

The University of Memphis
Memphis, TN 38152
Phone: 901-678-4341
Fax: 901-678-3591
Email: rbloomer@memphis.edu

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 o ($p=0.187$) minutes post protocol; % change from rest presented for each time post protocol. Values are mean \pm SEM.

Adapted from Bloomer et al. Glycine propionyl-L-carnitine increases plasma nitrate/nitrite in resistance trained men. Journal of the International Society of Sports Nutrition, 4: 22, Epub Dec 3, 2007.



White Paper:

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

Richard J. Bloomer, PhD

Sigma-tau HealthScience, USA
9841 Washingtonian Blvd., Suite 502, Gaithersburg, MD 20878
Phone +1 (301) 670-1519 • Fax +1 (301) 354-5373
Toll Free +1 (877) 246-7468
www.healthscienceusa.com • e-mail info@healthscienceusa.com

www.aminocarnitines.com • www.glycocarn.com
www.arginocarn.com • www.modernarteries.com

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www.healthscienceusa.com


AminoCarnitines®

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 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 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/body-building 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: *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.*

DR. RICHARD J. BLOOMER
Cardiorespiratory/Metabolic Laboratory
161F Roane Field House