

## **Dietary Supplements: An in depth review of the various physiological & ergogenic effects of today's most popular supplements**

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### **Creatine**

#### **What is it?**

A naturally occurring amino acid like compound synthesized from the amino acids glycine, arginine, and methionine. Creatine is stored primarily in muscle tissue (95%) with small amounts (5%) stored in the brain and testes. 2/3 of stored muscle creatine is in the form of phosphocreatine, with the remaining stored as free creatine.<sup>1,10,11</sup>

#### **Where does it come from?**

It is abundant in protein rich foods, most notably fish, pork, and beef.<sup>12</sup> If needs are not met by the diet, creatine can be synthesized from the aforementioned amino acids. Supplemental creatine is formed in the latter process in a lab.

#### **Safety?**

As possibly one of the most extensively studied dietary supplements to date, creatine has proven to be a safe and effective means of performance enhancement. Researchers have observed athletes and patients for up to five years ingesting creatine and have not reported any negative side effects; in fact, it has been shown to lessen the occurrence of injury to athletes<sup>9</sup>. In recent years research has focused on creatine for therapeutic benefits in various medical populations and diseases such as sarcopenia (age related muscle wasting), fibromyalgia, depression, neuromuscular disorders, muscular dystrophy, Huntington's disease, and many others.<sup>1,8,10</sup>

#### **Efficacy?**

Creatine has been (and continues to be) proven beneficial to athletes involved in intermittent, high intensity activities. It is also especially advantageous to strength/power athletes or those looking to increase muscle mass.

#### **Dosing/Timing**

For individuals just beginning supplementation, a loading phase of 20 grams (split into 4, 5 gram doses) for 3-5 days is recommended to increase creatine stores initially. After loading, a maintenance dose of 5g/day is recommended Post Workout.<sup>1</sup>

#### **Various Forms**

Creatine is available in many forms such as Creatine Ethyl Ester, Creatine Malate, Creatine Monohydrate, Creatine liquid drops etc... Monohydrate remains the most recommended and scientifically supported form.<sup>14,15</sup> Due to its overwhelming popularity, it would seem

appropriate to note that in a specific study carried out by Spillane et al., they concluded that creatine ethyl ester did not show any additional benefit at increasing muscle strength or performance above creatine monohydrate OR a maltodextrose placebo. Furthermore, serum creatinine (blood marker of creatine breakdown) values were highest in the creatine ethyl ester group without a significant increase in serum or muscle creatine levels. This demonstrated that after ingestion, a large portion of the supplemented CEE was being degraded within the GI tract.<sup>13</sup>

### **Additional Information**

#### **Uptake Enhancement**

Muscle creatine uptake is enhanced in the presence of insulin so it is suggested to be taken along with a rapidly digesting source of glucose, such as Gatorade powder (this is also suggested for the discussion that follows). Additionally, plasma (blood) creatine is transported into tissues via a sodium and chloride dependent transporter called CreaT.<sup>10,16</sup> There exist two isoforms of this transporter (CreaT1 and CreaT2), CreaT1 is most important to us since supplemental creatine is absorbed exclusively through it, while CreaT2 is found primarily in the testes.<sup>16</sup> The take home message is that CreaT is not only sodium but also chloride dependent, therefore, sodium and chloride in addition to glucose have been shown to further enhance creatine uptake.<sup>17,18</sup>

#### **Responders vs. Non Responders**

Anyone who has searched forums or spoken with friends in regards to results from creatine supplementation knows that there exists great variation between individuals. Some individuals even report that they do not receive any ergogenic effect from supplementation; these individuals are known as "non responders". Science offers us some insight into this phenomenon: In a study done investigating those that "respond" to supplementation, (defined as achieving a significant increase in total resting muscle creatine levels after a loading phase) and those that don't, it was concluded that responders generally:

- Possess a lower initial quantity of intramuscular creatine, therefore were able to absorb a greater amount through supplementation.
- Had a greater % of type 2 muscle fibers, and greater cross sectional fiber size.
- Possessed more fat-free mass.<sup>19</sup>

#### **In regards to creatine cycling:**

Since creatine levels have been shown to take roughly 4 weeks (30 days)<sup>20</sup> to return to baseline after cessation of supplementation it is suggested that to effectively cycle, one should stay off for at least this amount of time before reintroduction to their regimen.

## **Branched Chain Amino Acids (BCAA)**

### **What are they?**

The 3 BCAA's: Leucine, Isoleucine, and Valine are essential amino acids with a very unique role in various muscular processes. Most importantly of these roles, they provide a fuel source to working muscles, and a crucial role in muscle protein synthesis/decreased protein breakdown. They are unique in that, unlike other amino acids, upon absorption, they are not degraded in the liver and are transported directly to the muscle. This is illustrated in the fact that after a BCAA dose is administered, blood and tissue levels spike significantly.

### **Where do they come from?**

They are generally found in protein rich foods, but amounts vary widely with differing protein sources. The highest food sources are Whey Protein, Milk and Dairy, Beef, Salmon, and Soy.<sup>7</sup> (Soy protein is not recommended as a major source of BCAA intake because in large doses it inhibits protein synthesis<sup>2</sup>)

### **Safety?**

BCAA's are widespread throughout foods and are a component of a normal daily diet, therefore safety does not warrant much concern for healthy individuals. They are also ESSENTIAL amino acids, meaning we NEED to ingest them since our bodies cannot synthesize them.

### **Efficacy?**

Of the 3 BCAA's, Leucine is the protein synthesis "powerhouse" and is responsible for initiating protein synthesis<sup>3</sup>, therefore it may be the most essential of essential amino acids. The BCAA's also enhance insulin sensitivity, and are incredibly important in providing glucose to working muscles during sustained activity. Leucine is so efficient at initiating protein synthesis that a dose of Leucine+Glutamine has been shown to be equally as effective as a complete amino acid formula at increasing p70s6kinase phosphorylation (a marker of increased protein synthesis)and Leucine ALONE was almost as effective.<sup>21</sup>

### **Dosing/Timing**

Roughly 3 grams (or 0.05g/kg BW) of leucine has been shown to maximally stimulate protein synthesis<sup>3</sup>, therefore a source (supplemental or dietary, supplemental is suggested) supplying 3 grams PRE Workout, and 3-6 grams POST workout is recommended (post workout recommendation is higher because exercise increases leucine oxidation). A general daily recommended intake of BCAA's is 6-20 grams/day total.<sup>4</sup>

### **Additional Information**

BCAA's in pure form are a white powder, and are hydrophobic (do not mix well in water). As with creatine, it is beneficial to take them with a fast digesting carbohydrate source, as insulin increases their uptake into the muscle. (Insulin also plays an important role in protein synthesis<sup>5</sup>). \*Although leucine can be purchased and taken alone, it is

recommended to take all 3 branched chain amino acids together, as taking just one could create an imbalance. A ratio of 2:1:1 Leucine/Isoleucine/Valine, respectively, is recommended. Lastly, it should be noted that BCAA's are important, but are not an end all be all replacement to the intake of the other amino acids.

## **Arginine**

### **What is it?**

A conditionally essential amino acid that acts as a precursor to nitric oxide, creatine, ornithine, and other nitrogenous compounds, it is also claimed to increase growth hormone secretion. There are two primary enzymes that compete for arginine and determine the physiological effects it produces; NO synthase, and Arginase. NO synthase is largely responsible for arginine's positive qualities like signaling the production of nitric oxide/improving blood flow, promoting wound healing, improving immune function etc... In contrast, arginase inhibits the production of nitric oxide, contributes to endothelial dysfunction, increased oxidative stress, atherosclerosis, and other cardiovascular disorders.<sup>22,23</sup>

### **Where does it come from?**

Arginine is typically found in high amounts in plant proteins such as soybeans, nuts, flax seeds, (2-3 g Arginine/100 g Food) and animal proteins such as tuna, chicken, and salmon (1-2 g Arginine/100 g Food).<sup>6</sup> \*100 grams = roughly 3.5 oz.

### **Safety?**

As arginine is a commonly encountered amino acid through dietary intake, it does not pose a threat to healthy individuals through normal consumption. However, prior recommendations of benefit to individuals recovering from heart attack are no longer warranted. Long term high dose arginine ingestion in this population did not improve vascular stiffness or clinical outcomes and actually lead to an increased risk of death. This can in part be explained by the fact that arginase activity increases with age and increasing intake of arginine.<sup>24</sup>

### **Efficacy?**

In otherwise healthy individuals, supraphysiologic doses of Arginine speeds recovery from traumatic injury by increasing collagen synthesis, stimulating cell growth, and increasing T cell response.<sup>25</sup> Growth hormone stimulating effects on healthy adults though, are unlikely. In fact, a dose of 5g Arginine consumed PRE workout actually compromised the GH response to training.<sup>26</sup> Data on Performance enhancing effects of Arginine in healthy populations are scarce, not very promising and require further research. From the information currently available arginine may aid in long duration, endurance exercise, or for nutrient delivery and exercise recovery post workout.

### **Dosing/Timing**

Not enough positive data to warrant recommendations to healthy athletes for performance enhancement.

### **Additional Information**

Arginine is quite cheap, but due to the lack of proficient scientific data, it would generally not be recommended for healthy individuals who are on a budget. This is simply because there are much more proven, effective supplements that provide a more cost-efficient means of performance enhancement.

## **Beta-Alanine (BA)**

### **What is it?**

A fairly new supplement gaining popularity, BA is a naturally occurring beta amino acid (most other amino acids are in the alpha configuration); this may explain why it is not involved in the synthesis of any major proteins or enzymes. It is the rate limiting precursor to Carnosine synthesis, which means Carnosine levels are directly influenced by the amount of BA available. Therefore, BA supplementation has been shown to increase intramuscular Carnosine concentrations significantly.<sup>27,28</sup> In light of this, the ingestion of BA increasing the deposit of intramuscular Carnosine can be likened to that of the ingestion of creatine increasing levels of creatine phosphate.

### **Where does it come from?**

Carnosine is a dipeptide (linkage of two amino acids) consisting of BA and the amino acid Histidine, free BA in the body is usually created from the degradation of carnosine. It is most abundant in skeletal muscle, therefore animal flesh such as chicken, beef, pork and fish are high sources of dietary BA and carnosine.<sup>27</sup> It is important to note that only BA supplementation (not carnosine) has not been shown to be ergogenic.<sup>29</sup>

### **Safety?**

There are two important issues to address regarding BA supplementation:

1. BA requires the release of Histidine, to form Carnosine. Because of this, a "flushing"/pins and needles (also known as parasthesia) type reaction is typical. Since histamines are released in allergic reactions, it is a similar feeling but subsides within 5-15 minutes. This is normal and not dangerous albeit uncomfortable.
2. BA and the nonessential amino acid, Taurine, compete with receptors for transport. This is clinically relevant since these receptors are found in the brain, heart, and skeletal muscle. In animals, disproportionate intakes of BA to Taurine have been shown to decrease Taurine uptake. This has also been demonstrated in humans where, in response to BA supplementation, plasma (blood) Taurine levels increased. However, urinary Taurine excretion was not increased. This may not be a concern for athletes getting enough complete proteins (or adequate amounts) in their diet. For individuals who are not, supplementation of Taurine along with BA is STRONGLY recommended.<sup>29,30,31</sup>

### **Efficacy?**

Histidine alone is a relatively weak buffer (pH managers, they resist change in pH). When combined with BA though, it becomes much more efficient.<sup>32</sup> This is the premise of BA supplementation; if you can decrease the accumulation of hydrogen ions (acidity) in the working muscle, you can increase the time to fatigue. This is exactly what studies on BA supplementation have illustrated.

### **Dosing/Timing**

For buffering effects: 3-6g/Day approximately 1 hr. before exercise. It would also be wise to start slowly and with a lower dosage to minimize the "tingling" effect. Studies have shown this tingling effect is virtually eliminated with 1 gram doses; therefore, distributing your beta-alanine supplement into smaller dosages would also solve this problem. The maximum threshold to avoid this effect has been suggested at 10mg/kg bodyweight.<sup>4</sup>

## **Glutamine**

### **What is it?**

A conditionally essential amino acid that is the most prevalent free amino acid in blood and one of the most prevalent in muscle. Glutamine is often times confused with glutamate (or glutamic acid), this confusion usually leads to glutamine being credited for roles that glutamate is responsible for. For example, a study undertaken on piglets (which have intestinal function very similar to that of humans) examining intestinal metabolism found that 95% of the dietary glutamate presented to the mucosa was metabolized in first pass and that glutamate not glutamine is the major fuel for the intestinal enterocytes.<sup>33,34</sup> This has been further proven by human data.<sup>35,36</sup>

### **Where does it come from?**

Again, most protein foods like meats, fish, and dairy supply ample glutamine, along with beans, spinach, cabbage and beets.

### **Safety?**

As a conditionally essential amino acid, glutamine is safe for consumption.

### **Efficacy?**

When provided to otherwise healthy subjects, Glutamine is yet to yield improvements in body composition or athletic performance. In a study comparing the effects of Glutamine vs. a maltodextrin placebo on 1 RM squat, bench, peak knee extension torque, lean tissue mass, and protein degradation, variables were equally improved in both groups.<sup>37</sup> Additionally, individuals in a placebo controlled study receiving an acute dose of Glutamine at 0.3g/kg bodyweight (which would equate to a dose of roughly 22 g for a 160 lb. individual) 1 hour PRE workout, found no improvement in weightlifting performance.<sup>38</sup>

Furthermore, claims that Glutamine reduces protein breakdown and improves immune function are quite embellished. It is required in very high (>20 g/day) and sustained doses to effectively influence net protein balance or physiological measures of immune function.<sup>39,40,41</sup>

Glutamine has, however, proven to be as effective POST workout at restoring muscle glycogen levels as a glucose containing beverage. This could be a great asset to an individual on a carbohydrate restricted diet, especially since Glutamine taken alone was shown to NOT increase insulin.<sup>42</sup> The following recommendations are therefore based on Glutamine's ability to restore glycogen in the absence of carbohydrate.

### **Dosing/Timing**

Glycogen Resynthesis: 8g consumed immediately post exercise.<sup>4</sup>

### **Additional Information**

Glutamine tends to be a very expensive supplement, even when bought in bulk. Due to this, and the lack of clinical evidence to support its use, Glutamine supplementation is not recommended for general use beside that which has been provided.

#### ***Brief Author Biography***

Ben Esgro is a Certified Sports Nutritionist through the International Society of Sports Nutrition, he also holds a B.S in Nutrition with a minor in exercise science from West Chester University. He plans to pursue a Master's in Sports Nutrition next year at Marywood University. Ben is also a competitive Natural Bodybuilder. He can be contacted at [besgro@gmail.com](mailto:besgro@gmail.com).

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