

# Sports Pharmacy



DECODING THE SCIENCE OF ELITE HUMAN PERFORMANCE

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How Pharmacists can get involved with Sports Pharmacy

Dietary Supplement Facts vs. Fiction  
5 Common Questions in a Pharmacy World

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How L-Glutamine can enhance athletic performance

A Pharmacist's Approach to Branch-Chain Amino Acids

Whey Protein Too Good to be True?

Creatine Supplementation and athletic performance

HMB Supplementation and Muscle Growth



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### MISSION STATEMENT

# The Mission of Sports Pharmacists

**Brandon K. Welch, Pharm.D.**  
 Founder of Pharmacy Athlete

We are happy to announce our first edition of the Sports Pharmacy Magazine where we cover topics related to performance-enhancing supplements and nutritional interventions to help optimize the wellness of patient athletes. I believe pharmacists are an essential and cornerstone piece affecting the health outcomes of millions of patients. We've seen the versatility of our role during the most challenging times of the most recent pandemic. We were forced to educate the general public based on facts and clinical research related to the health crisis of COVID-19. We are not just pharmacists, but CLINICIANS. We fact check and support claims based off peer-reviewed studies and clinical research. I say all this to say, Pharmacists can be pivotal players in the arena of sports. We are poised to help intersect biochemistry with biomechanics and real-life science with athletic performance. Our patient athletes rely on results and we are here to deliver them in real-time.

Many athletes, at all levels of competition, place great emphasis on the use of dietary supplements and nutritional interventions to optimize their performance.

When looking at the use of supplements by elite athletes, it is important to bear in mind that many athletes are unaware what the active ingredient(s) are or of the amount of those ingredients. Consuming multiple supplements may increase the risk of exposure to harmful levels of specific substances or interactions causing adverse health outcomes. The indiscriminate use of supplements is a cause for concern and demands educational interventions at an early age for athletes, coaches, and parents/family members. Working with elite athletes involves being a part of a high-performance culture where performances are measured by results, and every small improvement counts. A discussion around medical, physiological, cultural, and ethical questions may be warranted, to ensure that the athlete has the information needed to make an informed choice.



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# How Pharmacists can get involved with Sports Pharmacy



**By** Dr. Hussam Hamoush, Pharm.D.  
Owner at Stonebriar Pharmacy



A typically football team in the NFL is allowed to have 53 active players on their roster. That's 53 athletes that must be always at peak physical performance. Within the NFL, there are plenty of rules and regulations centered around preventing the use of Performance Enhancing Drugs (PED). Do teams know which products are permitted and not permitted? With increasing scrutiny, fines, and suspensions, athletes need to be constantly aware of what goes into their system. How do teams make sure that they are protecting their players both financially and physically? This is how we introduce the idea of a Sports Pharmacist. Pharmacist can play an important role in promoting safe therapy, follow-up, and being to identify drugs that can be harmful, have adverse effects and drug interactions. The clinical role of pharmacy is expanding the more we go along in the profession. Students have expressed deep interest in the field of sports pharmacy because of the education they are provided. In pharmacy programs across the country, pharmacy has had an expanded role into the health care field. The field of "Sports pharmacy" is still a very new and underutilized specialty. In the past, pharmacists were predominately utilized towards doping control. Ambrose (2004) describes that pharmacist can play a key role in participating in doping control programs in addition to preventing athletes from inadvertently consuming a substance banned by their respective federal agency. Pharmacist can also help in ensuring the safe use of substance that could enhance an athlete's performance. With more and more false claimed ads that pop up on social media, a pharmacist will be able to decipher information that can prevent an athlete from taking an unknown substance that could potentially do more harm than good. And if a professional athlete received a suspension, that's missing money that is coming out of their paycheck. One of the major problems in sports today is a lack of what we like to call "Quality Information". Many products that are advertised as "Performance Enhancing" are dubbed so with a lack of evaluation, testing, or can be obtained via illegal means. All of which could lead to hardships for the athlete in the future. Another aspect of pharmacotherapy that an athlete would seek would be around injury recovery. Injuries happen all the time in sports. Pharmacists play a crucial role in ensuring patients are recovering appropriately from their injury as well following up to ensure adherence. Time lost is money lost for the athlete. With the growing number of Over-the-Counter medications that say they are going to "cut recovery time in half" can make false claims that could do more harm than good. Pharmacist can even help with finding the right delivery system for a patient. This can help reduce the risks of



## The role of pharmacy is growing, it's not about filling prescriptions anymore.

side effects that have the potential hinder an athlete from performing when they need to. For example, an anti-inflammatory can be taken topically instead of orally that can result in stomach pain and nausea.

What does this mean for the average person that isn't a professional athlete? How can a pharmacist help? With the specialty growing and more and more information being available to the consumer, there is an increased risk of potential harm that can come to the patient. A Sports Pharmacist would be able to check drug interactions, analyze lab data, and provide insight into the products claim for the validity of data. Social media has become an avenue for false claims by "influencers" that appeal to the amateur that has just began their fitness journey. False claims such as "use this to get ripped QUICK" or "This is how I lost

35 pounds in 1 month". With the pharmacist education and training, they will be able to decipher these false claims with good data that will save money, ensure safety, and find a way to get the best results.

As you continue to read the articles we provide for Sports Pharmacists, the information we give has been backed by studies, been peer-reviewed, and have come from a strong recommendation from multiple pharmacists. The role of pharmacy is growing, it's not about filling prescriptions anymore. Our role is an integral part of the health care team.

#### Citations:

1. Ambrose, PJ. Drug use in sports: A veritable arena for pharmacists *J. am. Pharm. Assoc* **2004**, 44,501-516. (PubMed)
2. Bomfim, J. Pharmaceutical Care in Sports. *Pharmacy*. **2020**



# Dietary Supplement Facts vs. Fiction

## 5 Common Questions in a Pharmacy World



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In a perfect world, one would consume all the nutrition they need to maximize health, wellness, and physical performance through food alone. Unfortunately, the world isn't always perfect!

Between busy schedules, food availability and taste preferences, consuming all the nutrients you need from food alone can be quite challenging – especially if you're highly, physically active and/or on certain medications which deplete your body of nutrients. Taking a 'food only' approach becomes even more difficult when one considers dietary challenges such as food sensitivities/intolerances which eliminate certain foods from your diet.

This is where dietary supplements can play a key role in helping you achieve your health and performance goals – they fill in gaps that may be missing from our diet alone.

That said, you may be wondering, "I've heard that supplements are unregulated & it's a 'wild, wild west' out there... Is this true?", "I've heard you can consume all the nutrition you need from food alone?" or "Do supplements just make expensive poop & pee?!"

Working as pharmacists and a dietitian in a proactive pharmacy setting, we receive questions like this all of the time. Are they true?

Below are 5 of the most common topics we get asked about as it relates to dietary supplements and the truth behind them!

### Fact vs. Fiction #1 – The Dietary Supplement industry IS regulated.

Answer: Fact!

This one often comes to a surprise to many people as the dietary supplement world is often portrayed as the 'wild, wild west' in the media. Truth be told there are actually a lot of regulations in place to police the supplement industry, stemming from the Dietary Supplement Health and Education Act (DSHEA) which was passed in 1994. With this act, many laws are in place as it relates to product labeling and good manufacturing practices (GMP's) to ensure product safety.

The bigger challenge, as it relates to dietary supplement regulations, is enforcing them; especially as it relates to both 1) Product Safety and 2) Ensuring the supplement label actually matches what's in the bottle. Unfortunately, due to limited resources, the FDA is not able to monitor every manufacture at the preferred level of inspection that one may desire. As a result, supplements often slip through the cracks.

One does not have to spend too much time on google to find articles about supplements that have been spiked with illegal substances banned by the World Antidoping Association (WADA), adulterated with cheap fillers and/or simply failing to meet label claims as it relates to ingredient potency.

For this reason, if you're an athlete and compete in a sport tested for banned substances, we encourage you to choose supplements that are either NSF Certified for Sport or Informed Choice Certified. These certifications ensure that your supplement has been tested for substances prohibited by WADA.

Here at Hometown Pharmacy and Avant Pharmacy & Wellness Center we carefully screen our products. We only work with highly

reputable companies, preferably ones which test every batch produced to ensure ingredient potency and safety profiles along with efficacious doses of key active ingredients.

Using professional brands is critical in helping us get real world relevant results as well as helping us to build relationships with key members of our community such as athletic clubs, schools and fellow healthcare organizations.

**Fact vs. Fiction #2 – Physically active individuals can consume all the nutrients they need from food alone.**

Answer: Fiction!

Ok, technically, one can consume almost all the nutrients they need to optimize health and performance from food alone. However, the practicality of this can darn near be impossible. Two examples of this include CoQ10 and Creatine – 2 supplements often consumed to support energy production. Let's look at each a bit closer.

CoQ10 is well recognized for its role in energy production. For individuals that are on statin based medications (i.e. atorvastatin, rosuvastatin, simvastatin or lovastatin), we always recommend taking 100-300 mg per day to help your body maintain the CoQ10 that can be depleted with the use of these medications. Unfortunately, to consume this from food alone, on a daily basis we'd have to eat the equivalent of > 2-6 lbs of organ meat, > 10-30 lbs of peanuts/nuts or ≈ 40-120 lbs of broccoli!<sup>1</sup>

Similarly, we often recommend creatine in our pharmacy. Research has shown creatine to support not only physical performance but also potentially mood, cognition and recovery from traumatic brain injury. To ingest the recommended 5-10 grams of creatine a day, one would have to consume > 2-4 lbs of meat per

day!<sup>2-3</sup> Creatine is not present in vegetables, underlying its importance for consumption for those who are vegetarians or vegan.

**Fact vs. Fiction #3 – Multivitamin-minerals just make expensive pee!**

Answer: Fiction!

You may have heard that supplements just make for expensive pee and poop. From a pragmatic standpoint, this couldn't be further from the truth.

Will you pee excess vitamins and minerals out? The answer to this is 'yes'. However, the key word in the statement is "excess." One only reaches a level of "excess" when all deficiencies are accounted for.

Taking into account that most individuals have less than a perfect diet, especially when you consider increased nutrient demands placed on the body with high levels of physical training and/or medications that can cause nutrient depletion, many individuals are operating with nutrient deficient 'machinery' on a daily basis – This is not ideal for performance!

Two examples of this can be seen with vitamin D and magnesium supplements; both of which play a key role in physical performance and are often deficient in the diets of most individuals.

According to research 50-66% of the adult population is deficient in magnesium; This is alarming as magnesium is essential for 600 reactions in the body, including energy production.<sup>4-5</sup> Similarly, vitamin D deficiency is widespread – especially for those living in northern latitudes, have limited sunlight exposure in general and/or higher melanin content in their skin.

For these individuals, taking vitamin D and magnesium supplements does not represent 'expensive urine/poop' but rather physical performance gains!

The only time where this may lead to 'expensive pee/poop', even when deficiencies are present, are if the vitamins/minerals are not in their preferred



**Dietary supplements are a great way to help physically active individuals meet their health and performance goals.**

form for absorption. For instance, magnesium, especially in the form of magnesium oxide, can often cause GI issues, leading to diarrhea. For this reason we recommend taking magnesium chelated to an organic acid such as di-magnesium malate, magnesium citrate or magnesium bisglycinate.

**Fact vs. Fiction #4: Creatine Supplements may cause health issues, have not been studied long term & should be used with caution.**

Answer: Fiction!

In statement #2, we briefly touched on creatine as it relates to amounts present in our normal food supply. Additionally, as it relates to creatine, we often have people ask us in the pharmacy if it's safe to consume. This question often stems from many early reports in the media and medical world which reported potential health concerns when consuming it long term.

Fortunately, creatine has been studied extensively since the early 90's. Research conducted in adolescent, adult and elderly populations has shown it to be both safe and effective.<sup>6</sup> In fact, in 2020, the US Food and Drug Administration classified creatine monohydrate as 'generally recognized it as safe'.<sup>7</sup>

The only note of caution would be in individuals with pre-existing kidney conditions. That said, creatine use has been shown to be beneficial for individuals with chronic kidney disease on hemodialysis.<sup>8-9</sup>

**Fact vs. Fiction #5: Protein in amounts > 20 grams/meal is 'wasted' by the body.**

Answer: Myth!

Protein supplements tend to be popular items in our pharmacies. Whether looking for a quick "grab and go" smoothie in the morning as you head out to work or a post workout protein shake, supplements such as these can work great.

As it relates to protein, one thing we're often asked is, "Is dietary protein consumption in amounts >20g per meal wasted by the body?"

The answer to this question is "no." This number is often cited due to research showing that 20 grams of egg protein maximally stimulated muscle protein synthesis in young men following an acute exercise session.<sup>10</sup> However, the amount of protein needed to maximally stimulate muscle growth will vary considerably based on age and type of protein consumed.

For instance, one needs to consume higher amounts of plant proteins to receive the same acute

anabolic effect as animal proteins such as whey. Additionally, with age, skeletal muscle becomes less responsive to protein; Thus older individuals appear to require additional protein to get the same anabolic effect as a younger individual.

Additionally, protein not used to support muscle tissue can be used for other functions within the body such as energy balance and immune support.

In conclusion, dietary supplements are a great way to help physically active individuals meet their health and performance goals. However, there are many misconceptions about the dietary supplement world which make navigating it pretty challenging. This underscores the importance of selecting dietary supplements from pharmacists, dietitians and other health care professionals well versed in the nuances of dietary supplements.

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# How L-Glutamine can enhance athletic performance

By Dr. Jessica Beal-Stahl, Pharm.D.



## AUTHOR BIO:

Jessica Beal-Stahl, PharmD, is the Chief Clinical Officer and Co-Founder for Personalized Athletics Lab, tying her passions of athletics and pharmacy together. She received her Doctorate of Pharmacy from Mercer University in 2009 and have been practicing as a Director of Clinical Services at an independent pharmacy in Merritt Island, Florida, since graduation. Jessica also knows what it's like to be a high-level athlete, having played D1 volleyball, medaled internationally in Olympic weightlifting, and recently set a world record in Olympic Weighting for snatch in her age/weight class. She holds additional certifications in Integrative Medicine, Nutrigenomics, and sports nutrition.

L-Glutamine, a nonessential amino acid, meaning the body can produce glutamine in human muscle. It is the single most common amino acid in human muscle and plasma; about 60% of skeletal muscle is made from glutamine. Besides the significant role it plays in protein synthesis; it boosts the immune function and supports intestinal health.

Glutamine is obtained through the catabolism of proteins in food. In states where tissue is being built or repaired, like the growth of babies, healing from wounds, or severe illness, glutamine becomes essential<sup>1</sup>.

Glutamine is synthesized by adipocytes, liver, and lungs from glutamate and ammonia by the enzyme glutamine synthetase and stored and released by skeletal muscle. Glutamine is a precursor for purines and pyrimidines, enabling the synthesis of DNA and RNA, mRNA synthesis, and DNA repair of nucleotide and nucleic acids.

PubChem notes one of the prominent role glutamine plays in muscle recovery is the transport of nitrogen atoms to where they are needed most<sup>2</sup>. To build muscle a positive nitrogen balance must be maintained. After a heavy workout, rushing nitrogen to damaged muscles stimulates tissue repair. If glutamine is lacking, damaged tissue may stay damaged because it does not have the materials to rebuild.

Glutamine is also the primary fuel source for lymphocytes to provide energy and optimal conditions for nucleotide biosynthesis and cell proliferation. It's critical to lymphocytes, especially when sick, as glutamine levels drop, causing a reduction in the immune cell's ability to defend the body. Unlike skeletal muscle, leukocytes do not possess the enzyme glutamine synthetase, so leukocytes cannot synthesize glutamine when needed<sup>3</sup>.

Glutamine's immune-boosting properties are also linked to its activity in the intestines. It contributes to maintaining the intestinal lining – which ensures the body absorbs the nutrients it needs and helps protect the gastrointestinal tract, the largest organ in the immune system.

There is abundant evidence suggesting additional glutamine is essential in specific stress situations such as severe illness, trauma, and overtraining due to decreased plasma concentrations<sup>4</sup>.

In hypercatabolic states, the elevated demand exceeds the capacity of the body to produce adequate amounts of glutamine<sup>5</sup> the impairment of immune function may occur<sup>6</sup>. It's been suggested as a potential cause of exercise-induced immune impairment and increased susceptibility to infection in athletes. Due to the important pleiotropic roles in metabolism and tissue homeostasis, glutamine is one of exercise immunology's most studied amino acids<sup>7</sup>.

Studies show chronic oral administration of free glutamine can attenuate the injury and inflammation induced by intense aerobic and exhaustive exercise. However, the effects on muscle

recovery from resistance training are unclear<sup>4</sup>. Due to higher training volumes and loads, some athletes find supplementing with glutamine beneficial as it may take up to a week after a workout for levels in your muscles to restore original levels prior to intense training sessions.

Few studies have examined the effect of glutamine supplementation alone as an ergogenic aid. Supplementation with glutamine reduced the magnitude of strength loss, accelerated strength recovery, and diminished muscle soreness more quickly than placebo; these effects were more pronounced in the men<sup>8</sup>. In adult weightlifters, no effect on muscle performance, body composition, or muscle-protein degradation; but glutamine may help with recovery of muscle strength and reduce muscle soreness after exercise<sup>9</sup>.

In “**Dietary Supplements and Sports Performance: Amino Acids,**” the International Society of Sports Nutrition (ISSN) stated glutamine might be able to stimulate muscle glycogen synthesis. But adequate carbohydrate alone is sufficient. Additionally, neither short-term nor long-term glutamine supplementation leads to a significant increase in muscle mass or strength<sup>10</sup>.

While no governing bodies have regulations or limits on the amount of glutamine, remember the quality of the product and manufacturing process is vital. A recent review article examining 50 studies found over 28% of the supplements tested were contaminated with undeclared substances posing a risk of unintentional doping for athletes<sup>11</sup>.

Most diets contain about 3-6 grams of glutamine per day. Animal products are the most significant source. Some athletes can have higher intakes of l-glutamine because of their high protein intakes from protein supplements, protein hydrolysates, and free amino acids products.

In most studies, glutamine had no reported side effects in adults or preterm infants<sup>12,13</sup>. Many patients with serious catabolic illnesses, such as infections, intestinal diseases, and burns, take glutamine safely with a daily oral dose ranging from 0.21 to 0.42 g/kg body weight glutamine (equivalent to 15–30 g/day in a person weighing 154 pounds) have provided no biochemical or clinical evidence of toxicity<sup>12</sup>.

Generally, glutamine is considered safe for the body when available in normal quantities. Some patients report mild side effects when newly added;

cough and changes in bowel movements are the most common adverse effects. While patients with liver and kidney diseases, glutamine supplements may worsen symptoms.

**Pharmacist Takeaway:** While glutamine has been highly studied and has additional benefits, especially the support of the gastrointestinal tract. Athletes may benefit from another supplementation vs glutamine alone as an ergogenic product.

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# A Pharmacist's Approach to Branch-Chain Amino Acids

By Dr. Matthew Liaw, Pharm.D.



## AUTHOR BIO:

Matthew Liaw is a pharmacist with ten years of service to Navajo people at Crownpoint Healthcare. He is also an amateur distance runner specializing in the 10k, half-marathon, and marathon. As a pharmacist, he has led a medication error subcommittee, run a pain management clinic, and led an antimicrobial stewardship program. The runner in him is a scientist who enjoys repeating physiology trials to see how valid they are for his training. Some of his favorite moments at the UNM physiology lab include testing how shoes affect running economy, testing the impact of an extended interval block, and comparing methods of body fat testing. His dream is to bring his expertise in pharmacy and passion for running together and become a sports pharmacist.

## BCAAs: Many Claims

Throughout the mid-2010s, branched-chain amino acids (BCAAs) have become popular in sports nutrition. The three proteinogenic BCAAs are leucine, isoleucine, and valine. They are essential amino acids for humans and cannot be synthesized in the body. Advocates claim benefits include fueling exercise, reducing muscle protein breakdown (MPB), promoting muscle protein synthesis (MPS), decreasing muscle damage, reducing fatigue, promoting a healthy immune system, and reducing muscle soreness. While the physiological benefits may have some rationale, strong evidence from human studies is often weak (Jeukendrup and Gleeson, 2019).

## Beneficial Claims during Exercise

As a fuel source, BCAAs can be converted to glucose for use in glycolysis. In theory, supplementation of BCAAs during endurance events can spare glycogen use and delay “hitting the wall.” However, studies have shown that the oxidation of BCAAs contributes little fuel to exercise (Wagenmakers et al., 1989). In addition, the availability of carbohydrates in the body reduces BCAA oxidation (Jeukendrup and Gleeson, 2019). This means that if an athlete is consuming carbohydrates in an event BCAA contribution is even lower. This leads to the conclusion that BCAA supplementation during exercise is unnecessary.

During intense and extended exercise sessions, muscle protein can be broken down for fuel. By having BCAAs in the blood, the body might not need to use muscle protein. In vitro studies showed the addition of BCAAs to incubation or perfusion mediums promoted protein synthesis and inhibited protein degradation. However, human trials have failed to

replicate the benefits (Frexes-Steed et al., 1992; Nair et al., 1992).

Reducing fatigue can be a benefit during exercise. Some proponents of BCAAs claim a benefit based on the Central Fatigue Hypothesis. The theory is that during prolonged exercise, fatty acids (FAs) are mobilized to serve as fuel. They block free tryptophan (fTRP) from binding to albumin sites thereby increasing the fTRP to BCAA ratio. The increase in this ratio allows tryptophan to cross into the brain via the LNAA transporter where it is converted into serotonin (Chaouloff et al., 1986; Hargreaves and Partridge, 1988). It is assumed that the increase in serotonin leads to central fatigue. BCAAs compete with fTRP for the LNAA transporter. By increasing systemic BCAA levels, less fTRP might pass into the brain to be converted (Jeukendrup). However, increased tryptophan has not been found to impact performance (Stensrud et al., 1992). A field trial performed in the Stockholm Marathon failed to show a significant performance change in BCAA supplementation compared to placebo. Subgroups suggested there might be a performance benefit in less trained athletes (Blomstrand et al., 1991). Subsequent studies failed to find a performance effect found by Blomstrand (Van Hall et al., 1995).

## Beneficial Claims Post-Exercise

Probably the most popular purpose for BCAA consumption is to promote protein synthesis. The body requires a positive protein balance to build muscle. Like other amino acids, BCAAs provide the building blocks for creating new proteins. They also stimulate the mammalian target of rapamycin (mTOR) pathway for muscle growth. Leucine is the strongest stimulant of this pathway out of the three BCAAs. However, the ingestion of BCAAs alone only provided a fraction of



the anabolic response compared to complete proteins like whey (Jackman et al., 2017). The conclusion was that while BCAAs can stimulate MPS, the body needs sufficient amounts of essential amino acids along with the BCAAs for optimal MPS.

Similar to decreasing protein breakdown during exercise, BCAAs have been touted to decrease muscle damage. There is some evidence that BCAAs can reduce muscle soreness, but the benefits to muscle function are not significant (Jackman et al., 2010; Howatson et al., 2012). Neither of these studies compared differences between BCAA supplementation compared to complete protein sources. Further studies are needed to determine if BCAAs are unique in reducing muscle soreness.

### The Athletes Perspective

Looking at BCAAs as a distance runner, the evidence does not favor the use of isolated BCAA supplementation. My personal preference would be to source BCAAs from whole protein sources. A hundred grams of chicken has about 1500mg of BCAAs and other amino acids (Jeukendrup and Gleeson, 2019). A hundred grams of peanuts can give 3300mg of BCAAs. If I were to use it for its perceived benefits, I would take the supplement within 30 minutes of completing an intense workout along with my post-workout nutrition. The combination of amino acids with carbohydrates increased MPS according to Koopman and colleagues (2005). During a marathon or ultramarathon, I might take a gel or drink with high amounts of BCAAs to delay fatigue and spare glycogen. These details become important when a pharmacist approaches an athlete on using medications along with BCAAs.

### The Pharmacists Perspective

What does this mean for the pharmacist discussing BCAAs with an athlete? Because BCAAs are found in foods, the athlete should separate them from medications that need to be taken on an empty stomach. Tryptophan is also found over the counter to aid sleep. If an athlete is supplementing tryptophan as a sleep aid, one can recommend separating the BCAA ingestion so as not to interfere with tryptophan's mechanism of action. For building muscle, recommend athletes make sure other types of proteins are included in a high-quality diet or a complete protein source.

As a product that is often found in food, BCAAs are usually considered a benign supplement. BCAAs are not banned by the World Anti-Doping Agency or US Anti-Doping Agency (WADA, 2022). Athletes must know the risk of contamination and the addition of other products. Most supplement doses are intended for people 18 years old and up. Because of this, there is a risk of excessive use in younger athletes. It is recommended this population avoid

products with proprietary blends (Periato, 2022). Remind the athlete to follow the directions and recommended amounts. Be aware of hazardous trends such as dry scooping where users dump powder supplements directly into the mouth. Some people claim this practice helps the body absorb the product faster thereby improving the workout. The risks for such a practice include accidental inhalation of the powder and digestive issues. Overall, BCAAs are a safe supplement and can be a convenient way to provide post-workout nutrition.

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# Whey Protein Too Good to be True?

By Keaton Higgins, Pharm.D. (c), ATC



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Keaton Higgins is a final-year pharmacy student at the University of Iowa and a certified athletic trainer, receiving his degree and accreditation through the University of Northern Iowa. During his time in pharmacy school, Keaton has worked tirelessly to discover opportunities that would allow him to integrate his passions of sports medicine and pharmacy into a fulfilling career. He regularly provides pharmacology lectures at his alma mater to pre-healthcare and athletic training students and will be presenting this summer at the National Athletic Training Association Clinical Symposia & AT Expo.

## Intro

I was in eighth grade when I started weightlifting consistently. In the early days, this new world brought upon more questions than answers on daily basis, and I was overwhelmed from the start:

What exercises are the best to do? How often should I work out certain muscle groups? What kind of clothes should I wear so that people don't make fun of me?

Overwhelming, to say the least. While these same thoughts are most likely going through the heads of most first-time gym goers, it does seem like that there is one thing that everyone there agrees on: protein powder. More specifically, **whey protein** - the most commonly used type of protein powder. From high performing athletes to post-operative patients in the hospital to novice exercisers like me back in grade school, whey protein supplements are routinely used by many different populations.

But why? And more importantly, what actually is it and what does it do?

## How It Works

Whey protein is a collection of eight different proteins found in milk that, after pasteurization and drying, is readily available in a powder form. This collection of proteins encompass all nine essential amino acids that we need to function properly.<sup>6</sup> The human body doesn't produce all of these essential amino acids naturally, so supplementation through consumption is necessary. This is one reason why whey protein supplementation is so advantageous. When consumed, whey protein is broken down into these essential amino acids, which are then used to repair and grow new muscle fiber in the body.

Which leads us to the question – shouldn't ALL athletes be supplementing their diets with whey protein?

The short answer is... no. The correct answer is... it depends.

## Effectiveness and Safety

There has been extensive research suggesting that in conjunction with physical exercise, whey protein has been shown to accelerate recovery of muscle function after resistance training<sup>2</sup> and increase muscle thickness.<sup>3</sup> Recent studies also suggests that compared to various other comparable supplements and placebos, whey protein consumption is associated with ergonomic effects such as more efficient generation of energy, increased coping of intense physical exercise, improved  $VO_{2\max}$ , and the ability to achieve ideal body weight goals while maintaining or gaining muscle mass.<sup>4</sup>

Perhaps most importantly for competitive athletes, whey protein is NOT considered a banned substance by WADA, USADA, NCAA or any other prominent regulatory body.

While whey protein is an acceptable supplement and has been shown to be effective in several different instances which would benefit high-performing athletes, there are red flags to watch out for when it comes to consumption.

As mentioned previously, whey protein is a dairy product derived from milk. Whey protein may cause significant gastrointestinal discomfort, especially for those with a sensitivity or intolerance to



lactose-containing products. Whey protein may also interact with certain medications that athletes may be taking. Isotretinoin and tetracycline antibiotics (doxycycline, minocycline) are commonly prescribed to help treat acne in the younger population, and whey protein may cause significant interactions leading decreased absorption and effectiveness of these medications. Studies have also shown a potential for hepatotoxicity with concurrent use of isotretinoin and whey protein supplements.<sup>5</sup>

### Dosing recommendations

The amount of protein that should be consumed in a single serving and throughout an entire day are both widely debated and heavily opinionated topics. However, most current research recommends between **20 to 40 grams of proteins per single serving** (with most studies trending towards the lower end),<sup>2</sup> and a daily goal of a minimum **0.8 grams per kilogram of body weight, and 1.2-2.0 grams per kilogram for active to very active adults.**<sup>1</sup> This translates to about 0.35 grams per pound of body weight per day for sedentary adults, and around 0.55-0.9 grams per pound per day for a more active population.

### Conclusion

Whey protein supplementation is a relatively safe and effective way to help achieve daily protein intake recommendations, build muscle, and maximize athletic potential. While athletes can use most whey protein products without the risk of worrying about regulations set forth by WADA, USADA or other governing bodies, there are still risks to consider when deciding to use whey protein supplements. These may include dietary allergies or insensitivities, concurrent medication use and additional caloric intake impacting weight-related goals.

It's also important to remember that whey protein supplements are just that – a way to supplement a balanced diet and lifestyle. It is not necessary to use whey protein powder to achieve particular goals if the same amino acids are already provided through diet choices. Foods rich in these essential amino acids include quinoa, eggs, lean meat, and beans to name a few. If these resources are limited or unavailable to the consumer, then whey protein can play an important role in providing these amino acids essential to muscle growth. It is also an effective way to ensure adequate daily caloric and protein goals are met, especially if time is scarce and there is little time to prepare a full meal.



Whey protein supplementation is a relatively safe and effective way to help achieve daily protein intake recommendations, build muscle, and maximize athletic potential.

If one were to choose to utilize whey protein supplements to help them obtain their performance goals, it is always important to discuss their particular products of choice with a trusted physician or pharmacist before doing so to protect their health and maximize their athletic potential.

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# Creatine Supplementation and athletic performance

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## Intro to Creatine

Creatine is an ergogenic supplement that has been used by many athletes for performance enhancing benefits. An ergogenic aid is a supplement or practice to increase performance capacity, the ability to recover from exercise or promote greater training adaptations. Creatine has been one of the more extensively studied dietary supplements in the sport's industry. There are upward more than 300 articles supporting the effects of creatine on exercise performance and training adaptations.

Creatine believe it or not was first discovered in 1832 by Michael Chevreul and the name creatine was derived from the Greek word for flesh, since it was found in meat<sup>1</sup>. In the 1960's and 70's Soviet Researchers found that creatine loading can improve anaerobic performance. In the mid to late 80's Karolinska Institute in Sweden started researching creatine loading to test it's true performance benefits<sup>1</sup>. In the early 1990s Great Britain Olympic Champions Linford Christie and Sally Gunnell said they had been using creatine as a performance enhancement supplement in the 1992 Barcelona games. In the mid 1990's, the banning of anabolic steroids helped creatine become a very popular sports supplement. Creatine gained its popularity for athletes in the 1990's with the goal of increase muscle gains in the weight room and to augment resistance training. The popularity began to explode as more studies starting showing the benefits it had on strength training, mainly with short, high intensity exercises. A survey conducted by division 1 athletes in the late 90's found that close to 50% of male athletes reported current or prior use of creatine. The popularity also showed merit by a cohort of high school athletes attesting to using creatine for performance benefits.

## Biochemistry

Creatine is a nitrogenous amine and a naturally occurring amino acid derivative found in almost all of the skeletal muscle tissue, with close to 95% body's creatine stored in the skeletal muscle. The endogenous forms of creatine are synthesized in the kidneys and the liver from the following amino acids: arginine, glycine and methionine<sup>2</sup>. Creatine production occurs in the kidneys and starts with the amino acid glycine. The compound is then transferred to the liver where a methyl group from methionine is added forming creatine. Creatine begins to circulate and pulled into skeletal muscle via transporters in the cell membrane. The rate of creatine production has been shown to be regulated by exercise capacity, catecholamines, and insulin-like growth factors. Once creatine is pulled into a muscle cell, creatine can be phosphorylated to create phosphocreatine in a reversible enzyme reaction facilitated by creatine kinase<sup>1</sup>. Phosphocreatine (creatine phosphate), a compound with a "high energy" phosphate link, is used in muscle for storage of P bonds.

## Creatine Kinase, catalyzes:



This is a reversible reaction, through the equilibrium constant lightly favors phosphocreatine formation. Phosphocreatine is produced when ATP levels are high. When ATP is depleted during exercise in the muscle, phosphate is shuttled from phosphocreatine to Adenosine Diphosphate (ADP), to replenish Adenosine Triphosphate (ATP). During high-intensity exercises that rely on short-duration repetitions, ATP needs become met by both bioenergetic pathways anaerobic glycolysis and Phosphagen through phosphorylation shuttle. Our anaerobic energy system that involves the metabolism of glycolysis is the dominant form of ATP production between 10 seconds to minutes, while the Phosphagen system or phosphocreatine predominates as an ATP source during most exercises less than 6 seconds.

The exogenous sources of creatine are animal based products that include red meat and fish. It has been well established that increasing dietary availability of creatine serves to increase phosphocreatine concentrations in the muscle. The availability of creatine and phosphocreatine in the skeletal muscles plays a remarkable role in contributing to energy metabolism during high intensity exercise. Theoretically, increasing the availability of phosphocreatine delivered to the skeletal muscle would enhance cellular bioenergetics of the phosphagen energy system that is most involved during high-intensity exercise performance. Research theorizes that by elevating the intake of phosphocreatine through creatine supplementation, one can increase time to exhaustion and enhance performance by delaying the phosphocreatine shuttle. The proposed mechanism by decreasing time to exhaustion is through ATP production via glycolysis by increasing phosphofructokinase activity or by buffering hydrogen ions.

### Creatine Dosing

Intramuscular stores of creatine can be maximized by supplementing loading doses of creatine monohydrate for 5 to 7 days with a dose of 20 to 25 grams or 0.3g/kg per day<sup>1</sup>. Studies have shown that the best increase of creatine is reported to be in the first 2 days of supplementation. During the loading phase, it is best to spread the dose throughout the day into four equal doses dissolved into an aqueous solution. After the completion of the loading phase, it's best to for the athlete to continue with a maintenance dose of 0.03g/kg daily<sup>1</sup>.

The duration of the maintenance phase can vary throughout studies from 28 days to 10 weeks. One thing to consider is the addition of carbohydrates or protein added to creatine supplementation, there can be an increase of muscle retention of creatine in the first few days, resulting in decreased need for loading.

### Side Effects of Creatine

According to the International of Sport's Nutrition's position statement on creatine monohydrate supplementation states there is currently no scientific evidence of unusual side effects or adverse events when used appropriately. With that being said, it is concluded that when used correctly, creatine can potentially be an acceptable ergogenic aid for young athletes.

Creatine is excreted by the kidneys which can lead some to believe it can be detrimental to renal function. Several studies have been conducted and they have assessed serum creatinine during creatine loading phase but there has been no significant of increases in serum creatinine levels in a healthy population. Although increases in urinary creatinine excretion and decreases in total urine volume output during creatine loading phase. The decrease in urinary output is hypothesized to result in fluid retention and weight gain during the initial phases of creatine supplementation<sup>1</sup>. It's important to note, creatine is osmotically active so, it's assumed fluid retention will occur.

It has been reported in the literature that there has been a case with a 20-y/o male that suffered from interstitial nephritis from creatine supplementation. This issue mainly was due to its inappropriate use of a loading dose (20g/day) of creatine taken over a course of 4 weeks<sup>1</sup>.

Another case report of a young healthy person developing acute liver failure when ingesting mega doses of creatine monohydrate along with other dietary supplements for weight training.

Concerns have arisen with athletes developing problems staying hydrated, getting muscle cramps and regulating body temperature due to a decrease in urinary volume and water retention when consuming creatine monohydrate.

Pharmacist counseling tip: Because more water is transporting to the muscles, less water is available for the rest of the body. Therefore, proper hydration is imperative. A healthy amount of water is anywhere from 2.5-3 liters.

When creatine has been studied in isolation and under acceptable doses, there have been no significant adverse effects to the kidneys or the liver.

### Effects of Creatine Monohydrate on Athletic Performance

There is a significant body of evidence that supports the ergogenic effect of creatine monohydrate on athlete performance. Resistance training has been measured in countless ways in the scientific literature including one repetition max, peak power production, pH balance regulation, increased lean muscle mass, and enhanced oxidative metabolic pathways. Beyond this, short-duration, maximum-intensity exercises have the most support behind creatine's benefits. Currently, studies consistently have lacked support on its effect on aerobic conditioning such as long distant running.

### Creatine Regulation

Creatine is a naturally occurring substance in the body so there is a very few regulations regarding the sports supplement. Currently, no sports body has any limits on the use of creatine. This can include: WADA, IOC, NCAA, NBA, MLB, NFL, UFC. The NCAA does not prohibit individual institutions from distributing creatine supplementation. The IOC ruled to allow creatine given the substance is readily found in animal protein. One thing to strongly consider is with creatine being labeled as a dietary supplement that falls under the umbrella of the Dietary Supplement Health and Education Act (DSHEA), it is not regulated by the FDA. It's important to be mindful of ingredients used in supplements that are not third-party tested to avoid any illegal contaminants.

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# HMB Supplementation and Muscle Growth

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## What is $\beta$ -Hydroxy $\beta$ -methylbutyrate?

$\beta$ -Hydroxy  $\beta$ -methylbutyrate (HMB) is a metabolite of leucine. Recently, it has become one of the dietary supplements that could potentially increase lean muscle mass and promote performance, especially when associated with strength training.

While most muscle growth-promoting hormones work on anabolism, HMB seems to act as an anti-catabolic agent. By minimizing the rate of proteolysis, HMB can lead to solid results when it comes to muscle hypertrophy.

Research on this topic covered animal and human subjects.

**This article will discuss evidence-based research on the effects of HMB on muscle growth and lean body mass.**

## The effects of HMB Supplementation on Animals

Similar to other substances, early research surrounding HMB focused on animals.

### Scientists evaluated the following parameters:

- Carcass weight
- Immune function
- Growth rates
- Side effects
- Morbidity and mortality
- Toxicity

Nissen et al.<sup>[1]</sup> concluded that supplementing lambs with HMB produces no difference in overall weight gain. Despite that, weight gain per unit improved.

When investigating muscle hypertrophy, the evidence was too unreliable to draw any conclusions.

## The effects of HMB Supplementation on Humans

### Untrained Individuals

Supplementing untrained individuals who underwent weight training for 3 weeks with HMB led to a dose-responsive decrease in lactate dehydrogenase (LDH), creatine kinase (CK), and 3-MH.

Another group of researchers found that HMB supplements lower resistance training-induced muscle damage. As for muscle growth, a dose-responsive increase was noted. Researchers found no changes in fat composition, overall strength, and body weight.

We should that interpreting these results based on the trends of LDH and CK can be deceiving due to their poor clinical significance.<sup>[2]</sup>

Nissen et al.<sup>[3]</sup> found that taking 1.5–3 grams of HMB per day prevents proteolysis associated with exercise. Researchers concluded these results due to a 20 to 60% decrease in LDH and CK serum levels, as well as a 20% decrease in urine 3-MH.t



**Three weeks of supplementation also produced a dose-responsive change in strength status.**

### Trained Individuals

The purpose of studying the effects of HMB on trained individuals is to see whether the anti-catabolic properties of HMB are still present. Since these individuals experience training-induced suppression of protein breakdown, the effects of HMB may not be similar to untrained individuals.

Nissen et al.<sup>[4]</sup> reported that 3 grams of HMB supplementation per day significantly enhanced muscle function and body composition when coupled with resistance training. The results were independent from the initial training status.

The authors of the study found these results to be somewhat surprising, especially when considering the limited potential for gains in strength-trained athletes relative to their untrained counterparts.

### HMB and muscle growth – Mechanisms of action

May slow down skeletal muscle proteolysis

Myocytes and the muscle tissue are constantly in a state of turnover. Therefore, lean muscle mass is the net result of the rates of protein synthesis and proteolysis.

To achieve muscle hypertrophy, one of the parameters has to change; either an increase in protein synthesis or a decrease in proteolysis.<sup>[5]</sup>

The vast majority of studies focused on findings substances that induce protein synthesis. This left a large window of opportunities for proteolysis-decreasing agents, such as HMB.

According to research, proteases may be the primary trigger of HMB's effect on muscle hypertrophy.<sup>[6,7]</sup>

Di Pasquale<sup>[8]</sup> theorizes that HMB may promote muscle growth by binding to the receptors of the following hormones:

- Cortisol
- Testosterone
- Growth hormone
- Insulin-like growth factor-1 (IGF-1)
- Insulin



Current evidence demonstrates that a dosage of 1.5–3 grams of HMB per day provides considerable gains in lean muscle mass and overall strength when coupled with resistance training.

Alternatively, HMB downregulates the enzymes responsible for muscle tissue breakdown.

### May regulate the production of cholesterol

Previously, there was a hypothesis about the effects of HMB on androgen levels. This hypothesis stems from the assumption that  $\beta$ -hydroxy  $\beta$ -methylglutaryl CoA (HMGCoA), a metabolite of HMB, can be a source of cholesterol and thus androgen production.

However, measuring the levels of serum testosterone after HMB supplementation showed no significant changes.

Alternatively, HMB can provide sufficient amounts of HMG-CoA for cholesterol production. In return, this will boost cell growth and function.<sup>[9]</sup>

While this theory makes perfect sense, studies found that HMG can lower low-density lipoprotein (LDL) levels. This argument may be enough to refute the previously mentioned theory.<sup>[9]</sup>

May lead to body fat loss

In vitro, scientists found that HMB above physiological levels can boost the oxidation of fatty acids in skeletal muscles.<sup>[10,11]</sup>

While this effect is not clear-cut in vivo, two studies demonstrated fat loss after HMB supplementation compared to control groups.<sup>[4,12]</sup>

High-dose leucine supplements coupled with a caloric deficit of 30% led to greater body fat loss compared to 3 different diets with similar total caloric intake.<sup>[13]</sup>

Despite the significant increase in HMB levels with such doses of leucine, there is no direct link that connects HMB to body fat loss. Moreover, the study that included high doses of leucine also had other amino acids, such as lysine. This may interfere with the credibility of these findings.

Without conducting further research in this field, drawing conclusions about HMB and fat loss is too premature.

### The side effects of HMB

According to the International Olympic Committee's medical advisory board, HMB is a legal substance. In a 1997 human study, researchers found no adverse effects of high-dose HMB taken for up to 7 weeks.<sup>[9]</sup>

Taking HMB supplements does not seem to affect renal, hepatic, or immune function indicators.<sup>[14]</sup>

Moreover, the ratios of urinary testosterone to epitestosterone showed no significant changes after 2 weeks of HMB supplementation.<sup>[15]</sup>

Aside from blood tests, questionnaires were handed to people taking these supplements. The analysis of these questionnaires showed no adverse effects.<sup>[9]</sup> Finally, animal studies showed positive improvement in health status after taking doses of up to 100 grams per day.<sup>[1,16,17,18] [18,19,22,24]</sup>

### Conclusion

Current evidence demonstrates that a dosage of 1.5–3 grams of HMB per day provides considerable gains in lean muscle mass and overall strength when coupled with resistance training. Preliminary research shows that these effects may be due to a decreased rate of proteolysis. However, further research is necessary to test this theory.

With that said, the available research is very promising, with a clear need for longer, better controlled clinical trials to objectify the effects of HMB supplementation on muscle growth.

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