

MD+ Creatine Advantage

version III

Creatine Advantage was formulated to Naturally Boost Energy, Decrease Fatigue, and Improve Body Composition and Mental and Physical Performance.

Creatine advantage information was updated September 14, 2021. By Mauro Di Pasquale, B.Sc. (Hons); M.D.



Creatine Advantage is the Ultimate Creatine Product and addresses several levels involved in maximizing energy and decreasing fatigue. The formulation contains dozens of additive and synergistic Ingredients for Maximizing the Body's Energy Systems, decreasing general and exercise induced fatigue, Improving Body Composition, and physical and mental performance.

To order go to <https://metabolicdiet.com/product/creatine-advantage/>

For information on my line of nutritional supplement products go to <https://metabolicdiet.com/shop/>

Creatine Advantage is manufacture in a GMP and NSF certified pharmaceutical grade facility.

The information below on the new Creatine Advantage version III is in a constant draft form as revisions are made as new information becomes available. This latest information will give you the flavor of just what Creatine Advantage will do for you in helping you achieve your health, body composition and physical and mental performance goals.

Table of Contents

Creatine Advantage version III Supplement Panel	3
Introduction	4
Low-dose creatine supplementation enhances fatigue resistance in the absence of weight gain.	5
More Than Just Creatine.....	5
Mitochondrial Effects	6
Coenzyme Q10 (ubiquinone-10, CoQ10)	6
L-Carnitine	7
Taurine	8
Alpha Lipoic Acid	9
Astaxanthin.....	10
Other Amino Acids.....	11
Increased Synthesis of PC and ATP	11
Increasing TCA Flux and ATP Synthesis	12
Insulin Boosting System.....	12
Creatine Advantage Also Contains:	13
Volumizing Ingredients.....	14
Branched Chain Amino Acids	14
Beta-Alanine and Carnosine.....	14
The Journal of Sports Medicine and Physical Fitness 2020 Oct 22.....	15
Acute carnosine and β -alanine supplementation increases the compensated part of the ventilation vs work rate relationship during a ramp incremental cycle test in physically active men	15
Citrulline Malate.....	15
Biotin	16
What's Not in Creatine Advantage	16
Safety of Long-Term Creatine Intake.....	16
References	17

Creatine Advantage version III Supplement Panel

Supplement Facts:		Serving Size 15 Grams	
		Servings Per Container: 35	
	Amount	% Daily	
	Per Serving	Value	
	Amount	% Daily	
	Per Serving	Value	
Calories	42		Creatine Monohydrate
Total Carbohydrates	2 g	1%	Glutamine Peptides (from Casein)
Vitamin C (as Ascorbic Acid)	50 mg	83%	Branched Chain Amino Acids
Vitamin B1 (as Thiamine Pyrophosphate)	30 mg	150%	(Leucine 600 mg, Valine 200 mg, Isoleucine 200 mg)
Vitamin B2 (as Riboflavin)	30 mg	150%	L-Taurine
Vitamin B3 (as Niacin, Niacinamide and Inositol Hexanicotinate)	20 mg	100%	D-Ribose
Vitamin B6 (as Pyridoxal-5-Phosphate)	5 mg	250%	Beta-Alanine
Vitamin B12 (as Methylcobalamin)	200 mcg	3333%	L-Histidine
Pantothenic Acid (as D-Calcium Pantothenate)	5 mg	50%	L-Inosine
Biotin	300 mcg	100%	N-Acetyl Tyrosine
Iron (as Ferrous Succinate)	3 mg	15%	N-Acetyl-Cysteine
Calcium (as Calcium Phosphate)	150 mg	15%*	L-Histidine
Magnesium (as Aspartate and Phosphate)	250 mg	62%	L-Carnitine Fumarate
Potassium (as Phosphate and Succinate)	210 mg	6%*	L-Carnosine
Phosphorus (as Calcium, Magnesium, Potassium Phosphate)	250 mg	25%	Citrulline Malate
Manganese (as Manganese Aspartate)	2 mg	100%	Betaine (Trimethylglycine)
Sodium (as Chloride)	25 mg	2%	Alpha Lipoic Acid
Chromium (as CHROMEMATE™ Polynicotinate)	25 mcg	21%	Coenzyme Q10
Zinc (as Monomethionine)	6 mg	40%	Creatine Advantage™ Complex - 820 mg*
Selenium (as L-Selenomethionine)	25 mcg	35%	Calcium Pyruvate, Choline Bitartrate, L-Phenylalanine, AMP (Adenosine Monophosphate), ATP (Adenosine Triphosphate), NADH, Astaxanthin.
Other Ingredients: Beet Powder, Natural Flavors, White Stevia Powder, and Erythritol.			
*Daily Value not established			
** Percent Daily Values are based on a 2000 calorie diet			

Introduction

The ergogenic as well as therapeutic effects of increasing muscle and body creatine by supplementation have been documented by studies spanning three decades. In those involved in exercise and sports, creatine supplementation has been shown to have ergogenic effects leading to improvements in athletic performance by increasing energy, strength and muscle mass, decreasing fatigue, and enhancing recover.^{12345,6,7,8,9,10,11121314151617}

A recent study concluded that creatine can maintain mitochondrial integrity, increase creatine phosphate resources, act as a cellular energy buffer, and protect two important cellular targets, mitochondrial DNA and RNA, from oxidative damage.¹⁸

Another recent study concluded that According to the available information, creatine has antioxidant properties and can be effective through direct and indirect mechanisms. It has a positive effect on oxidative stress and reduces ROS. Creatine can maintain mitochondrial integrity, increase CrP resources, act as a cellular energy buffer, and protect two important cellular targets, mtDNA and RNA, from oxidative damage.¹⁹

These and other beneficial effects of creatine supplementation, for example on the CNS, are enhanced in Creatine Advantage by stacking creatine with other ingredients.

Our formula not only contains the highest quality, pure crystalline creatine monohydrate so that it mixes instantly and leave's no chalky taste, but we've also added a host of other natural ingredients that make our formula much more effective and versatile than any other creatine products on the market

Creatine monohydrate is absorbed fairly well if just mixed with water. Using carbs increases insulin secretion and thus creatine utilization. However, by using the right formulation, as in Creatine Advantage, insulin levels are increased by the formulations' amino acids, which in turn maximizes creatine absorption. But as you'll discover, Creatine Advantage does much more than just raise creatine levels.

To understand why you need a number of synergistic ingredients besides creatine to maximize the energy systems in the body it's important to know some basics on creatine metabolism. Creatine is used by the body to make phosphocreatine, and the phosphocreatine is a high energy source that functions to replenish ATP (the primary energy source in the body) when it's depleted.

The body needs about 2 grams of creatine a day to account for the amount of creatine that is metabolized to creatinine irreversibly. The creatinine is then excreted in the body. Part of this turnover can be replaced through exogenous sources of creatine in foods, especially meat and fish, and of course by supplementing with creatine monohydrate or creatine phosphate (the two most common forms available in supplements with the monohydrate being by far the most widely available). The remainder is derived via endogenous synthesis from the precursors **arginine, glycine and**

methionine. Both the creatine and the creatine precursors (all three are in the glutamine peptides mix) are supplied in Creatine Advantage.

It's also important that you provide the body with the means to increase energy levels, preferably by breaking down and oxidizing body fat, so that phosphocreatine can be made from creatine plus phosphate. And it's important to simultaneously maximize the effects of insulin, GH, and IGF-I, which is difficult to do using carbs and sugars, not only to synergistically maximize the levels of these anabolic hormones, but also so that the creatine is most efficiently used.

Creatine Advantage doesn't overwhelm the body with creatine, since 3.5 grams a day is all that's needed to maximize creatine cellular levels - the usual doses of creatine used by athletes are mostly excreted²⁰ (as urinary creatine and a small amount of creatinine) and secondly the use of excessive amounts for long periods of time may be counterproductive as far as potential adverse effects.

An example of the usefulness of a steady lower dose of creatine is a recent study that found that lower dose Creatine supplementation had significant effects on body composition, muscle function, and body Creatine retention (see citation and abstract below).²¹

Low-dose creatine supplementation enhances fatigue resistance in the absence of weight gain.

[Rawson ES](#), [Stec MJ](#), [Frederickson SJ](#), [Miles MP](#). [Nutrition](#). 2011 Apr;27(4):451-5. Epub 2010 Jul 1.

Source

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Abstract

OBJECTIVE:

We examined the effects of 6 wk of low-dose creatine supplementation on body composition, muscle function, and body creatine retention.

METHODS:

Twenty healthy men and women (21 ± 2 y old) were randomized to receive creatine ($0.03 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$); $n = 10$, 4 women) or placebo ($n = 10$, 4 women) for 6 wk in a double-blind placebo-controlled fashion. Participants were tested on two occasions before supplementation to establish a reliable baseline, and then were retested after supplementation. Testing included body composition, maximal strength (three-repetition maximal concentric knee extension at 180 degrees/s), muscle fatigue (five sets of 30 concentric knee extensions at 180 degrees/s), and plasma creatine concentration.

RESULTS:

There were no significant differences in body mass, fat-free mass, fat mass, body fat percentage, total body water, or maximal strength in either group from before to after supplementation (all $P > 0.05$). After supplementation, plasma creatine increased significantly in the creatine group (+182%, $P = 0.03$), with no difference in the placebo group.

Compared with baseline values, creatine-supplemented volunteers were more resistant to fatigue during sets 2 (7%), 3 (9%), 4 (9%), and 5 (11%) (all $P < 0.05$). In placebo-supplemented participants, there was no improvement in fatigue resistance during sets 2 (0%), 3 (1%), 4 (0%), and 5 (-1%) (all $P > 0.05$).

CONCLUSION:

Ingesting a low dose ($\approx 2.3 \text{ g/d}$) of creatine for 6 wk significantly increased plasma creatine concentration and enhanced resistance to fatigue during repeated bouts of high-intensity contractions.

More Than Just Creatine

Using Creatine Advantage does more than just supply 3.5 grams of Creatine per serving. At the same time Creatine Advantage maximizes phosphocreatine and ATP production (the TCA cycle intermediates and the AMP), and protein synthesis (the amino acid content and glutamine peptides).

Added amino acids and dipeptides and other essential boosters allow an increase in the absorption and utilization of creatine and increase the volumizing, anticatabolic and anabolic effect of the Creatine Advantage formulation. The added energy ingredients and precursors make Creatine Advantage the ultimate creatine and energy mix, one that will maximize energy metabolism, muscle mass and performance.

But that's not all. Creatine Advantage, with its synergistic formulation, also has neuroprotective effects and may be useful for treating neurodegenerative diseases,^{22,23,24,25,26,27} likely due to its effects on phosphocreatine and ATP,²⁸ as well as protective and reparative effects on other cells and systems in the body.

For example, a study found that topical creatine has beneficial effects on skin damage because of its ability to recharge the energy mechanisms in these cells that deal with the protection and repair of skin damaged by free radicals.²⁹

Mitochondrial Effects

The effects of creatine are enhanced by stacking creatine with other ingredients. These added ingredients increase the use of creatine by the body, as well as increasing energy systems beyond just creatine phosphate, as well as providing extra cytoprotective and antioxidant protection.

For example, Creatine Advantage contains several ingredients, including creatine and alpha lipoic acid that have multiple functions, including ameliorating mitochondrial disorders.³⁰

As well, ingredients such as taurine, alpha lipoic acid, beta-alanine, L-carnitine fumarate, betaine, N-Acetyl-Cysteine, N-Acetyl-Tyrosine, and various amino acids, including histidine, and many other ingredients have potent cytoprotective, neuroprotective, antioxidant and fat burning effects on their own and work with the other ingredient to improve health, body composition and performance.

Coenzyme Q10 (ubiquinone-10, CoQ10)

Coenzyme Q10 (CoQ10), a coenzyme that is ubiquitous in animals, including humans, is a lipid-soluble antioxidant and acting as an electron carrier is a key component of the mitochondrial electron transport chain for adenosine triphosphate (ATP) production.³¹ It is also one of the key antioxidant nutrients that protect mitochondrial membrane lipids and proteins and mitochondrial DNA from free radical-induced oxidative damage.

As such it is necessary for proper energy metabolism. For example, myocardial CoQ₁₀ content is reduced by cardiac failure and aging. It is also reduced by statins, the popular cholesterol lowering drugs. Studies have suggested preventative supplementation of CoQ10 for cardiac health and for those on statins.^{32,33,34,35,36,37}

CoQ10 has been shown to decrease oxidative stress and mitochondrial damage leading to increases in mitochondrial mass in many tissues.^{38,39} As well, CoQ10 has been shown to affect the expression of genes involved in human cell signaling, metabolism and transport.

As such, since many neurodegenerative disorders, diabetes, cancer, and muscular and cardiovascular diseases have been associated with low CoQ10 levels, supplementation may be

beneficial in many conditions and diseases^{404142 434445} including alleviating intervertebral disc degeneration.⁴⁶

For example, CoQ10 supplementation has been shown to have anti-aging and beneficial effects on semen parameters, fertility, testicular damage, and reproductive hormones including testosterone.⁴⁷⁴⁸⁴⁹⁵⁰⁵¹⁵²⁵³⁵⁴⁵⁵ In a recent study CoQ10 while not found to directly increase testosterone, CoQ10 supplementation **“was found to ameliorate the reduction in testosterone induced by chemical reproductive toxicants, mainly by neutralizing the damaging effect of the generated free radicals.”**⁵⁶

CoQ10 has also been shown to have beneficial effects on oxidative stress, inflammation, the immune system, and on exercise performance.⁵⁷⁵⁸⁵⁹⁶⁰⁶¹⁶²⁶³⁶⁴⁶⁵⁶⁶⁶⁷

CoQ10 also regenerates and extends the action of vitamin E thus further protecting against membrane lipid peroxidation. Under the various forms of stress and inflammation, demand for coenzyme Q10 increases which must be met by dietary intake in order to optimize mitochondrial function.

As well, it has been shown that the reduced form of CoQ10 is an important physiological lipid-soluble antioxidant that scavenges free radicals generated chemically within liposomal membranes.^{68,69} It has also been shown that it reduces oxidative stress associated with strenuous exercise in rats, healthy adults and young athletes.⁷⁰⁷¹⁷²⁷³⁷⁴ As noted above, vitamin E and ubiquinone increase physical working capacity of experimental animals.⁷⁵

Generation of free radicals and subsequent lipid peroxidation have been proposed to contribute to delayed tissue damage. One study has found that ascorbate and ubiquinol levels were decreased after trauma.⁷⁶ In this study, changes in tissue levels of ubiquinol, but not ascorbate reflected the degree of trauma. The authors suggest that ubiquinol levels may provide a useful marker of the oxidative component of the secondary injury response.

A recent study found that CoQ10 supplementation **“significantly recovered mitochondrial function and concurrently decreased the generation of reactive oxygen species and lipid peroxides, inhibited the accumulation of lipid droplets and the formation of the NOD-like receptor family pyrin domain-containing three (NLRP3) inflammasome, and reduced interleukin-1 β release and cell death.”** Also, the authors concluded that their results clarified **“the causal role of CoQ10 in coupling the electron transport chain with β -oxidation”**.⁷⁷

Creatine Advantage also contains **L-carnitine**. Studies have shown that under certain conditions CoQ10 plus L-carnitine and in some cases L-carnitine alone, significantly increases total antioxidant, LH and testosterone levels as well as improving semen parameters.⁷⁸⁷⁹⁸⁰⁸¹⁸²⁸³⁸⁴⁸⁵⁸⁶

L-Carnitine

Creatine Advantage contains L-carnitine fumarate, with both parts of the ingredient involved in optimizing energy metabolism. The fumarate moiety increases the flux of the TCA cycle to increase ATP synthesis, as well as the potential to form glucose through gluconeogenesis.

L-carnitine is mainly known for shuttling fatty acid acyl units into mitochondria so that beta oxidation of these acyl units provides acetyl units to fuel the TCA cycle and through oxidative phosphorylation to increase ATP production. In this respect, L-carnitine functions much like a gas pump in that it puts fuel in the gas tank so that your car engine can use it to provide energy to run the car. LC also acts to maintain mitochondrial function and suppresses oleic acid-mediated MPT through acceleration of beta-oxidation.⁸⁷

But L-carnitine (LC) is much more than just the shuttle mechanism to get fatty acids into mitochondria, it also functions in the opposite direction when there's an overload of acyl and acetyl units in the mitochondria that can result in mitochondrial dysfunction and insulin resistance.⁸⁸ LC thus acts more like a regulator of mitochondrial function both by providing nutrients that can be used efficiently and removing nutrients that are clogging up the mitochondrial machinery. Studies have shown that the more fat is shuttled into the mitochondria and used as fuel, the more L-carnitine is needed. So, unless the body's metabolism is primed epigenetically to deal with utilizing fat as a primary fuel, and that also means a sufficient amount of LC to deal with the use of fat as a primary fuel (i.e. avoiding a relative carnitine insufficiency which can also be caused by aging and vegetarian diets), the result can be high rates of incomplete fat oxidation and intramuscular accumulation of fatty acylcarnitines, byproducts of lipid catabolism produced under conditions of metabolic stress including exercise.⁸⁹⁹⁰

Although it seems counter intuitive given LC role in fat metabolism, LC also increases insulin sensitivity and is a regulator of glucose metabolism and may be used to counter the metabolic syndrome and help treat type II diabetes.⁹¹⁹²

A recent study found that the combination of LC, alpha lipoic acid, and betaine, all in Creatine Advantage, had beneficial effects on health and body composition.⁹³ As well,, LC is essential for proper muscle function and some studies have shown that carnitine supplementation improves exercise performance.⁹⁴

LC has antioxidant properties directly but also ramps up endogenous antioxidant systems including glutathione, catalase, and SOD. The dual action decreases the effects of ROS produced with higher intensity resistance and aerobic exercise. L-carnitine also decreases the production of some of the pro-inflammatory cytokines and has anti-inflammatory and immunomodulating effects.⁹⁵⁹⁶⁹⁷

Taurine

Taurine, a sulfur-containing amino acid and the second most abundant amino acid, and the most abundant free amino acid, found in skeletal muscle tissue, has many properties that can enhance the training effect, including its abilities to increase growth hormone, protect joints, and protect the liver, as well as its antioxidant and anabolic effects.⁹⁸ Taurine has also been shown to have insulin like effects and to help control cell volume. The volumizing effect on muscle cells is felt to lead to an increase in protein synthesis.

Over the years, oral taurine administration has been shown to help muscle cramping in patients with liver cirrhosis and myotonic dystrophy. Several studies have suggested that it may also help to alleviate muscle cramps occurring during and after exercise. But there's more to the story.

Taurine is considered a potent antioxidant and cytoprotective agent that may be useful for combating the adverse effects of physical and psychological stress, and aging.^{99,100,101,102}

A study in rats showed that taurine is useful for reducing physical fatigue, muscle damage, and exercise induced muscle injury during exercise training, presumably due to its antioxidant effects and the beneficial effects that taurine has on metabolism and on muscle and cardiac functions.¹⁰³

A recent study on rats has shown that oral taurine supplementation may increase muscle performance and reduce muscle injury caused by exercise.¹⁰⁴ The aim of the study was to determine if increasing muscle levels of taurine would decrease free radical damage after exercise-induced injury. The authors found that first of all taurine levels rose in muscle after supplementation, and secondly that running performance was improved by the taurine supplementation. Thus it appears taurine supplementation may facilitate exercise performance and reduce some of the counterproductive muscle injury caused by exercise.

A recent study found that taurine supplementation in patients with heart failure increases their exercise capacity.¹⁰⁵ Another recent study found that taurine decreases oxidative stress in skeletal muscle after eccentric exercise.¹⁰⁶ Another study found that taurine may attenuate exercise-induced DNA damage and enhance the capacity of exercise due to its cellular protective properties.¹⁰⁷

On a preventative level, taurine administration has been shown to increase taurine concentrations in skeletal muscles, reduce the decrease in taurine concentration in skeletal muscles on exercise, and up-regulates physical endurance.¹⁰⁸

There is some evidence to show that taurine may enhance training further by decreasing training induced fatigue. A recent paper has shown that Na⁺-K⁺-ATPase activity is depressed with fatigue, regardless of training state, suggesting that this may be an important determinant of fatigue.¹⁰⁹ Another recent paper associated fatigue and training with reduced Ca²⁺-ATPase activity.¹¹⁰ Previous studies have shown that taurine stimulates Na⁺-K⁺-ATPase activity and also the pumping rate of the Ca²⁺-activated ATPase pump.

One study found that taurine administration reduced the decrease in taurine in skeletal muscles in exercise, increased duration of running time in rats, and was considered to reduce exercise-induced muscle fatigue.¹¹¹ Also taurine supplementation has been shown to increase skeletal muscle force production, protects muscle function and reduce oxidative stress.¹¹²

While the evidence is circumstantial at present and a direct study linking the two research findings needs to be done, it's quite possible that supplemental taurine, besides all the positive effects we know it has, may also reduce exercise induced fatigue.

For more information go to my updated article on [Taurine](#).

Alpha Lipoic Acid

Alpha lipoic acid (ALA) has potent antioxidant properties intrinsically and secondary to its ability to increase levels of intra-cellular glutathione, and its ability to recycle other antioxidants such as vitamin C, vitamin E and glutathione.^{113,114,115,116,117} ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.¹¹⁸

Alpha lipoic acid also has a number of useful and diverse properties. In a review¹¹⁹ the author states “LA improves glycemic control, polyneuropathies associated with diabetes mellitus, and effectively mitigates toxicities associated with heavy metal poisoning. As an antioxidant, LA directly terminates free radicals, chelates transition metal ions (e.g. iron and copper), increases cytosolic glutathione and vitamin C levels and prevents toxicities associated with their loss.”

ALA has significant anti-inflammatory properties and has been shown to inhibit IL-1, a proinflammatory cytokine and inhibit the synthesis of PGE2 by inhibiting COX-2 activity. This latter mode of action simulates the anti-inflammatory effects of the present class of NSAIDS such as Celebrex, Advil, Aleve, etc. As well, the anti-inflammatory effects of ALA are increased since it decreases both the pro-inflammatory cytokines^{120,121} and secondary cortisol elevations.

It has been shown to inhibit cross-linking among proteins, a process that contributes to the aging process in the body and especially in collagen-heavy tissues such as skin. Alpha-lipoic acid activates a collagen-regulating factor known as AP-1 that turns on enzymes that digest glycation-damaged collagen and thus make the skin more supple and youthful looking.

Besides having potent antioxidant and anti-inflammatory effects, ALA also has significant anabolic effects secondary to its beneficial effects on insulin sensitivity and growth hormone and IGF-I secretion, all factors involved in maintaining, repairing and regenerating musculoskeletal tissues.^{122,123,124,125}

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.^{126,127}

Astaxanthin

Astaxanthin, a powerful lipid based antioxidant complements and adds to the many beneficial effects of Creatine Advantage on energy metabolism, body composition, exercise performance and overall health.

Astaxanthin has been shown to have potential to improve health, enhance energy metabolism and exercise performance, increase fat metabolism during exercise, decrease oxidative stress and muscle injury, delay exhaustion, increasing improve body composition, enhance recovery, prevents redox imbalances, and attenuates muscle damage, counterproductive inflammation and fibrosis induced by rigorous physical training as well as immobilization.^{128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145}

Some of the benefits of Astaxanthin deserve special attention. For example, astaxanthin has a protective effect on mitochondria, the cellular powerhouses that produce the energy we need to live and function optimally. Protecting the mitochondria is especially important during exercise since destructive free radicals production increases almost exponentially and can damage not only the mitochondria, thus impairing energy systems, but also skeletal muscle as a whole impairing performance and recovery and increasing the chance of injury.¹⁴⁶

But that's not all because astaxanthin, through its effects on decreasing mitochondrial damage in other parts of the body such as the testes, also increases testosterone production and thus increases

the anabolic effects of exercise, and has also been shown to have positive effects on sperm parameters and fertility.¹⁴⁷

Unlike some other antioxidants, astaxanthin not only has intrinsic antioxidant and anti-inflammatory properties but it also increases the endogenous production of natural antioxidant defense mechanisms such as SOD and heme oxygenase-1.¹⁴⁸

As well, it works synergistically with other ingredients in Creatine Advantage. For example, in horses it's been shown that continuous dietary administration of astaxanthin and L-carnitine (both in Creatine Advantage) attenuates exercise-induced muscle damage.¹⁴⁹

For all these reasons astaxanthin plays a prominent part in the beneficial effects that Creatine Advantage has on all aspects of health, energy metabolism, nutrition, exercise, and anti-aging.

Other Amino Acids

Other amino acids that are a part of the glutamine peptides in Creatine Advantage contribute to overall health and repair in many ways. For example, proline and glycine are essential for collagen production. As well, the sulphur containing amino acids (also in the glutamine peptides) have significant antioxidant and other effects.¹⁵⁰

Increased Synthesis of PC and ATP

Creatine Advantage contains all the necessary products for the synthesis of both high energy phosphate compounds creatine phosphate and ATP, and for the efficient salvage of ATP after it's been metabolically degraded, including:

- **Inorganic phosphorus and phosphates – also important for normalizing and regulating thyroid hormone.**
- **Creatine**
- **Inosine**
- **Ribose**

For example, one study found that ribose supplementation acutely increased ATP resynthesis after high intensity exercise, and that that oral intake of ribose in humans after 1 wk of high-intensity training lead to higher resting ATP levels.¹⁵¹

It also contains the following nutrients to facilitate the glycolytic and TCA cycle energy processes:

- **Biotin** - a cofactor in many energy reactions involving glycogenolytic, glycolytic, TCA and anapleurotic enzymes.
- **Magnesium** - which has also been shown to increase energy systems, insulin sensitivity, protein synthesis and serum testosterone, GH and IGF-I levels.
- **Calcium** - which has been shown to facilitate muscle contraction and decreasing fatigue).
- **Potassium**, the transport of which is linked to aerobic glycolysis.

Increasing TCA Flux and ATP Synthesis

Creatine Advantage maximizes ATP production (as I mentioned above ATP is the main energy source in the body - the function of phosphocreatine is to replenish ATP, so it makes sense to increase ATP levels as well). It contains a proprietary blend of several ingredients that maximizes mitochondrial anapleurotic flux in the TCA cycle resulting in increased ATP production and increased energy availability for protein synthesis and other functions, including the formation of phosphocreatine.

These ingredients, including **coenzyme Q10** and several anapleurotic direct and indirect TCA cycle intermediates (such as **aspartate, citrate, malate, fumarate, succinate**, and the various anapleurotic and the various amino acids, including the **branched chain amino acids, glutamate, glutamine**, and other amino acids present in the **glutamine peptides** hydrolysate), impact on TCA Cycle (also known as the Citric Acid cycle and Krebs's Cycle) flux and maximize mitochondrial metabolism, increase aerobic ATP production, and enhance insulin and growth hormone/IGF-I secretion and formation.

The overall increase in anapleurotic flux produces an increase in aerobic energy production, insulin secretion, and protein synthesis, and results in an increased adaptive response, a surge in skeletal muscle cell growth, increased fat loss, and improved recovery.

Adenosine monophosphate (AMP), one of the ingredients in Creatine Advantage, activates AMPK (AMP-activated protein kinase). The AMPK pathway is active in sensing and regulating tissue energy metabolism, influencing fuel metabolism, especially fat, in tissues including muscle and liver, and increases insulin sensitivity in skeletal muscle,^{152 153154} AMPK also plays a part in decreasing the concentration of malonyl-coA in peripheral tissues, (as does exercise BTW) and thus decreases triglyceride accumulation and increases fatty acid oxidation.¹⁵⁵

The overall response to all of this is also an increase in energy output, which under conditions of energy deprivation, such as when you're trying to lose weight and/or body fat, increases fat oxidation further.

Insulin Boosting System

Creatine Advantage has a low carbohydrate based insulin boosting system (glutamine in the form of glutamine peptides - more stable in liquid form and more effective than free glutamine) and compounds to increase insulin sensitivity (**chromium, histidine** – which also provides intracellular buffering to stimulate anaerobic energy formation, **taurine**¹⁵⁶ – which also has significant antioxidant and protective effects, stimulates growth hormone secretion and increases cell volume, and racemic **alpha lipoic acid** (a combination of the two main enantiomers of ALA – ALA is also an excellent antioxidant) and thus make the insulin more effective.

All of these compounds increase the boosting effect that insulin has on intramuscular creatine phosphate levels. For example, a study found that co-ingestion of alpha-lipoic acid with creatine can enhance muscle total creatine content as compared to the ingestion of creatine and sucrose or creatine alone.¹⁵⁷

As well, there is a significant increase in insulin sensitivity and/or insulin secretion, when a protein hydrolysate, such as the **glutamine peptides**, is combined with creatine.¹⁵⁸ **Sodium** is also important for increasing creatine uptake in muscle and some studies has been found to be important for creatine uptake into relatively insulin insensitive muscles such as the soleus.¹⁵⁹

Creatine Advantage Also Contains:

Glutamine peptides (from casein rather than from wheat gluten so Creatine Advantage can be safely used by those with gluten sensitivity), which have anabolic (increases protein synthesis and muscle mass) and anticatabolic (decrease muscle breakdown) effects, above those normally associated with glutamine, as the peptides themselves have some physiological effects. Also the peptide form is better absorbed than free glutamine that is not peptide bonded.

As well, the glutamine in the glutamine peptides:

- Regulates protein synthesis and increases body composition and performance
- Increases both aerobic and anaerobic energy systems
- Has beneficial effects on the immune system
- Aids in the prevention and treatment of the overtraining syndrome.
- Increases insulin sensitivity when a protein hydrolysate is combined with creatine.¹⁶⁰

Glutamine has significant effects on body composition and performance as it favorably affects growth hormone and cortisol levels, protein synthesis, cell volume, muscle catabolism (inhibits it) and gastrointestinal and immune function.¹⁶¹¹⁶²¹⁶³¹⁶⁴¹⁶⁵ It's used for energy by most cells in the body but especially by the GI tract, liver, kidney and the immune system. The process for energy production is by successive deamination of glutamine to glutamate, then to alpha-ketoglutarate that enters the TCA/Krebs cycle and through the oxidative phosphorylation forms ATP, the main energy source on which the body functions.

Glutamine is also used as a basis for the synthesis of the ATP molecule itself, nucleic acids (DNA and RNA synthesis and repair), other amino acids and proteins, glucose through gluconeogenic pathways, carbamoylphosphate, and other metabolites. As well glutamine increases glutathione, a powerful endogenous antioxidant that mitigates the counter-productive effects of exercise on excessive muscle damage without affecting the positive effects of exercise.

The interconversions, reactions, pathways and signaling that glutamine is involved in are complex and impacts many metabolic processes that are beyond the means of this information piece. As an example, glutamate can be used (besides conversion to glutamine) in an alanine aminotransferase

reaction to produce alpha-ketoglutarate (AKG) and alanine or by the reverse reaction alpha-ketoglutarate can be aminated by ammonia or via a transamination reaction from other amino acids to form glutamate and pyruvate. The resulting alanine and pyruvate are involved in complex interactions and so the complexity of how glutamine affects metabolism soon increases exponentially.

A recent paper found that glutamine supplementation improves some parameters of sport and exercise performance, and chronic supplementation appears to be of special importance for

increasing tolerance to intermittent exercise, lowering feelings of fatigue, and optimizing recovery from muscle damage.¹⁶⁶ Glutamine may also act as a relevant resource for rehydration during strenuous and prolonged physical activity.

And glutamine plays well with other ingredients in Creatine Advantage. For example, a study found that a combination of creatine monohydrate plus glutamine together resulted in significantly increase muscle mass and strength.¹⁶⁷

Volumizing Ingredients

Creatine Advantage contains an advanced cell volumizing formula that results not only in increases in protein synthesis and an anabolic effect, but an increased transport of creatine inside muscle and other cells. This formula includes:

- **Glutamine**
- **Taurine**
- **Potassium**
- **Sodium**
- **Creatine** itself which has significant volumizing effects.

Branched Chain Amino Acids

Increased intracellular concentrations of branched chain amino acids (leucine, valine and isoleucine) stimulate formation of acetyl-coenzyme (CoA) and succinyl-CoA, thus increasing both glycolytic and anapleurotic flux and aerobic and anaerobic energy production. All three, but especially leucine, have a synergistic effect with creatine on increasing protein synthesis.

Beta-Alanine and Carnosine

Both Beta-alanine and Carnosine (beta-alanyl-L-histidine) were added to Creatine Advantage because of their powerful antioxidant, anti-inflammatory, and immune system effects, as well as their beneficial effects on physical and mental performance, healing and recovery.^{168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188}

Exercise is a catabolic process and unaided this catabolism isn't reversed right away even after you've finished training. Carnosine has an immediate effect on helping to change the catabolic state to one that's anabolic and aiding recovery in this and other ways. It also has beneficial effects on muscle damage and on increasing blood flow in muscle.¹⁸⁹

Carnosine has beneficial effects on exercise performance by helping to overcome muscle fatigue, likely due its effectiveness as a buffering agent, and perhaps its antioxidant, chelating, and enzyme regulating effects.¹⁹⁰

Carnosine levels tend to be higher in athletes such as sprinters^{191,192} and in bodybuilders¹⁹³ These studies also show that intramuscular carnosine may be an effective physiological H⁺ buffer and that there is a significant relationship between the carnosine concentration in human skeletal muscle and

high intensity exercise performance. A recent study found that beta-alanine supplementation increased muscle carnosine levels¹⁹⁴ and resulted in an improvement in exercise performance.¹⁹⁵

Since dietary carnosine is absorbed across intestinal epithelial cells, using carnosine itself would seem to be more useful than using beta-alanine. However, a recent study found that using carnosine and beta-alanine together results in a greater effect than using either one alone.¹⁹⁶ As such, I've included both in Creatine Advantage.

Ditto for the inclusion of Taurine as the combination of taurine and carnosine has been shown to be have protective properties towards testicular tissue and consequently for testosterone production.¹⁹⁷

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Acute carnosine and β -alanine supplementation increases the compensated part of the ventilation vs work rate relationship during a ramp incremental cycle test in physically active men

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PDF

BACKGROUND: Chronic supplementation with carnosine and β -alanine (Carn- β A) has been proposed to improve muscle contractility and reduce muscle fatigue mainly through an increase in intracellular pH buffering capacity. However, the acute ergogenic effects of Carn- β A supplementation are poorly investigated. This study aimed at evaluating the acute effects of a single Carn- β A supplementation on the cardiorespiratory and metabolic response during a ramp cycle-ergometric test.

METHODS: This randomized, double-blind, placebo-controlled study, involved 10 healthy males (age 22.2 ± 1.9 years, body mass 72.5 ± 7.9 kg, stature 1.72 ± 0.08 m, body mass index, 24.47 ± 1.91 kg/m², mean \pm standard deviation). All the participants performed two maximal incremental ramp tests on a cycle ergometer, with a prior randomized assumption of 2.5 g L-carnosine plus 2.5 g β -alanine (Carn- β A) or placebo (PLA). During exercise, gas exchange parameters were measured breath-by-breath, heart rate was monitored by electrocardiography and rate perceived exertion was determined on Borg scales. From the ramp test, peak cardiorespiratory and metabolic parameters and ventilatory thresholds (VT1 and VT2) were calculated off-line.

RESULTS: No differences between the experimental conditions emerged at peak exercise. However, despite acute Carn- β A supplementation did not affect the single ventilatory thresholds, the compensated portion of the ramp test (i.e., the difference between VT2 and VT1) was significantly larger ($P = 0.043$) in Carn- β A.

CONCLUSIONS: These findings demonstrate a positive effect of acute Carn- β A supplementation on the compensated part of the exercise. This should be taken into account by nutritionists and athletes searching for nutritional supplements, when a quick effect based on an acute dose is required.

Citrulline Malate

Citrulline Malate (CM), a mixture of citrulline and malate, was added for several reasons. Citrulline has several effects, including increasing ammonia clearance, increasing bicarbonate, ornithine, arginine, and citrulline levels. Malate, a tricarboxylic acid cycle (TCA) intermediate, has beneficial effects on energy metabolism mainly by facilitating aerobic ATP production through anaplerotic reactions.

Overall, studies suggest that citrulline malate supplementation can boost athletic performance and enhance recovery by eliminating the amino acid breakdown products of protein metabolism and augmenting the detoxifying capacity of liver cells in removal of ammonium and lactate from the blood.¹⁹⁸¹⁹⁹²⁰⁰²⁰¹²⁰²²⁰³²⁰⁴

The bottom line is that CM supplementation has beneficial effects on energy metabolism, body composition, exercise performance, decreasing fatigue, and enhancing recovery short term by facilitating the shift from the catabolic training state to the post exercise anabolic state.²⁰⁵²⁰⁶²⁰⁷²⁰⁸

Biotin

Biotin is a water-soluble vitamin that acts a cofactor for several of the carboxylases involved in fatty acid synthesis, gluconeogenesis, and branched-chain amino acid (BCAA) metabolism.

The ketogenic phase of my diets and any ketogenic/low carb diet increases biotin bioavailability and consumption, and hence, promotes energy production by gluconeogenesis and branched-chain amino acid metabolism, which can result in biotin deficiency. A recent paper concluded that “It is suggested that individuals that consume the ketogenic diet have an increased biotin requirement.”²⁰⁹

Many other ingredients that increase the effectiveness of Creatine Advantage in maximizing energy metabolism, performance and body composition – see the complete nutrition panel below. Their function in enhancing the effects of Creatine Advantage in maximizing energy metabolism, performance and body composition will soon be added to this information piece.

What’s Not in Creatine Advantage

Almost as important as what’s in Creatine Advantage, is what’s not in it. For example, guanidinopropionic acid (GPA), an ingredient that is used in some creatine products, is not a useful ingredient as it seems that its use can decrease creatine levels in heart muscle cells and likely muscle cells.²¹⁰ As well, in keeping with a lower carb approach, which besides decreasing fat oxidation also decreases GH and IGF-I levels, Creatine Advantage only contains 1.5 grams of carbs per 10 grams serving - just enough to maximize creatine uptake into muscle cells, but not enough to have counter productive effects.

Safety of Long-Term Creatine Intake

Studies have shown that the long-term use of creatine does not have any significant side effects, such as an increase in muscle cramping or injuries, nor does it impact on the body’s ability to manufacture creatine endogenously once the creatine is discontinued.²¹¹²¹²²¹³²¹⁴ Muscle creatine levels usually return to normal within 4 weeks.²¹⁵

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