Nitric Oxide Stimulating Dietary Supplements: 
Introducing 
Glycine Propionyl-L-Carnitine (GPLC-GlycoCarn®)

What is Nitric Oxide?
Nitric oxide (NO), initially known as endothelium derived relaxing factor (EDRF), is biosynthesized within the body from L-arginine and oxygen by a variety of nitric oxide synthase enzymes (Collier and Vallance, 1991). Nitric oxide is a gaseous chemical compound that acts as an important signaling molecule within the human body. Nitric oxide has been shown to decrease platelet and leukocyte adhesion, as well as to decrease the proliferation of smooth muscle cells. These effects are important in reference to decreasing clot and lesion formation within blood vessels, which may be associated with non-fatal and fatal outcomes (e.g., heart attack, stroke). Recent evidence also indicates that NO may be involved in both glucose and fatty acid oxidation (Jobgen et al., 2006). Although, perhaps the most well studied effect of NO is in facilitating vasodilation (opening of blood vessels).

The endothelium (inner layer) of blood vessels is involved in NO production, which acts on vascular smooth muscle cells to promote vasodilation. For this reason alone, nitric oxide has received considerable attention over the past 20+ years from scientists. In fact, NO was recognized as “molecule of the year” by Science in 1992. Additionally, the Nobel Prize in Physiology or Medicine was awarded in 1998 to Robert Furchgott, Louis Ignarro, and Ferid Murad for their discoveries related to NO. Over the past 5 years in particular, NO has received a great deal of attention from health and fitness enthusiasts, as well as from sports supplement companies who widely market products claiming to increase NO production. In this regard, the primary desired effect is the potential increase in blood flow.

Exercise and Nitric Oxide
The demands for increased blood flow with acute strenuous exercise are significant. Although several mechanisms are available to allow for optimal blood flow redistribution with acute exercise, NO indeed plays a major role. While supplement companies market products targeted at increasing NO, it should be understood by readers that both acute and chronic exercise have been reported to increase circulating NO. This is often determined by the combined measurement of nitrate+nitrite (NOx), which are stable products of the rapidly degraded NO.

Specifically, blood concentrations of NO increase in response to strenuous single bouts of exercise (Bode-Boger et al., 1994; Clarkson et al., 1999), a finding that is evident for both dynamic (Hickner et al., 1997) as well as for isometric (Gilligan et al., 1994) exercise. Studies involving chronic exercise training performed 3-4 days per week have also noted an increase in resting levels of NO, as measured by NOx (Edwards et al., 2004; Poveda et al., 1997; Tordi et al., 2006). What this means is that individuals who exercise on a regular basis have an enhanced production of NO at rest, which may help explain some of the positive health and performance outcomes apparent in exercise trained compared to sedentary individuals. Obviously, if enhancing NO is of importance, regular structured exercise should be a component of an individual’s routine, regardless of the use of NO stimulating supplements.

Traditional Drugs/ Dietary Supplements and Nitric Oxide

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Aside from exercise, pharmaceutical agents have been used with success to induce NO· biosynthesis, with the end goal of promoting vasodilation (Burgaud et al., 2003). Such agents are often used to treat various forms of cardiovascular disease (e.g., angina, peripheral arterial disease). In some studies, treatments have included high dosages of the NO· precursor amino acid, L-arginine, which has been delivered via intravenous injection (at least in those studies demonstrating a benefit). A simple review of those studies that do report a potential benefit of L-arginine in this regard is what constitutes the “research” performed by most supplement companies marketing NO· stimulating products. Indeed, actual testing of the various products of sale using a controlled research design is, for the most part, nonexistent.

It is evident that the majority of such products contain various forms of L-arginine as the chief ingredient. Unfortunately, as discussed below, this may not be appropriate when considering all variables know to affect the response to L-arginine treatment (e.g., dosage, route of administration, species studied). Equally important, although L-arginine is the precursor to NO· biosynthesis, it has been suggested that this amino acid is not the rate limiting component (Kurz and Harrison, 1997) and that nitric oxide synthase enzymes may be most important to NO· biosynthesis. Therefore, adding excess L-arginine may do little to promote increased NO· production, as most individuals already have adequate L-arginine available for NO biosynthesis. What they may need is an increase in certain enzymes that appear to ultimately control NO· production. The supposed “effect” that individuals may experience when using many of the marketed products may be more dependent on the sugar contained within the product, as opposed to the L-arginine. This is because sugar intake results in an insulin spike, and insulin itself has been shown to yield a vasodilating effect (Giugliano et al., 1997; Steinberg et al., 1994).

Despite this, it is evident that dietary supplements marketed to increase NO· production are rampant within the supplement industry. In fact, a quick scan of many of the popular bodybuilding magazines indicates that in any given month there can be more than 30 pages of advertisements that focus solely on this particular class of supplements! As with many dietary supplements, the scientific evidence for effect for these products is virtually nonexistent. Of course, some of the chief ingredients found within some of these products may have been shown to result in a measurable increase in NO· or an increase in blood flow. But a careful review of the original investigations indicates that the dosing suggested by the manufacturer of the product is often FAR less than that used in the original investigation. More importantly, the route of administration is often different. That is, many original investigations using a given ingredient have used intravenous injection and not oral intake, as is being marketed by supplement companies. This is of particular importance, as L-arginine at an oral dosage of only 10 grams per day has been noted to have an unpleasant taste and in some cases result in gastric distress (Robinson et al., 2003). It has also been reported that oral intake of L-arginine of 20+ grams per day results in arginine absorption that is highly variable across subjects, and does not result in any significant increase in vasodilation (Adams et al., 1995; Chin-Dusting et al., 1996), unlike findings from many studies involving intravenous injection. Other work involving direct comparisons between intravenous and oral intake of L-arginine agrees with these findings (Bode-Boger et al., 1998), indicating no effect of oral L-arginine intake on vasodilation, partly due the fact that oral L-arginine bioavailability is only ~68%. Hence, based on the available evidence, it seems unlikely that oral L-arginine intake will result in any improvement in blood flow. Lastly, some of the original investigations have used animals (typically rodents) as test subjects and not humans, or have involved experiments in vitro (i.e., outside of a living organism). Generalizations to humans cannot always be made from such studies. Collectively, the fact...
remains that no nutritional supplements marketed to increase NO have been shown in a controlled laboratory study involving human subjects to increase blood levels of NO. That is, until recently.

**Glycine Propionyl-L-Carnitine and Nitric Oxide**

Glycine Propionyl-L-Carnitine (GPLC) is a USP grade dietary ingredient which consists of a molecular bonded form of propionyl-L-carnitine and one of the carnitine precursor amino acids, glycine. It is marketed as GlycoCarn® through Sigma-tau HealthScience. Two recent studies have demonstrated an increase in blood levels of NOx with oral GPLC intake, at a daily dosage of 4.5 grams (Bloomer et al., 2007; in press). These findings agree with other recent work using PLC exclusively (Lofreddo et al., 2007) which demonstrated an increase in blood NOx in response to 6 grams per day of PLC given via intravenous infusion.

The first study to use GPLC involved previously sedentary men and women who were assigned to supervised aerobic exercise with or without treatment for eight weeks (Bloomer et al., in press). A significant increase in resting levels of blood NOx was noted for subjects receiving GPLC compared to placebo (in a double blind design). Subjects who received GPLC were also noted as having lower levels of lipid peroxidation, a measure of free radical mediated oxidation of lipids. This is important, as increased free radical production is associated with impaired NO bioavailability.

The second study to use GPLC involved resistance trained men who were assigned to GPLC and a placebo for four weeks each, with a two week washout period between each four week phase—also using a double blind design (Bloomer et al., 2007). At the end of each four week phase, resting blood samples were obtained, in addition to blood samples following static forearm exercise (used to induce a further increase in NO). Blood NOx was noted to be higher in response to the forearm exercise with GPLC compared to placebo, a finding that may have implications related to enhanced blood flow during acute bouts of exercise.

**Need for Further Research**

If a given oral dietary supplement is in fact capable of stimulating an increase in circulating NO (to date, GPLC is the only such ingredient reported in the scientific literature to do so), to observe a desired effect it must be assumed that 1) the increase in circulating NO will cause an increase in blood flow to working skeletal muscle, 2) the increase in blood flow will be associated with an increase in oxygen and nutrient delivery, and 3) the increase in oxygen and nutrient delivery will promote a) an increase in work capacity during exercise and b) enhanced recovery post exercise. Study pertaining to these variables in human subjects using this class of nutritional supplement is indeed in its infancy. Continued work over the next couple of years will hopefully provide new insight into addressing these interesting and important issues.

**Practical Applications**

It is well documented that NO acts in blood vessel dilation and improved blood flow. For athletes and fitness enthusiasts, this is essential because greater blood flow is associated with increased oxygen and nutrient delivery to skeletal muscle. This may be important both during the exercise bout (to aid in performance and to improve the muscle “pump”), as well as during the recovery period (to aid in nutrient delivery to help facilitate exercise recovery). In this way, products aimed at increasing NO may prove helpful. To date, GPLC is the only dietary ingredient reported to promote such an effect, which may be enhanced if consumed with carbohydrate rich meals, as insulin has been shown to promote vasodilation (Giugliano et al.,
1997; Steinberg et al., 1994) and to enhance carnitine retention (Stephens et al., 2006; 2007), which may apply to GPLC (a novel form of carnitine). Continued research on this ingredient will provide additional information pertaining to the potential for enhanced blood flow, and subsequent enhanced performance and recovery associated with exercise.
References


Bio

Richard J. Bloomer holds a PhD in Exercise Physiology and is currently an Assistant Professor within the Department of Health and Sport Sciences at The University of Memphis. He held prior positions at Duke University Medical Center and Wake Forest University. His research focus is centered on oxidative stress and antioxidant therapy.

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Dietary Glycine Propionyl-L-Carnitine HCl, USP (GPLC-GlycoCarn®) for Human Health and Performance

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Dietary supplementation with the naturally occurring nutrient L-carnitine has been extensively studied as an aid to improve fatty acid metabolism and aerobic exercise capacity, to provide antioxidant benefits, and to enhance blood flow to active tissues (e.g., skeletal muscle and heart). While multiple forms of carnitine have been the focus of ongoing scientific study over the past several decades, and several are currently available for retail sale, Propionyl-L-Carnitine (PLC) has been shown to provide an optimal vasodilatory effect to blood vessels, and to support healthy heart and skeletal muscle function. Unfortunately, PLC itself is currently classified as a drug in Europe and elsewhere through Sigma-tau Industries. Additionally, PLC is likewise scheduled to achieve similar drug status within the USA as a treatment for blood vessel disorder (intermittent claudication; impaired blood vessel supply to lower extremities). Fortunately, a purely unique, patented and safe USP dietary form of PLC has been developed which is molecularly bonded to glycine, one of the precursor amino acids to carnitine biosynthesis. This form offers the benefits associated with PLC, including enhanced fatty acid metabolism, antioxidant function, and blood flow. This bonded form is called Glycine Propionyl-L-Carnitine (GPLC) or GlycoCarn®, which is essentially structured to simultaneously deliver two parts PLC and one part glycine. This exclusive third generation form of AminoCarnitine® is branded and marketed as a raw material called GlycoCarn® by Sigma-tau HealthScience and is a certified USP dietary supplement. Since 2005, we have been studying the health and performance effects of GlycoCarn® within human subjects, using both noninvasive (e.g., exercise tolerance testing) and invasive measures (e.g., blood sampling and muscle biopsies). We have been particularly interested in the benefits of GlycoCarn® related to the following, with a brief rationale provided for each.

Antioxidant Function: A well-described effect of PLC is the ability of this nutrient to reduce the potentially harmful effects of free radicals. When free radical production overwhelms antioxidant defense, a condition of “oxidative stress” occurs, which is associated with damage to important molecules such as lipids, proteins, and DNA. Increased oxidative stress is thought to play a role in both acute illness and chronic disease, and is strongly associated with the aging process. Therefore, the focus of many individuals in recent years has been to decrease oxidative stress via antioxidant intake.

Fatty Acid Metabolism: Carnitine is critical for the transport of activated long chain fatty acids into the mitochondria of the cell (i.e., the energy producing component of the cell). In theory, increased fatty acid metabolism would result in the increased “burning” of fat as an energy source, leading to improvements in blood triglycerides, body fat, and energy levels. This is particularly true for individuals who may have problems in these specific areas (i.e., high blood triglycerides values, excess body fat, poor energy levels).

Vasodilatation (i.e., increased blood flow): An exciting finding in recent studies using PLC is improved blood flow following treatment. This appears mediated by an increase in the important signaling molecule known as nitric oxide (NO·), which acts in blood vessel dilation (i.e., opening), allowing for enhanced blood flow. This is of particular importance for individuals with compromised blood flow due to cardiovascular disease, as well as for athletes seeking to enhance blood flow to aid oxygen and nutrient delivery to working skeletal muscles during and following acute bouts of exercise.

The text below describes our initial work using GlycoCarn®, in addition to how GlycoCarn® may have applications in the dietary supplementation regimen of otherwise healthy individuals.

To date, we have completed two human clinical trials using GlycoCarn®, and one other is currently underway in another laboratory within the USA. Additionally, we are now completing an additional human trial using another AminoCarnitine® called ArginoCarn®, which is also a USP registered dietary ingredient. This commitment to funding scientific research underscores the interest of Sigma-tau in evaluating the efficacy of their ingredients.
Our first study involved sedentary men and women who were assigned to supervised aerobic exercise with or without GlycoCarn® treatment for a period of eight weeks. The main findings of benefit in subjects using GlycoCarn® included a significant increase in resting levels of blood nitrate/nitrite (a surrogate marker of nitric oxide), as well as a drastic decrease in lipid peroxidation (a byproduct of free radical mediated damage), in comparison to subjects assigned to a placebo condition. We also noted an average decrease in blood triglyceride values ranging from 11-22%, which occurred in a dose dependant manner (however, these latter findings were not of statistical significance).

To follow up on this research, we studied if GlycoCarn® could yield the same increase in blood nitrate/nitrite in exercise-trained men, as in our previous group of sedentary subjects. We did this both at rest and following a protocol of forearm exercise used to further stimulate an increase in blood flow. Our findings were very interesting. That is, nitrate/nitrite was higher at rest in subjects when consuming GlycoCarn® compared to placebo and increased to a greater extent following exposure to the forearm exercise. Such findings may have important implications for exercising individuals who desire enhanced blood flow during an acute exercise bout. We believe that these findings are very timely considering the current interest in “nitric oxide stimulating products”, which continue to be one of the most popular dietary supplement classes in the fitness/bodybuilding world. To our knowledge, despite the marketing hype, there exist no published reports in scientific format indicating an increase in blood nitric oxide with any of the advertised products. GlycoCarn® is the only dietary supplement to date shown to yield an increase in blood nitrate/nitrite in human subjects.

In relation to the above studies, it should be noted that data from our first study will be published in early 2008 in The International Journal for Vitamin and Nutrition Research, while data from the second study is now published in the Journal of the International Society of Sports Nutrition. Interested individuals may secure a full text copy of these studies online or by contacting me directly at rbloomer@memphis.edu.

Considering the available evidence, it can be stated that GlycoCarn® can 1) provide antioxidant function to decrease the potentially harmful effects of free radicals, 2) enhance nitric oxide production which may allow for improved blood flow and 3) improve blood triglyceride values which may be related to enhanced fatty acid metabolism, in particular within individuals with previously elevated blood triglycerides. Hence, GlycoCarn® may be considered as a multi-component dietary supplement. In these regards, Life Extension’s Optimized Carnitine® and Peak ATP w/GlycoCarn®, both of which contain GlycoCarn® as the primary ingredient, may be considered as one component of a complete supplementation regimen in otherwise healthy individuals. Of course, as with all dietary supplements, individual response will vary. That is, some may experience extraordinary benefits while others note little benefit. Experimentation on the part of the individual, coupled with the approval and supervision by a qualified health care professional is always necessary.
Bio
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Figure 1. Plasma nitrate/nitrite before and after an ischemia-reperfusion protocol in 15 resistance trained men supplemented with GPLC and placebo in a cross-over design.
Note: Condition main effect (p=0.0008); No time main effect (p=0.7099) or interaction effect (p=0.8809); paired time contrasts at 3 (p=0.033) and 10 (p=0.036) minutes post protocol; rest (p=0.189) and 0 (p=0.187) minutes post protocol; % change from rest presented for each time post protocol. Values are mean ± SEM.


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Oxidative Stress and Exercise:

Role of Glycine Propionyl-L-Carnitine (GPLC-GlycoCarn®)

Introduction
Oxidative stress occurs when the production of reactive oxygen species (ROS), often referred to as “free radicals”, exceeds antioxidant defense (Halliwell and Cross, 1994; Sies, 1997). The antioxidant system is comprised of both endogenous (within the body) and exogenous (outside of the body) defense mechanisms. Oxidative stress may progress to oxidative damage involving cellular proteins (contractile, structural, and enzymatic), lipids, DNA, and other molecules in ways that might lead to abnormal cellular function. The degree of oxidative damage, as well as the time course for elevation in oxidative stress biomarkers has varied across studies, and appears dependant on the type, intensity, volume and duration of exercise, the exercise training and nutritional status of the research subjects, and the tissues being investigated (Bloomer and Goldfarb, 2004). With excessive oxidative damage, the onset of poor health and a variety of diseases exists (Dhalla et al., 2000). It should be noted that despite the potential for excessive ROS production to be problematic, low levels of ROS appears necessary for important physiological functions such as cell signaling, immune response, and apoptosis (Volaard et al., 2005). While ROS are constantly produced in small quantities within biological systems, their presence increases when exposed to both environmental and physical stressors (Halliwell and Cross, 1994). Exercise is one such stressor; hence, the use of antioxidant agents to combat ROS has been very popular in recent years.

Exercise and ROS Production
The topic of exercise-induced oxidative stress has received much attention over the past 30 years since it was first reported that lipid peroxidation was increased following 60 minutes of cycling exercise (Dilliard et al., 1978). Based on the available evidence, it is clear that exercise of sufficient intensity (typically >60% VO$_2$max or 50% one repetition maximum) and duration increases the formation of ROS, having the potential to create an imbalance between oxidant and antioxidant levels. Interestingly, while acute exercise appears to increase ROS transiently, this same exercise stimulus is needed to allow for an up-regulation in endogenous antioxidant defenses (Powers et al., 1999). In this way, the generation of ROS acts as the “signal” to allow for these important adaptations in antioxidant defense, which may have significant implications for protection against future elevations in ROS.

The specific sites of ROS generation with acute exercise have been previously discussed in detail (Bloomer and Goldfarb, 2004; Jackson et al., 2007). These include both primary sources in which ROS are generated in direct response to a given condition, as well as secondary sources in which ROS production may occur in response to damage induced through other mechanisms, such as eccentric muscle actions which are common with strength/bodybuilding type exercise.

A major pathway for ROS generation during exercise involves oxygen, where oxygen is ultimately used for ATP production. Under normal physiological conditions, most of the oxygen consumed by cells is reduced to water in the mitochondria. However, some of the oxygen (1-5%) passing through the mitochondrial respiratory chain may give rise to superoxide, which may lead to other harmful ROS. This is especially apparent during acute sessions of strenuous exercise when oxygen uptake may increase 10-20 fold. In addition to generation through mitochondrial electron transport, ROS can be produced through other primary sources including prostanoid metabolism, and enzymatic reactions involving NADPH oxidase and xanthine oxidase, which are radical species generators (Jackson, 2007).
Secondary sources of ROS initiation can arise from exercise which involves muscle injury, such as high force eccentric muscle actions. This involves to a large extent the invasion of phagocytic cells into damaged tissue in an attempt to promote healing. In addition, muscle injury may be accompanied by disruption of iron containing proteins such as erythrocytes and myoglobin, which can lead to an increase in free iron which is known to catalyze radical reactions. Therefore, exercise that creates significant trauma such as high impact aerobic exercise or high force eccentric actions, may lead to destruction of these proteins, allowing for increased free iron availability to aid in the production of ROS. Finally, any imbalance in calcium handling, such as excessive intracellular calcium accumulation, may lead to ROS production. This appears to occur through the activation of phospholipase and proteolytic enzymes.

In the above ways, intense physical activity has been reported in several investigations to lead to an oxidative stress, as previously reviewed in detail (Bloomer and Goldfarb, 2004; Finaud et al., 2006; Volaard et al., 2005). One concern that many athletes have is the impact of ROS formation on physical performance. While few direct human investigations have focused on this area of research, the following section provides a brief summary for consideration.

**Association between ROS and Physical Function**

While human data are scarce, animal studies have noted impaired contractile function, reductions in muscle force output, and greater fatigue rates in isolated skeletal muscle as a function of increased ROS (Reid et al., 2001). It is important to keep in mind that oxidative alteration to proteins in particular can lead to impaired physical performance (Goldhaber and Qayyum, 2000), as proteins are involved in enzymatic reactions as well as actual muscle contraction (actin and myosin filaments).

Two human studies have investigated the relationship between oxidative stress and exercise overtraining/overreaching. In this work, four weeks of aerobic overtraining was linked to decreased blood antioxidant status (Palazzetti et al., 2003). Findings of increased total peroxides have been noted in professional football players over the course of a five month competitive season (Schippinger et al., 2002). Clearly, additional work using human subjects is needed in this area of research.

Because the potential for impaired performance exists due to heightened oxidative stress, methods to reduce the degree of oxidative stress resulting from exercise have been studied. The most common method is the intake of antioxidant nutrients. The following section describes the antioxidant defense system, which is comprised of both endogenous and exogenous components.

**Antioxidant Defense**

Although ROS are constantly generated and can increase with physical exertion, the extent of oxidative damage is largely dependent on the ability of the body to defend against ROS production. This defense is collectively referred to as the antioxidant defense system, and includes both enzymatic and non-enzymatic antioxidants. Common antioxidant enzymes include superoxide dismutase (SOD), of which three primary forms are known to exist: a cytosolic copper-zinc enzyme (Cu-ZnSOD), a mitochondrial enzyme requiring manganese (MnSOD), and an extracellular SOD (EC-SOD). Other antioxidant enzymes include glutathione peroxidase (GPx) and catalase (CAT), both of which function to inactivate hydrogen peroxide prior to reacting with the transition metals.

The major non-enzymatic antioxidant within the body is glutathione, which typically exists primarily in the reduced form (GSH). Dietary intake (via whole food or nutritional supplements) supplies further antioxidants in the form of vitamins (e.g., A, C, E), minerals (e.g., selenium, zinc), flavonoids, carotenoids (e.g., beta-carotene), and phenols. It should be noted that many of these antioxidants function together to provide cellular protection within the body. For example, vitamin C acts to “recycle” vitamin
E when vitamin E forms the vitamin E radical while performing its function as a potent chain-breaking antioxidant, intercepting lipid peroxyl radicals.

As mentioned earlier, regular exercise can increase endogenous antioxidant defense, often coupled with decreased ROS formation (Ji, 2002; Powers et al., 1999). This often leads to a decrease in oxidative stress at rest and following acute exercise. While most studies have focused on adaptations resulting from aerobic exercise, positive findings are also available in reference to anaerobic exercise (e.g., weight training).

Glycine Propionyl-L-Carnitine (GPLC) as an Antioxidant Agent

Antioxidant micronutrient intake has been widely used in an attempt to decrease oxidative stress resulting from exercise (Urso and Clarkson, 2003). One antioxidant nutrient that has received considerable attention is L-carnitine, with the amino acid precursor, glycine, also noted as having antioxidant properties. In fact, previous work involving animals has noted decreased protein and lipid peroxidation following glycine use (Malyshev et al., 1996; Senthilkumar et al., 2004; Zhong et al., 1996).

More specifically, propionyl-L-carnitine (PLC), a propionyl ester of L-carnitine, has potent antioxidant properties (Reznick et al., 1992; Vanella et al., 2000), which protect tissue from oxidative stress-induced injury. This effect has been suggested to be partly related to the role of PLC to enhance blood flow (Loffredo et al., 2007), possibly mediated by an increase in nitric oxide, a finding that has been replicated in two recent studies using a combination of PLC and glycine (Bloomer et al., 2007; Bloomer et al., in press).

This unique combination of PLC and glycine is a molecularly bonded USP grade nutritional ingredient called glycine propionyl-L-carnitine (GPLC). Aside from the effect of oral GPLC to increase blood nitric oxide production, GPLC has been reported to decrease ROS mediated oxidation of lipids in a recent study (Bloomer et al., in press). In this study, subjects received oral GPLC at a dosage of either 1.5 or 4.5 grams per day over the course of an eight week intervention period. With both dosages, the level of oxidative damage to lipids measured in a rested state was significantly lower at the end of the intervention period as compared to pre intervention. The same was not true for subjects receiving a placebo. These findings highlight the significant antioxidant properties of GPLC. While these preliminary results are of interest, future work is needed to investigate the impact of GPLC on decreasing oxidative stress resulting from strenuous exercise.

Practical Applications of GPLC

The dietary ingredient GPLC has been show to possess both antioxidant properties (Bloomer et al., in press) and to increase blood nitric oxide (Bloomer et al., 2007; Bloomer et al., in press). This dual action role makes this ingredient one to consider for both general health enthusiasts and athletes who are interested in improving antioxidant defense while potentially stimulating an increase in blood flow due to the increased levels of nitric oxide. Additional ongoing clinical research with this interesting ingredient will provide more information as to its role in modulating exercise performance and exercise recovery.
References


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Glycine Propionyl-L-Carnitine HCl (GPLC-GlycoCarn®): A Vasodilatory and Antioxidant Agent

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Introduction
Bodybuilders are constantly seeking methods to improve exercise performance and recovery. Aside from advanced training techniques, well-planned dietary strategies, optimal rest, and in some cases pharmaceutical assistance, the use of nutritional supplements is often considered paramount. This is because many products are currently available that appear to provide assistance in this regard. Some products contain new ingredients that are relatively unknown by those within the bodybuilding community. However, in some cases these new ingredients may be of great interest to bodybuilders, strength athletes, and general fitness enthusiasts. One such ingredient is Glycine Propionyl-L-Carnitine (GPLC) or GlycoCarn®. Since 2005, we have been studying the effects of GPLC within men and women, and have noted some interesting findings which may have implications for exercise performance and recovery. This article highlights some of the potential benefits associated with oral use of GPLC.

What is Glycine Propionyl-L-Carnitine (GPLC)?
Dietary supplementation with the nutrient L-carnitine has been studied extensively, for the following specific reasons:

1. To enhance blood flow to skeletal muscle and heart (possibly leading to greater “pumps” and greater oxygen and nutrient delivery both during and following exercise—to aid in both performance and recovery).
2. To provide antioxidant actions (possibly minimizing the degree of “oxidative stress” caused by excess free radical formation; possibly leading to reduced muscle soreness and enhanced recovery following strenuous exercise).
3. To improve fat metabolism (possibly sparing muscle glycogen during aerobic exercise bouts, leading to maintained/improved performance).

Although several forms of carnitine are available, Propionyl-L-Carnitine (PLC) has been shown in many studies to provide vasodilatory and antioxidant activity. Recently, a patented and safe USP dietary form of PLC has been developed by Sigma-tau HealthScience, Inc. which is molecularly bonded to glycine, one of the precursor amino acids to carnitine biosynthesis. Known as one of the AminoCarnitines®, GPLC has received considerable attention in recent months from bodybuilders and sport supplement companies alike. Based on preliminary evidence, the main functions of this ingredient appear related to a potential for enhanced vasodilation and antioxidant activity.

GPLC and Nitric Oxide
It would be safe to say that most, if not all bodybuilders are at least somewhat familiar with the gaseous molecule nitric oxide (NO), often marketed as a workout enhancer. A quick scan of the popular bodybuilding publications indicates that in any given month, 30-40 entire pages are devoted to advertisements for this class of dietary supplement alone! Nitric oxide was initially known as endothelium derived relaxing factor (EDRF), and is synthesized within the body from the amino acid L-arginine and oxygen by nitric oxide synthase enzymes (Collier and Vallance, 1991). Nitric oxide acts as a very important signaling molecule within the human body, with several key biological functions (Thomas et al., 2008) including the regulation of muscle atrophy/hypertrophy (Salanova et al., 2008) and the facilitation of vasodilation (opening of blood vessels; McAllister and Laughlin, 2006). These actions have been the focus of many drugs targeted at enhanced blood flow (Burgaud et al., 2003), as well as the thrust...
for the “nitric oxide stimulating” dietary supplements currently being marketed. In this regard, the majority of such products contain forms of L-arginine as the primary “active” ingredient. However, it should be noted that while L-arginine is the precursor to NO biosynthesis, this amino acid may not be the rate limiting component (Kurz and Harrison, 1997). Rather, nitric oxide synthase enzymes may be most important to NO biosynthesis. This suggests the need for other ingredients to be included within a “complete” nitric oxide stimulating supplement. The potentially missing ingredient may in fact be GPLC.

We have now completed two studies using oral intake of GPLC in which we have demonstrated an increase in blood levels of nitrate/nitrite (NOx; a measure of NO) (Bloomer et al., 2007; Bloomer et al., in press). Our findings agree with recent work using PLC via intravenous infusion (Lofreddo et al., 2007), in which blood NOx was reported to be increased significantly. Explanation for these findings of increased NOx with GPLC treatment appear related to an increase in endothelial nitric oxide synthase (eNOS) (de Sotomayor et al., 2007), the major enzyme responsible for NO production. Other explanations are related to the antioxidant activity of GPLC (Pignatelli et al., 2003), as we have recently noted (Bloomer et al., in press).

Our first study to use GPLC included sedentary men and women who performed supervised aerobic exercise with or without GPLC treatment for an eight week intervention period (Bloomer et al., in press). A significant increase in resting levels of blood NOx was noted for those subjects receiving GPLC compared to placebo (see Figure 1). Our second study to use GPLC included well conditioned men who were assigned to GPLC and a placebo for four weeks each, with a two week washout period between each assignment (Bloomer et al., 2007). Following each four week period, resting blood samples were taken from subjects, in addition to blood samples following forearm exercise (used to induce a further increase in NO). Blood NOx was higher in response to the forearm exercise with GPLC compared to placebo (see Figure 2).

These initial findings related to the role of GPLC to increase NOx at rest and in response to a physical stressor may have implications related to enhanced blood flow during and following intense exercise. Those testing the ingredient in the gym share stories of “better pumps”, “harder workouts”, and “rapid recovery between sets” when using GPLC. However, several key research questions remain to be answered concerning the use of nitric oxide stimulating supplements containing GPLC, including whether 1) the increase in circulating NO will cause an increase in blood flow to working skeletal muscle, 2) the increase in blood flow will be associated with an increase in oxygen and nutrient delivery to active tissue, and 3) the increase in oxygen and nutrient delivery will lead to an increase in work capacity during exercise and enhanced recovery post exercise. Continued research pertaining to these variables in athletes is necessary for this field to move forward.

GPLC and Antioxidant Activity
Aside from the potential outcome of increased blood NO, GPLC has been demonstrated to possess antioxidant properties (see Figure 3; Bloomer et al., in press). When the production of reactive oxygen species (ROS), often referred to as “free radicals”, exceeds antioxidant defense, a condition known as “oxidative stress” occurs (Halliwell and Cross, 1994). The antioxidant defense system includes components naturally found within the body, as well as nutrients consumed in whole foods and nutritional supplements. Excess oxidative stress may lead to damage to cellular proteins (contractile, structural, and enzymatic), lipids, DNA, and other molecules in ways that could potentially lead to impaired cellular function. Both acute aerobic (Finaud et al., 200; Volaard et al., 2005) and anaerobic (Bloomer and Goldfarb, 2004) exercise increase the production of ROS, with the extent dependent on the type, intensity, volume and duration of exercise, the training and nutritional status of the research subjects, and the tissues being investigated (Bloomer and Goldfarb, 2004).

Because ROS may be involved in muscle injury (Zerba et al., 1990) and subsequent recovery, one concern that many athletes have is the impact of ROS formation on physical performance. While few
human studies have focused directly on this issue, but rather noting a *relationship* between oxidative stress and exercise overtraining/ overreaching (Palazzetti et al., 2003; Schippinger et al., 2002), animal studies have noted impaired muscle function, reductions in muscle force output, and greater fatigue rates in isolated skeletal muscle as a function of increased ROS (Reid et al., 2001). Because of this, the use of antioxidant agents to combat ROS induced through exercise has been very popular in recent years (Urso and Clarkson, 2003). As noted earlier, GPLC has been shown to possess antioxidant properties (Bloomer et al., in press), a finding confirmed by prior work using PLC alone (Reznick et al., 1992; Vanella et al., 2000).

**GPLC and Fatty Acid Oxidation**

It is well known that L-carnitine is critical for the transport of activated long chain fatty acids into the mitochondria of the cell (i.e., the energy producing component of the cell), to undergo energy production (Calvani et al., 2000). Increased fatty acid metabolism would be associated with an increase in fat “burning”, which may be associated with a lesser reliance on muscle glycogen for fuel during longer duration exercise. Although this has yet to be shown in a controlled research setting using GPLC, statements from athletes using GPLC have been positive. Additional research is needed in order to rule out the common “placebo” effect and to validate the findings observed through field testing on athletes.

**Practical Applications of GPLC**

The dietary ingredient GPLC has been shown to increase blood NOx in two separate studies (Bloomer et al., 2007; Bloomer et al., in press) and to possess antioxidant properties (Bloomer et al., in press). It may also impart favorable effects on energy metabolism, although this needs confirmation. The “multi-action” potential makes this ingredient one to consider in the supplementation arsenal of bodybuilders and general health and fitness enthusiasts who are interested in potentially stimulating an increase in blood flow due to increased circulating NO·, while improving antioxidant defense. Supplement companies may choose to include GPLC in a “stacked” product inclusive of nutrients with documented success related to exercise performance (e.g., creatine and possibly beta alanine) and recovery (e.g., amino acids and carbohydrate), as well as overall health (e.g., vitamin C, vitamin E, alpha lipoic acid, etc.). Additional ongoing clinical research is now being conducted to determine whether or not GPLC, alone or in combination with other nutrients, can improve exercise performance and exercise recovery.
References


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Nitric Oxide Stimulating Dietary Supplements: Where is the evidence?

Nitric Oxide Supplements
ABSTRACT

Dietary supplements purported to increase nitric oxide production have gained enormous popularity within the athletic (e.g., bodybuilding) community in recent years. Although anecdotal reports suggest a potential benefit from using such products, the scientific evidence is sparse. To the knowledge of this author, only one ingredient consumed in oral form by human subjects has been reported within the scientific literature to promote an increase in blood nitric oxide. This ingredient is a unique form of L-carnitine called glycine propionyl-L-carnitine (GPLC). This article discusses the scientific evidence for nutritional supplements to increase nitric oxide production, as well as the physiological rationale as to why nitric oxide may be important related to athletic performance. Directions for future scientific work in this area of sport supplementation are presented.

INTRODUCTION: WHAT IS NITRIC OXIDE?

Nitric oxide (NO), first referred to as endothelium derived relaxing factor (Furchgott and Zawadzki, 1980), is biosynthesized from the amino acid L-arginine, oxygen, and a variety of cofactors, by nitric oxide synthase enzymes (Collier and Vallance, 1991). Nitric oxide is a gaseous chemical compound that acts as an important signaling molecule within the human body, known to facilitate a variety of critical functions as previously described in detail (for recent reviews please see Bian et al., 2008; Thomas et al., 2008). In this regard, high concentrations of NO favor cell cycle arrest and apoptosis, while brief production at low (nanomolar) concentrations favor a wide array of beneficial physiological functions including enhanced blood flow and immune defense, decreased platelet and leukocyte adhesion, decreased smooth muscle cell proliferation, regulation of neurotransmission and muscle atrophy/hypertrophy, and the stimulation of satellite cells (Anderson, 2000; Bian et al., 2008; Salanova et al., 2008; Thomas et al., 2008). These effects appear mediated via both a cyclic guanosine monophosphate (cGMP) dependent and independent signaling cascade (Bian et al., 2008).

In relation to sport supplementation, NO is of great interest primarily related to the ability of this molecule to facilitate vasodilatation, by acting on vascular smooth muscle cells (Bian et al., 2008). This major discovery, initially by Furchgott and Zawadzki (1980), has led countless other scientists from around the world to devote their research agendas to work related to NO. In fact, NO was recognized as “molecule of the year” by Science magazine in 1992, and the Nobel Prize in Physiology or Medicine was awarded in 1998 to Robert Furchgott, Louis Ignarro, and Ferid Murad (with the unfortunate omission of Salvador Moncada) for their work related to NO as a signaling molecule within the cardiovascular system. Over the past 5 years in particular, NO has received significant attention from the athletic community (primarily bodybuilders), fueled largely by the aggressive marketing campaigns of sport supplement companies who manufacture products touted to “stimulate nitric oxide production”. In this regard, the primary desired effect is the potential increase in blood flow to active skeletal muscle, mediated by the claimed increase in NO. It is hypothesized that this proposed increase in blood flow would then lead to an increase in oxygen and nutrient delivery (e.g., amino acids and glucose) to skeletal muscle in order to aid exercise performance and to help facilitate recovery.

EXERCISE AND NITRIC OXIDE
Before considering the impact of a dietary supplement on NO production, it is important to understand the role of exercise itself in facilitating increased NO. This is most often determined by the combined measurement of nitrate (NO$_3^-$) and nitrite (NO$_2^-$) in blood or urine, which are considered stable products of the rapidly degraded NO (half life equal to 3-4 seconds).

Previous reports indicate that acute exercise results in increased blood NO (Bode-Boger et al., 1994a; Clarkson et al., 1999; Rognmo et al., 2008), a finding evident for both dynamic (Hickner et al., 1997) and isometric (Gilligan et al., 1994) exercise. Moreover, studies involving chronic exercise training performed 3-4 days per week have also noted an increase in resting levels of NO (Edwards et al., 2004; Poveda et al., 1997; Tordi et al., 2006). These findings may help to explain some of the positive health and performance outcomes apparent in exercise trained individuals compared to their sedentary counterparts. Hence, what may be perhaps the most important initial recommendation is the performance of regular, structured exercise by all individuals interested in reaping the potential benefits of increased circulating NO.

While NO is indeed thought to play a role in enhanced blood flow during an acute bout of exercise (again, the chief marketing point of most sport supplement companies selling such products), other mechanisms are indeed involved (e.g., flow mediated dilation, muscle contraction-induced distortion of resistance vessels) as previously described (Joyner and Wilkins, 2007). In fact, these other mechanisms are believed to be primarily responsible for allowing for optimal blood flow redistribution and hyperemia with acute exercise, with NO playing only a minor role (Tschakovsky and Joyner, 2008). Therefore, even if such nutritional supplements did result in a significant and measureable increase in NO, the question becomes, would this have any physiological relevance in the context of an acute exercise bout? Clearly, no data presently exist to address this question.

**PHARMACEUTICALS, DIETARY SUPPLEMENTS AND NITRIC OXIDE**

Aside from exercise, pharmaceutical agents have been used with success to either induce NO biosynthesis or to enhance/maintain the actions of NO, with the primary end goal of promoting vasodilatation (Burgaud et al., 2002). These include nitrates (transdermal long acting, sublingual rapid acting), propionyl-L-carnitine (intravenous), and L-arginine (intravenous), as well as agents used for the treatment of erectile dysfunction (e.g., Viagra®, Cialis®). In most cases, the above drugs are used to treat ailments involving impairments in blood flow including various forms of cardiovascular disease, such as angina arising from myocardial ischemia, as well as peripheral arterial disease.

In some studies, treatment with high dose L-arginine, the NO precursor amino acid, has been associated with enhanced vasodilatation (Bode-Boger et al., 1994b; Giugliano et al., 1997). However, it should be noted that the route of administration in such studies has been intravenous injection and not oral intake. In fact, a review of studies involving oral intake of L-arginine at dosages ranging from 10-20 grams indicates no benefit of this amino acid with regards to either increased circulating NO or enhanced blood flow (Adams et al., 1995; Chin-Dusting et al., 1996; Robinson et al., 2003). In addition, an oral dosage of only 10 grams per day has been noted to have an unpleasant taste and in some cases result in gastric distress (Robinson et al., 2003). It is evident that sport supplement companies are simply basing their “research” related to their products on investigations involving intravenous injection of L-arginine. Obviously, the route of administration is important in this regard. For example, work involving direct comparisons between intravenous and oral intake of L-arginine indicates no effect of oral L-arginine intake on vasodilatation, partly due the fact that oral L-arginine bioavailability is only ~68% and varies across subjects (Bode-Boger et al., 1998). Moreover, while the dosage of L-arginine used in intravenous studies has often ranged from 6-30 grams given in a bolus dose, most of the dietary
supplements sold on the market today include only 3 grams of arginine per serving. At this low dosage, it is highly unlikely that oral intake of such supplements will have any impact on NO or on the desired changes fostered by the proposed increase in this molecule.

Equally important, although L-arginine is the precursor to NO biosynthesis, it has been suggested that this amino acid is not the rate limiting component (Kurz and Harrison, 1997). Rather, nitric oxide synthase enzymes may be most important to NO biosynthesis. Therefore, adding excess L-arginine may do little to promote increased NO production, unless individuals have enzymatic insufficiency. In fact, a recent report indicates that 3 grams per day of L-arginine results in no increase in NO availability and actually reduces exercise time to fatigue (Wilson et al., 2007). Any anecdotal effect that individuals claim to experience when using many of the marketed products may be more dependent on the sugar contained within the product, rather than the L-arginine. This is because sugar intake results in an insulin spike, and insulin itself has been shown to yield a vasodilating effect (Giugliano et al., 1997; Steinberg et al., 1994). In fact, intravenous L-arginine itself at a dosage of 30 grams over 30 minutes has been shown to increase insulin release (Giugliano et al. 1997) and promote vasodilatation. It is possible that some “cocktail” products which contain several ingredients aside from sugar and L-arginine may promote an effect on NO and subsequent vasodilatation. However, only well designed, controlled scientific studies will determine whether or not such products can substantiate the radical claims currently being made for such products.

Despite the lack of scientific data, it is evident that dietary supplements marketed to increase NO production are rampant within the supplement industry. In fact, a quick scan of many of the popular bodybuilding magazines indicates that in any given month there are 30 or more entire pages of advertisements devoted solely to this class of dietary supplement. Indeed, this is an area of interest with the athletic community.

**GLYCINE PROPIONYL-L-CARNITINE AND NITRIC OXIDE**

One novel ingredient that has emerged as a potential candidate to result in a measureable increase in NO production is glycine propionyl-L-carnitine (GPLC). GPLC is a molecular bonded form of propionyl-L-carnitine and the amino acid glycine. We have recently reported in previously sedentary men and women (Bloomer et al., in press) and in resistance trained men (Bloomer et al., 2007) that oral intake of GPLC at a dosage of 4.5 grams per day results in increased plasma NO, as measured by NO\(_3^- + NO_2^-\). Our findings agree with other recent work using PLC exclusively (Lofreddo et al., 2007) which demonstrated an increase in blood NO in response to 6 grams per day of PLC given via intravenous infusion.

The mechanisms of action for this effect appear mediated by a decrease in NADPH oxidase activation (Pignatelli et al., 2003), which subsequently leads to superoxide radical generation (Zalba et al., 2001) and decreased NO bioavailability. It has also been reported that PLC augments endothelial nitric oxide synthase (eNOS) (de Sotomayor et al., 2007), leading to increased NO production. Additional work to investigate the mechanisms associated with the increase in plasma NO with GPLC treatment is needed.

**CONCLUSION**

With the exception of two published studies reporting an increase in plasma NO with oral intake of GPLC (Bloomer et al., 2007; in press), there exist no published reports to indicate that the dietary supplements currently being marketed as “nitric oxide stimulators” have proven efficacy. Several interesting research questions remain to be answered with regard to this class of dietary supplement. This includes GPLC, for which enhanced performance and recovery related to exercise has yet to be noted. For example, can such products 1) Stimulate an increase in NO production? 2) Stimulate an increase in blood flow? 3) Stimulate an increase in oxygen and nutrient delivery to target tissue? 4) Enhance
aerobic and anaerobic exercise performance? 5) Enhance exercise recovery? and/or 6) Enhance muscle mass? Only continued funding by committed supplement companies will provide the opportunity for these and other questions to be addressed. Without such work, and subsequent evidence showing measureable improvements in these variables, this field will remain much more hype than effect. Current marketing campaigns by many of the top sport supplement companies are presented as though these questions have already been answered in the affirmative. Clearly, this is not the case.
REFERENCES AND NOTES


**Article Type:** Invited Review
Glycine Propionyl-L-Carnitine (GPLC-GlycoCarn®) and Exercise Metabolism

Introduction

Athletes and fitness enthusiasts are constantly looking for methods to improve exercise performance and to lose additional body fat. In this quest, individuals look towards advanced exercise training methods, dietary strategies, and nutritional supplements. Pertaining to the latter, several products are available, some with a substantial body of evidence in support of their use (e.g., creatine, caffeine), and many more with little to no evidence indicating beneficial effects on either exercise performance or body composition.

The novel ingredient Glycine Propionyl-L-Carnitine (GPLC) is a component of several new nutritional supplements which are now commercially available, with the potential to influence the above parameters. While controlled research studies to support the use of GPLC as a performance enhancer have yet to be conducted, two recent reports indicate a potent effect of this compound on elevating blood nitric oxide (Bloomer et al., 2007; Bloomer et al., in press), as well as decreasing free radical medicated modifications to blood lipids (Bloomer et al., in press). Both of these findings may be linked to improved exercise performance, as nitric oxide is responsible for increasing blood flow to active tissues (Collier and Vallance, 1991), and free radicals are known to interfere with physical performance (Goldhaber and Qayyum, 2000) and to promote greater fatigue rates in skeletal muscle (Reid et al., 2001).

Glycine Propionyl-L-Carnitine is marketed as GlycoCarn® through Sigma-tau HealthScience, Inc. This ingredient is USP grade certified and consists of a molecular bonded form of propionyl-L-carnitine and one of the carnitine precursor amino acids, glycine. Propionyl-L-carnitine is a form of carnitine with high specificity towards both skeletal muscle and heart tissue, and has been reported to possess benefits beyond those observed with typical L-carnitine (Brevetti et al., 1999; Fritz, 1979). The following text discusses how this novel ingredient might aid exercise performance, while simultaneously leading to body fat loss in certain individuals.

GPLC and Fatty Acid Transport

The process of fat “burning” involves a complex interplay of several factors including 1) Fatty acid mobilization from storage sites (i.e., fat cells), 2) Transport of fatty acids to the target tissue, 3) Uptake of fatty acids into the cell, 4) Activation of fatty acids via an ATP dependent process, 5) Movement of activated long chain fatty acids into the inner mitochondrial matrix (via the carnitine dependent enzymes called carnitine acyl transferase 1 (CAT1) and carnitine acyl transferase 2 (CAT2), 6) Degrading fatty acids into the final products which will be used for energy production (acetyl CoA and the electron carriers NADH and FADH₂) via a process called beta oxidation, and 7) Krebs cycle and electron transport chain (the pathways where ATP energy is produced from the products created within beta oxidation). Based on the above, it is evident that this is a rather complex process. Where GPLC may play an important role is step number 5,
in which carnitine is essential for the actual transport of fatty acids inside the mitochondrial matrix in order to be oxidized. Without adequate carnitine, this process does not proceed as desired. To this end, GPLC has been noted to result in a modest decrease in body fat percentage in subjects supplemented with this compound for a period of eight weeks, when combined with aerobic exercise (Bloomer et al., in press).

**GPLC and Aerobic Exercise Performance**

The ability of GPLC to aid in fatty acid transport during exercise has specific implications related to both fatty acid usage and glycogen depletion. That is, when additional fat is used as a fuel source, not only is there a greater possibility of fat loss, but there exists less reliance on stored glycogen (i.e., stored carbohydrate) to fuel exercise. This is particularly important as it relates to long duration exercise during which time glycogen stores may be compromised. An equally important consideration is related to the potential for lower lactate production during exercise, which occurs as a component of carbohydrate (glucose and glycogen) oxidation through a process known as glycolysis. Therefore, less reliance on carbohydrate during exercise may lead to both extended exercise duration (due to more glycogen remaining available for fuel) and less acute muscle pain/burning (due to lower lactate accumulation). Ongoing research studies addressing GPLC and these issues are now being conducted/designated at Universities across the USA.

**GPLC and Anaerobic Exercise Performance**

First of all, for many athletes participating exclusively in anaerobic exercise such as weightlifting (e.g., bodybuilders), carbohydrate intake is often low in comparison to aerobic athletes. Therefore, the ability of GPLC to enhance fat oxidation to minimize glycogen loss appears to be an important consideration, due to the fact that individuals consuming a low carbohydrate diet may not have abundant glycogen stores to begin with.

In terms of anaerobic performance measures such as reduced recovery intervals between sets and increased rep number per set, GPLC may prove beneficial based on recent work demonstrating an increase in blood nitric oxide production when resistance trained men were supplemented with GPLC (Bloomer et al., 2007). In this study resistance trained men received GPLC or a placebo for four weeks each, with a two week washout period between each four week phase. At the end of each four week phase, blood samples were obtained at rest and in response to isometric forearm exercise. Blood nitric oxide was elevated to a greater extent in response to the forearm exercise with GPLC compared to placebo. This was the first study to demonstrate that a dietary ingredient can stimulate an increase in blood nitric oxide in resistance trained men.

Although this study only measured blood nitric oxide and did not measure indices of exercise performance, it is important to note the potential benefits of increased nitric oxide related to exercise performance, as well as exercise recovery. In terms of performance, the increase in nitric oxide may be associated with an increase in blood flow to working skeletal muscle, which in turn may be associated with a greater delivery of oxygen and nutrients such as fatty acids,
glucose, and amino acids. The increase in oxygen and nutrient delivery may increase work capacity during an acute bout of exercise due to greater ATP production. In terms of recovery, greater nutrient delivery may facilitate glycogen resynthesis, as well as promote an anabolic environment (decreased proteolysis and increased protein synthesis). While controlled studies using GPLC have yet to be conducted to test the ability of this ingredient to improve anaerobic exercise performance in trained athletes, PLC alone has been reported to increase lower body strength (Barker et al., 2001). However, the subjects in this study suffered with peripheral artery disease; therefore findings may not be generalized to athletes, as individuals with disease are often carnitine deficient with altered carnitine metabolism. Additional work is needed using GPLC in a sample of trained athletes in order to determine the benefit of this ingredient related to these important issues of exercise performance and recovery.

**What are Athletes Saying about GPLC?**

Although the following claims and statements in no way represent data obtained in controlled, scientific experiments, athletes conducting “in the gym” testing of GPLC over the past several months have made some interesting comments. A few include “better pumps”, “enhanced vigor”, “great workout”, “increased stamina”, “I feel I can keep on going”, “shortened recovery between sets”, “just a different feeling all together”, “a major ingredient in my formula for success” and so on. This may be one ingredient with the potential to make a real impact on the sports supplement market. Keep your eyes open for new products emerging monthly which contain GPLC.

**Future Research with GPLC Related to Exercise Performance**

Although many athletes may not be highly interested in the scientific research, it is important to understand that anecdotal (i.e., in the gym) accounts related to sport supplements (or anything for that matter) will be more widely accepted if they are supported by hard evidence, gathered in a controlled scientific environment. This is exactly what is currently being done concerning GPLC—rigorous laboratory based scientific research. Two to three new studies involving GPLC should be completed within the next year, pertaining specifically to the exercise performance enhancing aspects of this ingredient. Stay tuned!
References


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