

Nutra-Iso® Nutritionals

Bioactive Nutrition by Quintessence Nutraceuticals, Inc.

HOW DO NUTRA-ISO® NUTRITIONALS WORK?

Nutra-Iso® Nutritionals (Nutra-Iso®) is a natural nutraceutical medical food ingredient extracted from FDA-USDA GRAS approved whole grain derivatives. These bioactive nutraceutical isolates (phytonutrients and phytochemicals) are formulated into consumer products for mitigating specific chronic health conditions related to nutritional imbalances. For example, the bioactive phytonutrient and phytochemical isolates extracted from rice bran derivatives have been clinically documented to lower and stabilize blood glucose levels in pre-diabetic and early stage diabetic populations, as well as balancing cholesterol and lowering triglycerides. In a sixty-day clinical trial, it was documented that these bioactive nutraceutical isolates reduced Fasting Blood Glucose Levels an average of 33% and reduced A1c levels an average of 1.6 points. In a similar clinical trial, triglyceride levels were reduced 19.4% and HDL levels (good cholesterol) were increased 16% while LDL levels (bad cholesterol) were reduced 8%. The bioactive nutraceuticals embodied in Nutra-Iso® for mitigating such pre-diabetic nutritional conditions meet the regulatory compliances under DSHEA/FDA for all claims made and are hypoallergenic and gluten free.

Like many pharmaceuticals, the precise mode(s) of action for Nutra-Iso® formulations for addressing chronic health conditions remain under continuing scientific investigation, but the system biology behind specific nutraceutical components extracted for inclusion in these formulations has been documented and scientifically reported. For example, the general mode of action in lowering and stabilizing blood glucose levels centers on the role of selected Nutra-Iso® isolates in decreasing insulin resistance. There is medical consensus that oxidative stress and insulin resistance are principle precursors to the diabetic condition. The American Association of Clinical Endocrinologist estimates that 90% of Type 2 diabetics are insulin resistant. Scientifically documented “triggering mechanisms” for insulin resistance include:

1. *Elevated fatty acids* inhibiting insulin signaling and glucose uptake by interfering with the translocation of the glucose transporter, GLUT-4. Numerous scientific reports demonstrate that oversupply of lipids raises the circulating level of free fatty acids (FFA) and contributes to the development of Type 2 diabetes¹. Increase in plasma lipid levels impairs insulin activity, increase in plasma FFA reduces insulin-stimulated glucose uptake, whereas a decrease in lipid content improves insulin activity in skeletal muscle cells, adipocytes and liver².
2. *Oxidative stress* disrupting mitochondrial signaling leads to cellular insulin resistance³. Many biochemical pathways strictly associated with high blood glucose levels can

¹Diabetes: 46 1997; Diabetes: 50 2001; Banting Lecture; Diabetes: 51 2001.

²Nature: 414 2001.

³Nature: 440 2006.

increase the production of free radicals⁴. Prolonged oxidative stress in muscle and fat has been shown to significantly reduce insulin-stimulated glucose transport⁵. In further support of the pathological role of oxidative stress, many of the adverse effects of high glucose levels on endothelial function, such as reduced endothelial-dependent relaxation and delayed cell replication, are reversed by anti-oxidants *in vivo*⁶. Nutra-Iso® Nutritional ingredients are high in a bioactive and synergistic complex of antioxidants.

3. *Glucose metabolism* inhibition due to increased oxidative stress and plasma cholesterol levels. Scientific evidence suggests that specific nutraceutical isolates embodied in the bioactive ingredients of Nutra-Iso® work synergistically to provide healthy glucose metabolism by reducing oxidative stress and plasma cholesterol levels in individuals with pre-diabetic health conditions⁷. Supporting scientific evidence was further reported in the Journal of Agriculture Food Chemistry⁸. The total ferulic acid, phenolic and tocotrienol isolates embodied in Nutra-Iso® ingredients appear to be among the key bioactive catalysts for achieving enhanced glucose metabolism through synergistic interaction to reduce oxidative stress and plasma cholesterol levels.

Scientific research, in both animal and human subjects, generally concludes that there are multiple enzymatic and metabolic actions that play interactive roles in reducing insulin resistance, thereby helping improve blood glucose metabolism, reducing blood glucose and serum insulin levels, and therein reducing the health risks associated with chronic health concerns related to the diabetic condition. Research concludes that this is also the case in formulations comprised of Nutra-Iso® ingredients, as the bioactive nutraceutical isolates in these formulations interact in several ways to reduce insulin resistance, including:

- *Direct effect on insulin resistance* – In animal studies, insulin levels decreased by up to 70% after taking active ingredient extracts naturally embodied in Nutra-Iso®⁹. The Insulin/Glucose ratio is a measure of insulin efficiency and an indicator of insulin resistance. In one study, the insulin/glucose ratio was decreased by 65%¹⁰. In other animal studies, plasma glucose levels were decreased 22 to 26%¹¹. In other scientific research the amino acid Arginine has been found to increase insulin sensitivity and thereby reduce insulin resistance¹². The bioactive ingredients in Nutra-Iso® contain biologically significant levels of Arginine.

In addition, the tocotrienol complex embodied in Nutra-Iso® is significantly higher than essentially all natural sources and competitive nutritional supplements. Analyses

⁴Clinical Chemistry & Laboratory Medicine: 39 2001; Acta: Hungarian Journal Physiology: 85 1997; Scandinavian Journal of Clinical & Laboratory Investigation: 59 1999.

⁵Journal Biological Chemistry: 272 1997; American Journal of Physiology: 35 1997.

⁶Journal of Clinical Investigation: 97 1996; Diabetes Care: 25 2002.

⁷Journal of Nutritional Biochemistry: 13:175-187, 2002.

⁸Journal of Agriculture and Food Chemistry: 54: 1914-1920, 2006.

⁹Journal of Agriculture and Food Chemistry: 2006.

¹⁰Journal of Nutrition: 2006.

¹¹Journal of Agriculture and Food Chemistry: 2000; Atherosclerosis: 1991.

¹²Diabetes Care: 2001.

conducted by Brunswick Laboratories (and validated again by AIB International Laboratories) documented the Nutra-Iso® Nutritional ORAC Profile for antioxidants at 20,496 micromoles, over 30% higher than other natural sources. This antioxidant complex functions in a synergistic bioactive manner to help balance blood glucose metabolism and reduce the oxidative stress that often leads to insulin resistance and related diabetic health conditions¹³.

Certain nutritional components have been documented to aid blood glucose stabilization:

- *Antioxidant activity* – Nutra-Iso® Nutritionals contain very high levels of a number of natural polyphenols. These polyphenols have been found to have significantly higher antioxidant capacity than traditional supplemental vitamins (Vitamin E, C, etc.). In particular, Nutra-Iso® is high in natural tocotrienols, ferulic acid, gamma-oryzanol, inositol and several phytosterols. These antioxidants, in combination with over 80 additional natural antioxidants from the whole grain derivatives in Nutra-Iso® Nutritionals, have been clinically documented to play a synergistic role in reducing insulin resistance, blood glucose levels and serum lipid parameters in human subjects with the diabetic condition¹⁴.
- Independent laboratory analyses have documented the high natural antioxidant levels found in Nutra-Iso® bioactive ingredients¹⁵. Vitamin E is known to have eight homologues that are active in glucose metabolism, four each of tocopherols and tocotrienols. The primary bioactive function of the tocotrienol complex is its capacity as an antioxidant in improved cellular function and protection of the lipid cell membrane, thereby promoting healthy cellular function and more balanced blood glucose metabolism. Findings indicate that α -tocotrienol (contained in Nutra-Iso®) is at least 3- fold more efficient as a scavenger of peroxy radicals than conventional vitamin E [α -tocopherol]¹⁶. Nutra-Iso® contains significant levels of natural tocotrienols. In addition, scientific studies have further reported that these tocotrienols have been scientifically documented to lower total cholesterol and LDL cholesterol in blood plasma¹⁷. Studies suggest that this is accomplished by inhibiting the activity of the enzyme HMG-CoA which is responsible for cholesterol synthesis in the liver¹⁸. Micromolar amounts of tocotrienol, but not tocopherol, have been shown to suppress the activity of HMG-CoA¹⁹. These findings provide insight into how lipid metabolism modification associated with the active ingredients in Nutra-Iso® affects blood glucose metabolism and cholesterol levels. The sixty day clinical trials of the active ingredients embodied in Nutra-Iso® found an 8% reduction in LDL cholesterol.

¹³United States Patent Number 9,192,180 B2 "Nutritionally Enhanced Fraction from Rice Bran and Method of Lowering Insulin Resistance Using Same." Paul R. Reising and Glenn H. Sullivan, 2015.

¹⁴Journal of Nutritional Biochemistry: 2002; Journal of Agriculture and Food Chemistry: 2001.

¹⁵USDA, Journal of Agriculture and Food Chemistry: 2004; Brunswick Lab ORAC Test Values, 2011.

¹⁶Nutrition, Lipids, Health and Disease: 1995; pp 8-35.

¹⁷American Journal of Nutrition: 1991.

¹⁸Journal of Biological Chemistry: 1993.

¹⁹Journal of Medical Chemistry: 1992; Journal of Medical Chemistry: 1994.

- *Gamma-Oryzanol* – Nutra-Iso® Nutritional contains very high levels of natural gamma-oryzanol. Scientific studies have confirmed that oryzanol is a natural antioxidant superior to tocopherols²⁰. The biologically active portion of gamma-oryzanol is ferulic acid. Recent findings in animal studies reported that ferulic acid significantly decreased the levels of glycogen in the liver and skeletal muscle along with diminishing the activities of hepatic glucose-6-phosphate dehydrogenase, catalase and peroxidase in when compared with controls²¹. In addition, gamma-oryzanol has been shown to affect bile acid secretion and fecal excretion of cholesterol²². In recent scientific studies it has been found that the active ingredients embodied in Nutra-Iso® have reduced triglyceride and LDL levels 19.4% and 8% respectively. These reductions were found to be statistically significant²³.
- *Magnesium* – Nutra-Iso® is naturally high in magnesium which has been scientifically documented to play a supporting role in regulating blood glucose levels²⁴. An American Diabetes Association ‘Expert Panel’ concluded that magnesium may play an important role in reducing insulin resistance. Clinical researchers have also found an association between low magnesium levels and insulin resistance in Type 2 diabetics²⁵.
- *Chromium and Selenium* – Chromium Picolinate (a naturally occurring amino acid metabolite) and Selenium are both contained in Nutra-Iso® consumer formulations for addressing glucose imbalances, oxidative stress and insulin resistance. Chromium has been documented to play a supporting role in balanced glucose metabolism mitigating what is sometimes referred to as the glucose tolerance factor²⁶. This essential mineral functions to help stabilize blood glucose levels through proper insulin utilization within the cells, enabling the insulin to enter the cell more readily. The principal function of Selenium is to inhibit the oxidation of lipids as a component of the enzyme glutathione peroxidase. It is a vital antioxidant, particularly in synergism with tocotrienols, and helps protect the body’s immune system by preventing the formation of free radicals.
- *Fiber* – Nutra-Iso® is high in dietary fiber providing 4 grams per serving and 8 a total of grams in a daily dose. Dietary fiber has been found to lower free fatty acid levels in human subjects, thereby playing an important role in helping to decrease insulin resistance²⁷. Moreover, fiber has been shown to balance the rate of nutrient absorption. This balanced absorption helps the digestive system manage the secretion of intestinal hormones that play an important role in glucose metabolism and increasing insulin sensitivity²⁸. The bioactive ingredients embodied in the fiber derivative portion of the proprietary formulation of Nutra-Iso® help manage glucose metabolism.

²⁰Journal of Food Science Technology: 1993.

²¹Methods and Findings in Experimental and Clinical Pharmacology: 2008.

²²Atherosclerosis: 1989.

²³Journal of Agriculture and Food Chemistry: 2000.

²⁴White Paper, American Journal of Clinical Nutrition: 1987; Diabetes Care: 2003.

²⁵Diabetes Care: 1998.

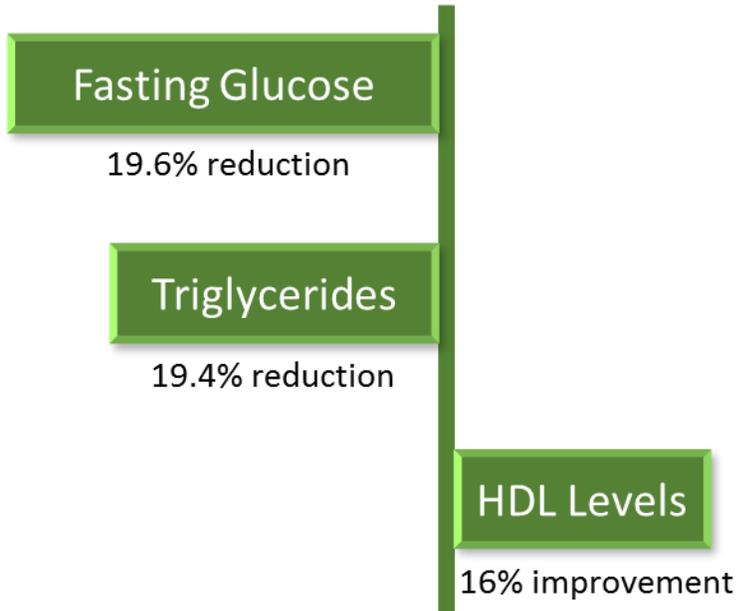
²⁶Dietary Chromium Overview: 2006.

²⁷Journal of Nutritional Biochemistry: 2002.

²⁸American Journal of Clinical Nutrition.

RICE BRAN CLINICAL RESULTS

30 Day Study Results



60 Day Study Results

