td>
<td>Contributes to healthy lifestyle by improving blood glucose regulation as part of a balanced diet</td>
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<td>Recommended dosage</td>
<td>1,000 mg/day, in 3 doses to be taken before meals</td>
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<tr>
<td>Safety and quality</td>
<td>No side effects have been reported in clinical studies. No risks have been identified in extensive toxicological tests. Glucevia™ is guaranteed to be made from 100% Fraxinus excelsior and in compliance with current standards regarding the absence of GMOs and allergens as well as acceptable levels of heavy metals and pesticide residues. Before sale of the product, it must be ensured that the product meets all local legal requirements.</td>
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**BENFOPURE BENFOTIAMINE**

**SCIENTIFIC LITERATURE**

Benfotiamine (S-benzoylthiamine-O-monophosphate) is an analogue of Vitamin B1, also known as Thiamine. Benfotiamine is a lipid-soluble compound that is more readily available for nutritional use and is significantly more active than traditional forms of Thiamine.

**Benfotiamine “mode-of-action”:**

- Assists the body in responding to the toxic breakdown compounds of excess sugar
- Reduces elevated levels of intracellular glucose and the potential for AGE (Advanced Glycation End-Products) formation
- Stimulates transketolase, an enzyme that helps convert the toxic compounds to harmless ones

Benfotiamine is a novel, lipid-soluble analogue of Thiamine, unique in its enhanced availability for the body compared to traditional water-soluble forms of Thiamine.

Thiamine, is a water-soluble vitamin of the B complex, and is an essential nutrient for most organisms. It is a required cofactor for the body’s production of several critical enzymes, including those in pathways involved in intracellular glucose metabolism.

**BENFOTIAMINE INCREASES THIAMINE CONCENTRATION IN THE BODY**

In a human study, the use of Benfotiamine increased thiamine diphosphate (TDP, the biologically active form of Thiamine) levels by 77% in the supplemented group versus the control group taking traditional water-soluble Thiamine. This study indicates Benfotiamine has higher bioavailability than Thiamine and is readily converted to Thiamine in the body.

**BIOAVAILABILITY OF BENFOTIAMINE COMPARED TO THIAMINE**

The total amount of Thiamine in the body is roughly 30 mg. After oral ingestion, Benfotiamine is digested in the gastrointestinal tract to a form which is more lipid-soluble than thiamine which permits this Benfotiamine-form to readily cross cell membranes in the intestines and enter the blood stream. A significant percentage of this lipid-soluble form is captured within red blood cells, where it is converted to free Thiamine as needed by the body.
The bioavailability of Thiamine in blood plasma is reported to be approximately 3.6 times greater after a dose of Benfotiamine than after a dose of Thiamine.

In 1991, Bitsch and colleagues evaluated the bioavailability of Benfotiamine in comparison to thiamine mononitrate (a common form of Thiamine). The Thiamine blood plasma concentration after Benfotiamine ingestion exceeded that of thiamine mononitrate by 55% and in hemolysate by 99%. This indicates that Benfotiamine provides more Thiamine to the blood than the more commonly used forms of Thiamine such as is found in multi-vitamins and B-complex supplements.

Another study in 1996 reported the mean blood plasma concentration of Thiamine after Benfotiamine consumption was 5 times higher than after Thiamine consumption. In red blood cells, Thiamine concentration ranged from 3.5 to 14.8 times higher after Benfotiamine ingestion.

After a single oral ingestion in mice with radiolabeled Benfotiamine or Thiamine hydrochloride (a commonly used form of Thiamine equivalent to 105 mg Thiamine/kg), the compounds appeared to be incorporated into all organs in a comparable way. However, Benfotiamine was incorporated at a higher amount than Thiamine hydrochloride.

REFERENCES


**METABOLISM PROTOCOL**

**INSULIN SENSITIVITY**
- Chromium*
- Alpha Lipoic Acid*

**BLOOD SUGAR**
- Glucovia®
- Glucodox™
- Berberine*

**PERIPHERAL NERVE FUNCTION**
- B6 (pyridoxyl 5 phosphate)*
- Benfotamine*

**INSULIN SUPPORT**
- Chromium* Vanadium*
- R-Alpha Lipoic Acid*
- Trans Resveratrol*
- Vitamin D*
- B6*
- B12*
- Biotin*
- Cinnamon*

**SUPPORTING ESTROGEN LEVELS**
- DIM*
- Turmeric*
- Taurine*

**SUPPORTING HEALTHY ESTROGEN LEVELS IN TURN SUPPORTS HEALTHY INSULIN LEVELS**

**CHROMIUM**
Interaction between chromium and insulin and insulin receptors supports glucose uptake into the cell.

**BENFOTIAMINE** supports the production of transketolase, an enzyme responsible for efficiently converting potentially harmful byproducts of glucose breakdown into easily eliminated, harmless compounds. This is one way benfotiamine helps support the small blood vessels and nerves in the distal extremities.*

**GLUCEVIA** is standardized to 10% Nuzhenide and GI3, two compounds that were shown in preclinical animal studies to support the rate of glucose absorption in liver and muscle.

**GLUCODOX™** demonstrates energizing action through its ability to stimulate the production of AMPK.* AMPK acts as the body’s master regulator of glucose uptake.

In addition, Glucodox™ supports the transformation of pre-adipocytes to adipocytes, which aids in supporting healthy leptin levels.*

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*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.
Metabolism and Metabolic Syndrome: The multifaceted nature of metabolic support involves many systems. This protocol outlines each individually. The needs of the patient will dictate the combination of systems that should be supported. Keep in mind there is product crossover with each of these protocols.

**TESTS: BASIC METABOLISM PROFILE:**
- CBC • CMP • Lipids • Hgb alc.
- Thyroid panel (TSH, T4, T3 uptake, Free T3)

**EXPANDED CARIAC ASSESSMENT:**
- hs-CRP • Homocysteine • Fibrinogen
- Vitamin D (25 OH)
- Cortisol • DHEA-s • Insulin • B12 & Folate.
- NMR instead of regular lipid panel

[NMR LipoProfile® test is an advanced cardiovascular diagnostic test that uses nuclear magnetic resonance (NMR) spectroscopy]
WEIGHT PROTOCOL

**WELLTRIM**® IG (IGOB131®) AFRICAN MANGO EXTRACT: Supports body weight and waist circumference as well as plasma total cholesterol levels, LDL cholesterol, metabolic function, adiponectin and, perhaps most importantly, C-reactive protein.* Healthy CRP levels can ultimately support healthy leptin levels.*

**WHITE KIDNEY BEAN (BEANBLOCK®):** Beanblock® contains an active ingredient, Alpha-amylase inhibitor isoform 1 (Alpha-AI1), that targets certain enzymatic activity which can lead to the breakdown and absorption of specific macronutrients such as starch. Affecting starch absorption can support healthy metabolic processes and satiety.*

**GREEN COFFEE BEAN:** Supports healthy levels of glucose-6-phosphate, which is responsible for converting glycogen into glucose.*

Source: J Agric Food Chem. 2010 Apr 14;58(7):4141-4

**GREEN TEA PHYTOSOME®:** Supports genetic signaling associated with Adiponectin and healthy fat accumulation by supporting lipolysis within adipocytes.*


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**CORTISOL/DHEA RATIO**

**HEALTHY RATIO=**
- Healthy levels of abdominal adiposity
- Healthy levels of T4 to T3 conversion (T3 is one of the body’s most powerful metabolic hormones, 5x more potent than its precursor T4)

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Metabolic health is an intricate puzzle dependent on the balance of our energy system. Think of energy production and use as an equation. When the equation is balanced, we see overall metabolic health result. Insulin sensitivity, liver health, nourishment, hormonal health and glycation levels are invaluable components of the equation.

**Suggested Use:** As a dietary supplement, take 3 capsules daily, or as directed by your healthcare practitioner.

**Supplement Facts**

Serving Size 3 Capsules  
Servings Per Container 30

<table>
<thead>
<tr>
<th>Amount per Serving</th>
<th>% Daily Value</th>
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<tbody>
<tr>
<td>Vitamin B6 (as Pyridoxal 5-Phosphate) 55 mg</td>
<td>2,750%</td>
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<tr>
<td>Chromium (as Cr Polynicotinate) 1,000 mcg</td>
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<tr>
<td>Glucemia® (Fraxinus excelsior) 1,000 mg</td>
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<tr>
<td>GlucoDox™ 200 mg</td>
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</tr>
<tr>
<td>R-alpha lipoic acid 100 mg</td>
<td>*</td>
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<tr>
<td>BenfoPure® Benfotiamine 75 mg</td>
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</tbody>
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*Daily Value not established.

**Other ingredients:** microcrystalline cellulose, hypromellose (capsule), vegetarian leucine. Color of this product may vary due to color variations of the ingredients.

**WARNING:** If pregnant or nursing, consult your healthcare practitioner before taking this product.

Keep out of reach of children. Store in a cool, dry place.

**CAUTION:** Discontinue use 2 weeks prior to surgery.

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DISCLAIMER (MUST READ):

All information provided in this book, particularly any information relating to specific medical conditions, health care, preventive care, and healthy lifestyles, is presented for general informational purposes only. It should not be considered complete or exhaustive and does not cover all disorders or conditions or their treatment, nor all health-related issues.

The information provided in this book is not intended as a substitute for the advice provided by your own physician or health care provider, and may not necessarily take your individual health situation into account. You should not use the information in this book as a means of diagnosing a health problem or disease, or as a means of determining treatment. You should also not use the information as a substitute for professional medical advice when deciding on any health-related regimen, including diet or exercise. You should always consult your own licensed health care provider for these purposes, or for any specific, individual medical advice.