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NUTRACEUTICALS

THE SCIENCE BEHIND GLYCODRIVE™

Overcoming the Carbohydrate Consumption Remorse

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THE SCIENCE BEHIND GLYCODRIVE™

Carbohydrates can be some of the most prevalent and palatable foods to consume. They are a rich, energy-dense, and premium source of energy in the human body. So much so, that our bodies have evolved to develop cravings for them and then preserve these calories for moments of high demand. In fact, excess carbohydrates are naturally stored as fat for future periods of famine. Nowadays, with the prevalence of famine being low in our regular lives, the consumption of grand amounts of carbohydrates is typically discouraged. With the exception of elite performance athletes, the over consumption of carbohydrates poses a potential risk of fat gain, insulin resistance, diabetes and an overall decrease in health and aesthetics. Consequently, there has been a trend for low-carbohydrate diets to combat this problem. However, despite this, carbohydrate consumption is still difficult to taper due to our evolutionary desire for them.

Overconsumption of carbohydrates for the average individual may occur simply by a lack of willpower, but there are several strategic reasons to intentionally overconsume carbohydrate calories. In a bulking phase, bodybuilders will typically overconsume all macronutrients in order to accrue additional mass. Endurance athletes will overconsume carbohydrates post-exercise in order to load the storage form of carbohydrates (glycogen) in their muscles. Additionally, some individuals consume meals with higher frequency which contributes to an increased demand on insulin signaling and potentially contributing to meal intolerance, more specifically glucose intolerance. Each of these strategies on their own can pose a risk that carbohydrates are not adequately being stored in muscle but rather ending up in adipose tissue as lipids and contributing to insulin resistance, leptin resistance, an inhibition of your metabolic rate, and potentially obesity.

GlycoDrive™ is a capsule product to be consumed prior to carbohydrate-heavy meals, particularly prior to post-exercise meals in order to maximize three distinct biological mechanisms to maintain your overall health and reduce the risks posed by overeating. The three mechanisms of GlycoDrive™ include: 1) enhancing carbohydrate oxidation so that less carbohydrates are left for storage, 2) increase the rate of muscle glycogen synthesis so that carbohydrates are being stored in muscle as glycogen rather than being converted to fat, and finally 3) maintaining a healthy sensitivity to insulin to reduce the health detriments of the carbohydrate overconsumption. Combining these mechanisms together will allow for the optimal destiny for a carbohydrate-rich meal. GlycoDrive™ contains five main ingredients to accomplish this effect.

Fenugreek

Fenugreek is an Indian plant that comes from the species, Trigonella foenum-graecum L, and is common in Indian cuisine. The seeds of fenugreek contain a relatively high concentration of a compound called

4- hydroxyisoleucine (4-OH-Ile), which is not something that is produced in humans. Mechanistic research of this compound reveals its unique ability to augment the insulin response to a carbohydrate meal either during resting or during post-exercise conditions. It is believed that the mechanism of this occurrence is due to a direct stimulation of the pancreatic beta cells.

Clinical research has explored the effects of 4-OH-Ile in human populations both at rest and after exercise. In one particular crossover study, where each participant experiences both experimental and control conditions, 148 mg of 4-OH-Ile or a placebo was combined with a 266 g of carbohydrates. The 266 g of carbohydrates represents caloric intake of over a thousand calories of carbohydrates. Over a 4-hour period glucose and muscle glycogen measurements were made. Despite an identical increase in plasma glucose in both trials during those 4 hours, the increase in muscle glycogen content was significantly greater in the trial containing 148 mg of 4-OH-Ile. During the placebo trial, muscle glycogen content increased by 53% whereas during the 4-OH-Ile trial, the increase in muscle glycogen content was 85% **(Figure 1)**. More convincingly, this effect was consistent for each participant in the study, and not just on average. When calculating for the rate of glycogen synthesis, it was determined that the 4-OH-Ile significantly increased the rate of glycogen synthesis 63% higher than the native rate of muscle glycogen synthesis.

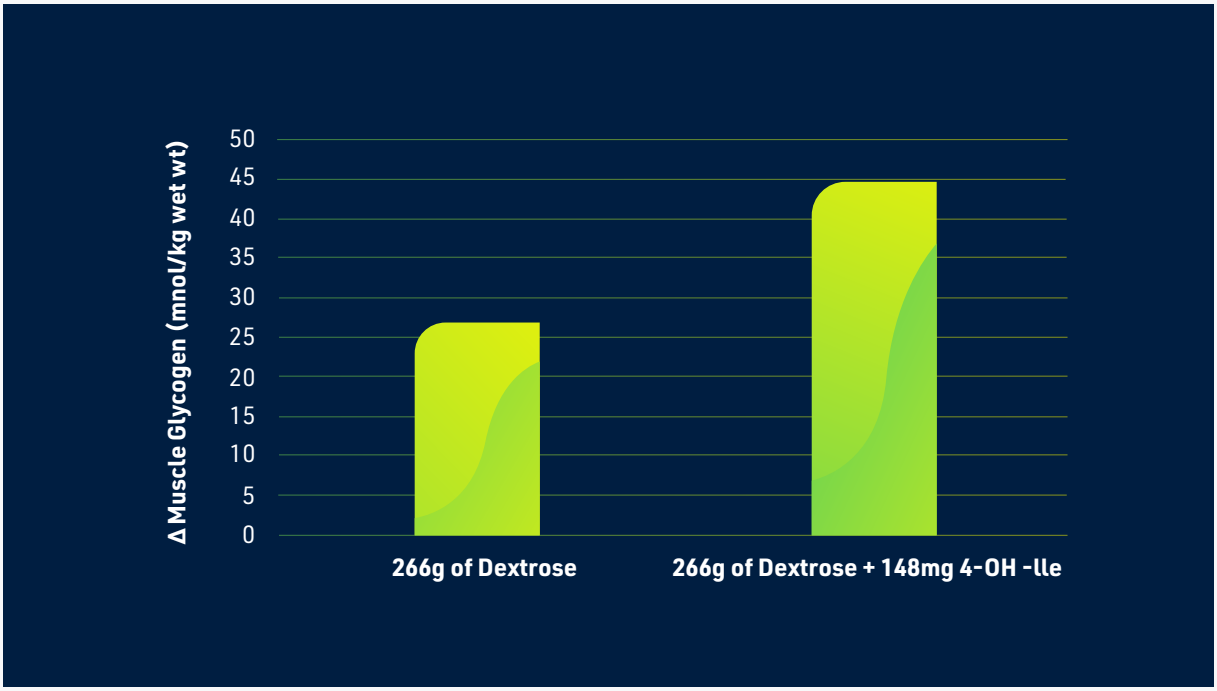

Figure 1. Muscle glycogen content 4 hours post-meal ingestion with and without 4-OHIle.

An increase in insulin stimulation alone does not account for the accelerated glycogen synthesis. This is because glycogen synthesis increased to a degree far greater than any insulin response. More so, insulin grossly signals all body tissues including fat cells to dispose glucose and not just muscle. Consequently, the authors suggested that 4-OH-Ile augments the insulin sensitivity and amplifies the glucose transport mechanism in muscle cells. Further mechanistic studies have explored this phenomenon and demonstrated that 4-OH-Ile helps activate the pathways involved with insulin sensitization.

GlycoDrive™ contains a natural supply of 4-OH-Ile through a fenugreek seed extract that has been standardized to 60%. Using 250 mg of this extract yields 150 mg of 4-OH-Ile, comparable to exactly the dose used in the human studies.

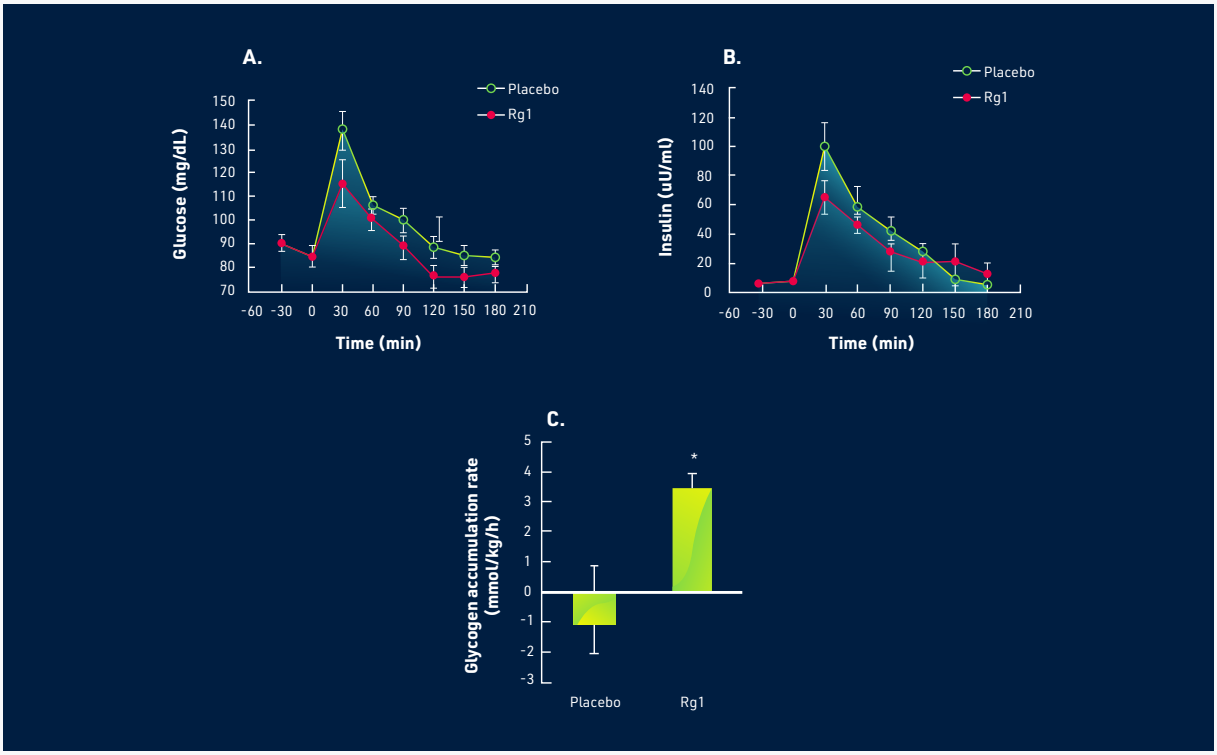

Figure 2. A. glucose and B. insulin response to a meal with Rg1 or placebo. C. glycogen accumulation rate with Rg1 versus placebo. *p<0.05 vs placebo.

ActiGin™

ActiGin™ is a branded proprietary combination of Panex notoginseng and Rosa roxburghi, with several clinically tested functional benefits. One of which is the promotion of glycogen synthesis. The major ginsenoside component of Panex notoginseng is called Rg1. In a human trial, the ergogenic effects of

Rg1 were tested in 14 untrained healthy men on measurements of meal tolerance and glycogen recovery post-exercise. A meal consisting of 2 g of carbohydrates per kg of body weight was consumed after an exercise challenge. Biopsied muscle tissue was obtained 3 hours later for evaluation. The results revealed that Rg1 significantly reduced the peak of glucose appearance in the blood, significantly reduced the insulin requirement to dispose the blood glucose levels and also, significantly increased the rate of glycogen accumulation **(Figure 2)**.

After further analysis into this mechanism, the investigators noticed an increase in mitochondrial carbohydrates metabolism in the Rg1 trial during the postprandial phase **(Citrate synthase activity, Figure 3)**. This indicates that not only was there an increased glycogen accumulation with Rg1 after the meal, but there was also a significant increase in metabolizing the carbohydrates as a result. Combined, the enhanced glycogen synthesis along with the increase in carbohydrate catabolism provides a clear explanation to why glucose did not peak as high in the bloodstream and why less insulin was required to dispose of it. Consequently, this mechanism provides a clear rationale for a decrease in depositing carbohydrates in fat tissue or de novo fatty acid synthesis and thus preserving overall health, exercise performance, and aesthetics.

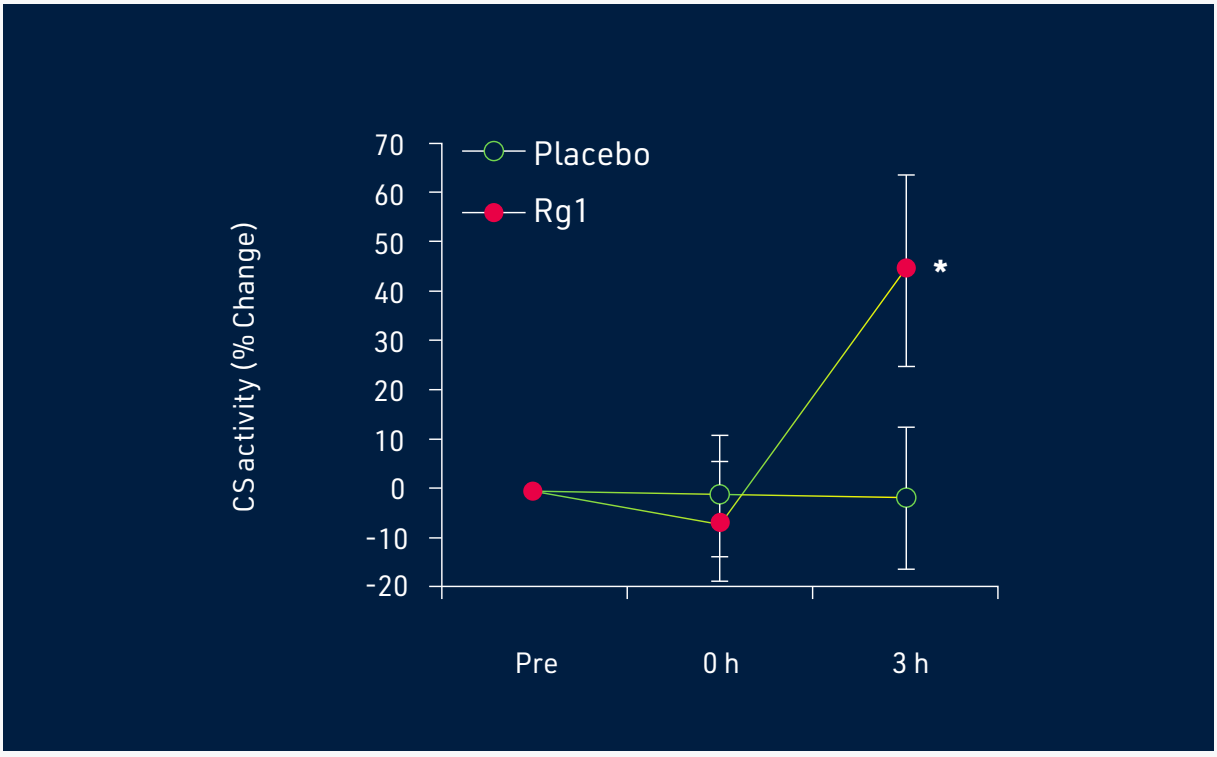

Figure 3. Citrate synthase (CS) activity as a measurement of mitochondrial activity with Rg1 versus placebo. *p<0.05 vs placebo.

The ActiGin™ used in GlycoDrive™ is the exact proprietary, branded ingredient and validated dose that was used in the aforementioned clinical trials. Including ActiGin™ in a carbohydrate-heavy meal, can significantly improve glycogen storage, increase carbohydrate metabolism and diverge carbs from being converted to fat. When used as part of your post-exercise carbohydrate loading, it can also confer some extra exercise performance benefits.

Vanadyl Sulfate

Chronic overeating (especially with carbohydrates) results in the repeated stimulation of insulin release and subsequent insulin signaling the target tissues to dispose of blood glucose. Over time, when this response continues to be overstimulated, the magnitude of its effectiveness becomes diminished. Once this occurs, tissues become less and less sensitive to insulin and as a result, more and more insulin is required to be released. This phenomenon is called "insulin resistance" and is associated with fat gain and other medical conditions, such as leptin resistance, obesity, diabetes and metabolic syndrome. Therefore, for carbohydrate-heavy eaters, bulking bodybuilders and high-frequency meal consumers, this can be a scary risk. For this reason, consuming supplements that support insulin sensitivity can actively reduce the risk of such negative health consequences.

YOU SHOULD KNOW

Frequently overconsuming carbohydrates, if left unchecked, can dramatically lead to fat gain over time. This unhealthy habit dysregulates how carbs in your body are directed and can perpetuate fat gaining. The specialized ingredients in GlycoDrive™ help regulate your system to appropriately use and/or store extra carbohydrates in muscle rather than storing them as fat.

At a molecular level, repeated and frequent stimulation of insulin release eventually leads to the suppression of its own insulin signaling at the target tissues. This can occur by stimulating PTP enzymes involved with degrading certain insulin signaling molecules. Vanadium containing compounds are known to inhibit such PTP enzymes and thus can prevent the degradation of insulin signaling molecules. Specifically, vanadate treatment has been shown to increase the activity of the insulin receptor and prolong signaling through the receptor by maintaining IRS-1 levels.

The insulinomimetic properties of vanadium compounds have been well documented in vitro and in vivo for years. Among its several insulin sensitizing effects, vanadium has also been shown to stimulate glucose uptake, glycogen synthesis in muscle and glucose oxidation in both adipose and muscle tissue.

Taken together with previous studies, vanadium works to decrease any hyperglycemia via its insulinomimetic effects on liver and muscle glucose metabolism. Supplementing with vanadium in the form of vanadyl sulfate supports a healthy degree of insulin sensitivity despite chronic overeating.

Banaba Leaf

Banaba leaf comes from the species Lagerstroemia speciosa and appears to mimic the effects of insulin by binding to the insulin receptor and activating the glucose transporters in muscle. The hypoglycemic effect of banaba have been demonstrated in several animal as well as a number of human studies. The active component, corosolic acid is believed to confer the effects.

A human study indicates that 10 mg of Corosolic acid 5 minutes before 75 g of glucose significantly improved glucose tolerance over 90 minutes, indicating an improvement in insulin sensitivity. A clinical study with participants exhibiting high blood glucose levels, 48 mg of banaba standardized to 1% corosolic acid was shown to reduce blood glucose levels by 20%. Clinical studies have also been conducted on healthy nondiabetic subjects showing a significant reduction in 60 minute postprandial blood glucose levels. Additional proposed mechanisms include that corsolic acid increases glycolysis which then helps to burn excess carbohydrates that are consumed and also inhibits sucrose, the enzyme that breaks down sugar, which is great for meals high in added sugar.

GlycoDrive™ includes 50 mg of banaba extract standardized to 1% corosolic acid. This dose is in accordance with several studies that show a reduction in blood glucose through improved insulin signaling.

Chromium

Chromium is considered an essential mineral that is involved in the metabolism of carbohydrates, lipids and proteins. Supplementation with chromium can be a simple method to improve blood sugar control. A significant number of studies have shown that chromium can normalize blood sugar levels, improve blood sugar utilization and decrease insulin requirements in individuals with glucose intolerance and insulin resistance. In one study, blood sugar responses to a carbohydrate meal of white bread were measured with and without a single dose (400 micrograms) of chromium. The addition of chromium resulted in a 23% reduction in blood sugar after the meal. Thus, taking chromium with carbohydrate-rich foods may be an effective way to lower the glycemic index of that meal.

Among its many functions, chromium increases insulin-stimulated glucose uptake in muscle cells by increasing insulin binding to the insulin receptor, enhancing the reactivity of the insulin receptor, and improving the downstream insulin signaling pathways. For example, the enhancement of insulin action by chromium is associated with phosphorylation of IRS-1 and PI3K. These lead to the translocation

of glucose transporters from the cytosol to the membrane. Since chromium acts to potentiate insulin signaling, it also aids with glycogen formation. The magnitude of glycogen synthesis is regulated by glucose availability and glycogen synthase activity.

Chromium in the form of picolinate has been shown to significantly enhance activation of glucose transporters, called GLUT4, to improve the rate of glucose delivery into muscle after stimulated with insulin. The comparative data results of chromium picolinate versus other forms of chromium demonstrated that it is the most effective form to facilitate glucose control. It was also observed that chromium picolinate is better absorbed physiologically, than chromium chloride and chromium acetate. Chromium oxide is not absorbed at all.

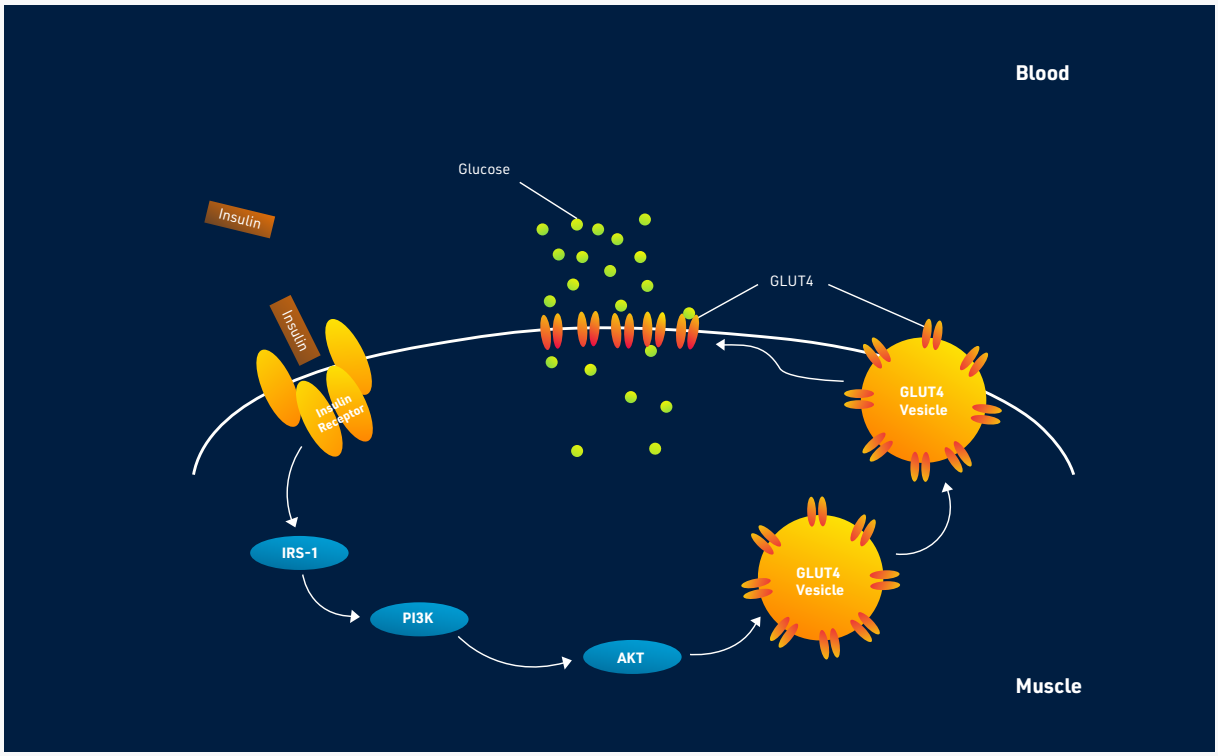

Figure 4. Insulin stimulated glucose uptake pathway. Insulin binds and activates an insulin receptor which activates insulin receptor substrate-1 (IRS-1) which activates phosphatidylinositol-3-kinase (PI3K) which then activates AKT to translocate vesicles containing GLUT4 transporters to the cell membrane. GLUT4 on the membrane then transports glucose molecules from the blood stream into the cell.

GlycoDrive™ uses the research-backed dose of 500 µg of chromium in the form of chromium picolinate to enhance insulin sensitivity, glucose transport, and glycogen synthesis.

CONCLUSION

The overconsumption and high frequency of carbohydrates intake dramatically increases the risk of several conditions related to insulin resistance and accumulated fat deposits. GlycoDrive™ is a product to minimize the negative health impact of carbohydrate-heavy, and carbohydrate-frequent meals. For whatever your reason for high carbohydrate eating, consuming GlycoDrive™ before each meal will help decreased the release of insulin, improve the sensitivity of insulin, enhance glucose delivery to muscle rather than fat, increase the synthesis of glucose into muscle glycogen and finally, increase carbohydrate metabolism to decrease the impact of the added carbohydrates to your system. Overall, Glycodrive™ gives you "More For Your Muscles".

Rob Riches
Blue Star Nutraceuticals® Athlete

References

Broca C, Gross R, Petit P, Sauvaire Y, Manteghetti M, Tournier M, Masiello P, Gomis R, Ribes G. 4-Hydroxisoleucine: experimental evidence of its insulinotropic and antidiabetic properties. Am J Physiol 277; E3614-623, 1999.

Broca C, Manteghetti M, Gross R, Baissac Y, Jacob M, Petit P, Sauvaire Y, Ribes G. 4-Hydroxyisoleucine: effects of synthetic and natural analogues on insulin secretion. Eur J Pharmacol 290: 339-345, 2000.

Broca C, Breil L, Cruciani-Guglielmacci C, Manteghetti M, Rouault C, Derouet M, Rizkalla S, Pau B, Petit P, Ribes G, Ktorza A, Gross R, Reach G, Taouis M. Insulinotropic agesnt ID-1101 (4- hydroxyisoleucine) activates insulin signaling in rat. Am J Phsyiol Endocrinol Metab. 287(3); E463-E471, 2004.

Cohen N, Halberstam M, Shlimovich P, Chang CJ, Shamoon H, Rossetti L. Oral vanadyl sulfatye improves hepatic and peripheral insulin sensitivity in patients with non-insulin-dependent diabetes mellitus. J Clin Invest. 95(6); 2501-2509, 1995.

Frauchiger MT, Wenk C, Colombani PC. Effects of acute chromium supplementation on postprandial metabolism in healthy young men. J Am Coll Nutr. 23(4); 351-357, 2004.

Fukushima M, Matsuyama F, Ueda N, Egawa K, Takemoto J, Kajimoto Y, Yonaha N, Miura T, Kaneko T, Nishi Y, Mitsui R, Fujita Y, Yamada Y, Seino Y. Effect of corosolic acid on postchallenge plasma glucose levels. Diabetes Res Clin Pract. 73 (2); 174-177, 2006.

Hou CW, Lee SD, Kao CL, Cheng IS, Lin YN, Chuang SJ, Chen CY, Ivy JL, Huang CY, Kuo CH. Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementations of the Ginseng-Based Steroid Rg1. PLoS One 10(1); e0116387. doi10.1371/journal.pone.0116387, 2015.

Jackson TK, Salhanick Al, Sparks JD, Sparks CE, Bolognino M, Amatruda JM. Insulin-mimetic effects of vanadate in primary cultures of rate hepatocytes. Diabetes. 37(9); 1234-1240, 1988.

Jette L, Harvey L, Eugeni K, Levens N. 4-Hydroxyisoleucine: a plantderived treatement for metabolic syndrome. Curr Opin Ivestig Drugs. 10(4); 353-358, 2009.

Judy WV, Hari SP, STogsdill WW, Judy JS, Naguib YM, Passwater R. Antidiabetic activity of standardized extact (Glucosol) from Lagerstroemia speciose leaves in Type II diabetics. A dosedependence study. J Ethnopharmacol. 87(1); 115-117, 2003.

Quann EE, Silvestre R, Kirwan JP, Sharman MJ, Judelson DA, Spiering BA, Vingren JL, Maresh CM, VanHeest JL, Kraimer WJ, Volek JS. Effects of chromium supplementation on glycogen synthesis and insulin signaling after high-intensity exercise. Med Sci Sports Exerc. 38(12); 2102-2109, 2006.

Ruby CB, Gaskill SE, Slivka G, Harger SG. The addition of fenugreek extract (Trigonella foenum-graecum) to glucose feeding increases muscle glycogen resynthesis after exercise. Amino Acids 28; 71- 76, 2005.

Sauvaire Y, PetitP, Broca C, Manteghetti M, Baissac Y, FernandezAlvarez, J, Gross R, Roye M, Leconte A, Gomis R, Ribes G. 4-Hydroxyisoleucine: a novel laminon acid potentiator of insulin secretion. Diabetes. 47(2); 206-210, 1998.

Slivka D, Cuddy J, Hailes W, Harger S, Ruby B. Glycogen resynthesis and exercise performance with the addition of fenugreek extract (4-hydroxyisoleucine) to postexercise carbohydrate feeding. Amion Acids. 35(2); 439-444, 2008.

Tsuchibe S, Kataumi S, Mori M, Mori H. An inhibitory effect on the increase in the postprandial glucose by banaba extract capsule enriched corosolic acid. J Integ Stud Diet Hab. 17; 255-259, 2006.

Volek JS, Silvestre R, Kirwan JP, Sharman MJ Judelson DA, Spiering BA, Vingren JL, Maresh CM, Vanheest JL, Kraemer WJ. Effects of Chromium Supplementation on Glycogen Synthesis after HighIntensity Exercise. Med Sci Sport Exerc. 38(12); 2102-2109, 2006.

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Dr. David Gundermann is an award winning nutritional product development scientist, clinical researcher, and known expert in muscle health and metabolism. He developed his passion for health & fitness at a very early age growing up in a family of accomplished competitive athletes.

As Director of Research and Development at Blue Star Nutraceuticals®, he leads all efforts concerning product formulation, key ingredient research, flavor science, long-term scientific assessment, and proprietary development.

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