

NutraIso® Nutritional Bioactive Nutrition by Quintessence Nutraceuticals

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How Do NutraIso® Nutritional Work?

NutraIso Nutritional (NutraIso) is a natural nutraceutical dietary supplement 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 the bran and germ of derivatives of rice have been scientifically documented to lower and stabilize blood glucose levels and HbA1c in nutritionally 'at risk' populations, as well as balancing cholesterol and lowering triglycerides. The bioactive nutraceuticals embodied in NutraIso for mitigating such chronic health conditions meet the regulatory guidelines under FDA-DSHEA for all claims made, are hypoallergenic, gluten free and non-GMO.

Like many pharmaceuticals, the precise mode(s) of action for NutraIso 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 NutraIso 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 Endocrinologists 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 diabetes (Diabetes 46 1997; Diabetes 50 2001; Banting Lecture; Diabetes 51 2001). Increases in plasma lipid levels impairs insulin activity, increases in plasma FFA reduces insulin-stimulated glucose uptake, whereas a decrease in lipid content improves insulin activity in skeletal muscle cells, adipocytes and liver (Nature 414 2001).
2. Oxidative stress disrupting mitochondrial signaling leads to cellular insulin resistance (Nature 440 2006). Many biochemical pathways strictly associated with high blood glucose levels can increase the production of free radicals (Clin Chemistry & Lab Med 39 2001; Acta: Hung. J. Phys. 85 1997; Scand J. Clin & Lab Invest 59 1999). Prolonged oxidative stress in muscle and fat has been shown to significantly reduce insulin-stimulated glucose transport (J. Biol. Chem. 272

1997; Am. J. Physiol. 35 1997). 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 antioxidants in vivo (J. Clin. Invest. 97 1996; Diabetes Care 25 2002). NutraIso 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 NutraIso bioactive ingredients work synergistically to provide healthy glucose metabolism by reducing oxidative stress and plasma cholesterol levels in individuals with prediabetic health conditions (J. Nutritional Biochemistry (13:175-187, 2002). Supporting scientific evidence was further reported in the Journal of Agriculture Food Chemistry (54: 1914-1920, 2006). The total ferulic acid, phenolic and tocotrienol isolates embodied in NutraIso Nutritional 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 NutraIso 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 NutraIso (J. Ag. Food Chem. 2006). 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% (J. Nutr. 2006). In other animal studies, plasma glucose levels were decreased 22 to 26% (J. Ag and Food Chemistry. 2000; Atherosclerosis. 1991). In other scientific research the amino acid Arginine has been found to increase insulin sensitivity and thereby reduce insulin resistance (Diabetes Care, 2001). The bioactive ingredients in NutraIso contains biologically significant levels of Arginine.

In addition, the tocotrienol complex embodied in NutraIso is significantly higher than essentially all-natural sources and competitive nutritional supplements. Analyses conducted by Brunswick Laboratories, and validated by AIB International Laboratories documented the NutraIso 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 conditions.

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

- Antioxidant activity-NutraIso contains 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, NutraIso is high in natural tocotrienols, ferulic acid, gamma-oryzanol, inositol and several phytosterols. These antioxidants, in combination with over 70 additional natural antioxidants from the whole grain derivatives in NutraIso, 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 condition (J. Nutritional Biochemistry, 2002; J. Ag and Food Chemistry, 2001).
- Independent laboratory analyses have documented the high natural antioxidant levels found in NutraIso bioactive ingredients (USDA, J. Ag and Food Chemistry, 2004; Brunswick Lab ORAC Test Values, 2011). 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 NutraIso] is at least 3-fold more efficient as a scavenger of peroxy radicals than conventional vitamin E [α -tocopherol] (Nutrition, Lipids, Health, and Disease. 1995; pp 8-35). NutraIso Nutritional contains significant levels of natural tocotrienols.

In addition, scientific studies have further reported that these tocotrienols have been clinically documented to lower total cholesterol and LDL cholesterol in blood plasma (Am. J. of Nutrition, 1991). Studies suggest that this is accomplished by inhibiting the activity of the enzyme HMG-CoA which is responsible for cholesterol synthesis in the liver (J. Bio. Chemistry, 1993). Micromolar amounts of tocotrienol, but not tocopherol, have been shown to suppress the activity of HMG-CoA (J. Med. Chem. 1992; J. Med. Chem. 1994). These findings provide insight into how lipid metabolism modification associated with NutraIso's active ingredients affects blood glucose metabolism and cholesterol levels. A sixty-day clinical trial of the active ingredients embodied in NutraIso found an 8% reduction in LDL cholesterol (J. Nutritional Biochemistry (13) 2002).

- Gamma-Oryzanol- NutraIso contains very high levels of natural gamma oryzanol. Scientific studies have confirmed that oryzanol is a natural antioxidant superior to tocopherols (J. Food Science Technology, 1993). 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 when compared with controls (Methods Find Exp Clin Pharmacol 2008). In addition, gamma-oryzanol has been shown to affect bile acid secretion and fecal excretion of cholesterol (Atherosclerosis. 1989). In recent scientific studies it has been found that the

active ingredients embodied in NutraIso have reduced triglyceride and LDL levels 19.4% and 8% respectively. These reductions were found to be statistically significant (J of Ag and Food Chemistry, 2002).

- Magnesium- NutraIso Nutritionals are naturally high in magnesium, which has been scientifically documented to play a supporting role in regulating blood glucose levels (White Paper, American Journal of Clinical Nutrition, 1987; Diabetes Care, 2003. An American Diabetes Association 'Expert Panel' concluded that Magnesium may play an important role in reducing insulin resistance. Clinical researchers also have found an association between low magnesium levels and insulin resistance in Type 2 diabetics (Diabetes Care, 1998).
- Chromium and Selenium- Chromium Picolinate (a naturally occurring amino acid metabolite) and Selenium are both contained in NutraIso 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 factor (Dietary Chromium Overview, 2006). 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- NutraIso is high in dietary fiber, providing 4 grams per serving and 8 grams total 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 resistance (J. Nutritional Biochemistry, 2002). Moreover, dietary 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 sensitivity (American Jour. Clinical Nutrition). The bioactive ingredients embodied in the fiber derivative portion of NutraIso's proprietary formulation help manage glucose metabolism.

NutraIso received United 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.

NutraIso Clinical Trial Results: Prediabetic and Type2 Diabetic

Table 1. Mean diabetes-related blood chemistry results between treatment after 90 days of NutraIso consumption. Each dose was provided twice daily, e.g. the 5g dose is equivalent to 10 daily grams of NutraIso, the 10g treatment equivalent to 20 daily grams and the 15g dose is equivalent to 30g daily of NutraIso.

	GLUC mg/dl			HbA1c (%)			INSULIN uUI/ml		
	Average	Difference	% Difference	Average	Difference	% Difference	Average	Difference	% Difference
GROUP 1									
Control	165.27			7.03			8.67		
5 gr	145.41	-19.86	-12.02	6.56	-0.47	-6.69	6.44	-2.23	-25.72
10 gr	129.67	-35.60	-21.54	6.27	-0.76	-10.81	9.16	0.49	5.65
15 gr	127.10	-38.17	-23.10	5.97	-1.06	-15.08	12.17	3.50	40.37
GROUP 2									
Control	217.54			8.33			5.69		
5 gr	228.96	11.42		8.61	0.28		5.94	0.25	4.39
10 gr	213.39	-4.15	-1.91	8.70	0.37	4.44	8.23	2.27	38.09
15 gr	178.84	-38.70	-17.79	7.94	-0.39	-4.68	13.32	7.36	123.49

Values in yellow are statistically significant ($p < 0.05$) from values obtained in the control treatment.

Table 2. Longitudinal comparison of the “before” (0 days) and “after” (90 days) diabetes-related blood chemistry results at finalization of the NutraIso consumption period. Each dose was provided twice daily, e.g. the 5g dose is equivalent to the 10 daily grams of NutraIso, the 10g treatment equivalent to 20 daily grams and the 15g dose is equivalent to 30g daily of NutraIso.

Treatment	FASTING GLUCOSE mg/dl			HbA1c (%)			FASTING INSULIN uIU/ml		
	Average	Difference with control		Average	Difference with control		Average	Difference with control	
		mg / dl	%		percent points	%		uIU/ml	%
GROUP 1 (HbA1c ≥ 6.1% & < 7.5)									
Control									
0 days	142.49			6.68			5.99		
90 days	165.27	22.78	15.99	7.03	0.35	5.24	8.67	2.68	44.74
5 grams									
0 days	143.86			6.80			7.70		
90 days	145.41	1.55	1.08	6.56	-0.24	-3.53	6.44	-1.26	-16.36
10 grams									
0 days	126.96			6.60			8.35		
90 days	129.67	2.71	2.13	6.27	-0.33	-5.00	9.16	0.81	9.70
15 grams									
0 days	134.80			6.74			8.31		
90 days	127.10	-7.70	-5.71	5.97	-0.77	-11.42	12.17	3.86	46.45
GROUP 2 (HbA1c ≥ 7.5)									
Control									
0 days	227.90			8.62			4.13		
90 days	217.54	-10.36	-4.55	8.33	-0.29	-3.36	5.96	1.83	44.31
5 grams									
0 days	248.82			9.14			2.00		
90 days	228.96	-19.86	-7.98	8.61	-0.53	-5.80	5.94	3.94	197.00
10 grams									
0 days	267.05			9.45			2.22		
90 days	213.39	-53.66	-20.09	8.70	-0.75	-7.94	8.23	6.01	270.72
15 grams									
0 days	263.89			9.41			0.92		
90 days	178.84	-85.05	-32.23	7.94	-1.47	-15.62	13.32	12.40	1347.83

Values in yellow are statistically significant (p<0.05) from baseline (0 days) values obtained for the same treatment at the beginning of the trial.