

HMB + ATP = huge muscles?

Interaction of Beta-Hydroxy-Beta-Methylbutyrate Free Acid and Adenosine Triphosphate on Muscle Mass, Strength, and Power in Resistance Trained Individuals 



Introduction

Emerging research is indicating that a combination of β -Hydroxy β -Methylbutyrate (HMB) and adenosine triphosphate (ATP) may be a strong option for people looking to enhance their exercise capacity through supplementation.

HMB is a metabolite of the branched-chain amino acid [leucine](#), and may help with reducing muscle protein breakdown. ATP is the energy currency of the body. This molecule stores and releases chemical energy to fuel metabolic processes that keep you alive. Availability of ATP to the muscle is a primary dictator of how much volume of work or exercise you can perform. Supplementing with creatine is effective because it can be used to quickly replenish ATP in hard-working muscles, so that they can continue contracting. A preliminary study looking at oral supplementation [with ATP](#) on exercise performance has shown promise, but getting optimal amounts of energy to the muscle is only part of the equation.

Muscles still must be given time to recover from exercise-induced damage. The greater the amount of fatigue brought on by training, the higher the recovery demands will be between exercise sessions. For athletes, minimizing time between training sessions while maximizing

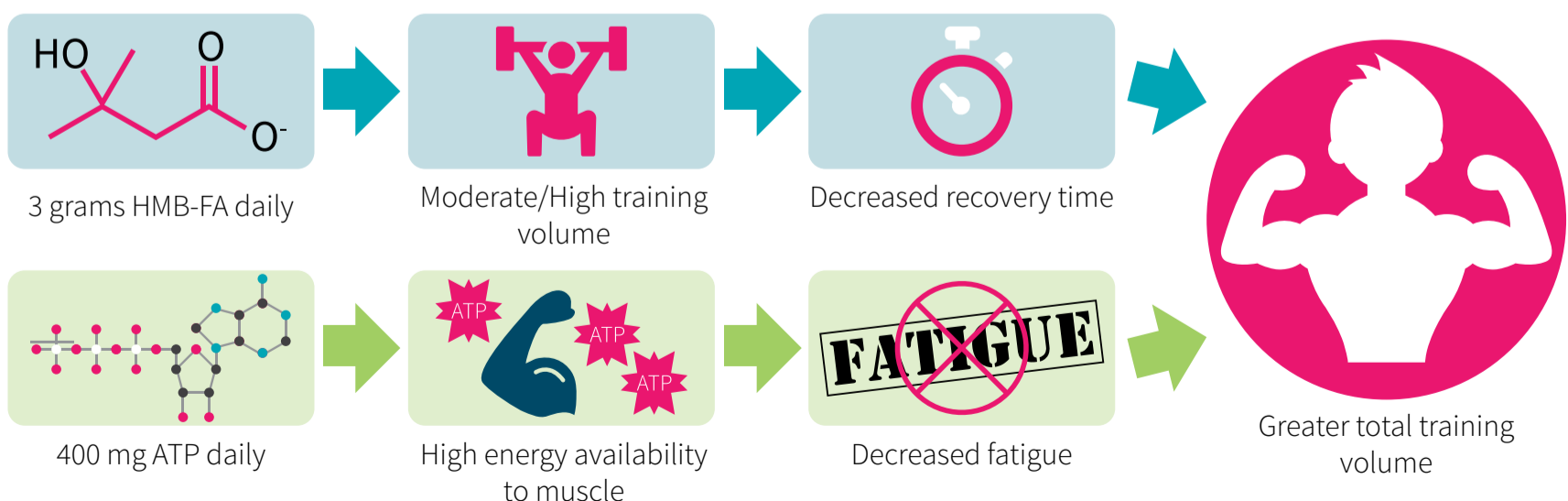
training volume is a critical component of attaining peak performance. This is where HMB may come in, as evidence indicates that it can [aid in perceived muscle recovery time](#). It is possible that, when combined, HMB and ATP may act synergistically (as shown in Figure 1). ATP provides muscles the energy they need to keep working and HMB reduces the recovery time between bouts of training. The study under review aimed to investigate this potential synergistic effect.

A synergistic combination of ATP and HMB may prove to be a potent ergogenic aid. Supplementing with ATP can ensure a high availability of energy to working muscles while HMB may help to reduce recovery time between exercise sessions.

Who and what was studied?

Seventeen resistance-trained men (average age of approximately 21) were recruited into this randomized, double-blind, placebo, and diet-controlled study. They had an average squat, bench press, and dead-lift of 1.7 times, 1.3 times, and 2.0 times their body weight. Anyone taking any anti-inflammatory or performance-enhancing supplement was excluded from the trial. Age, height, body mass, and body mass index showed no significant differences between placebo

Figure 1: HMB and ATP ergogenic synergy



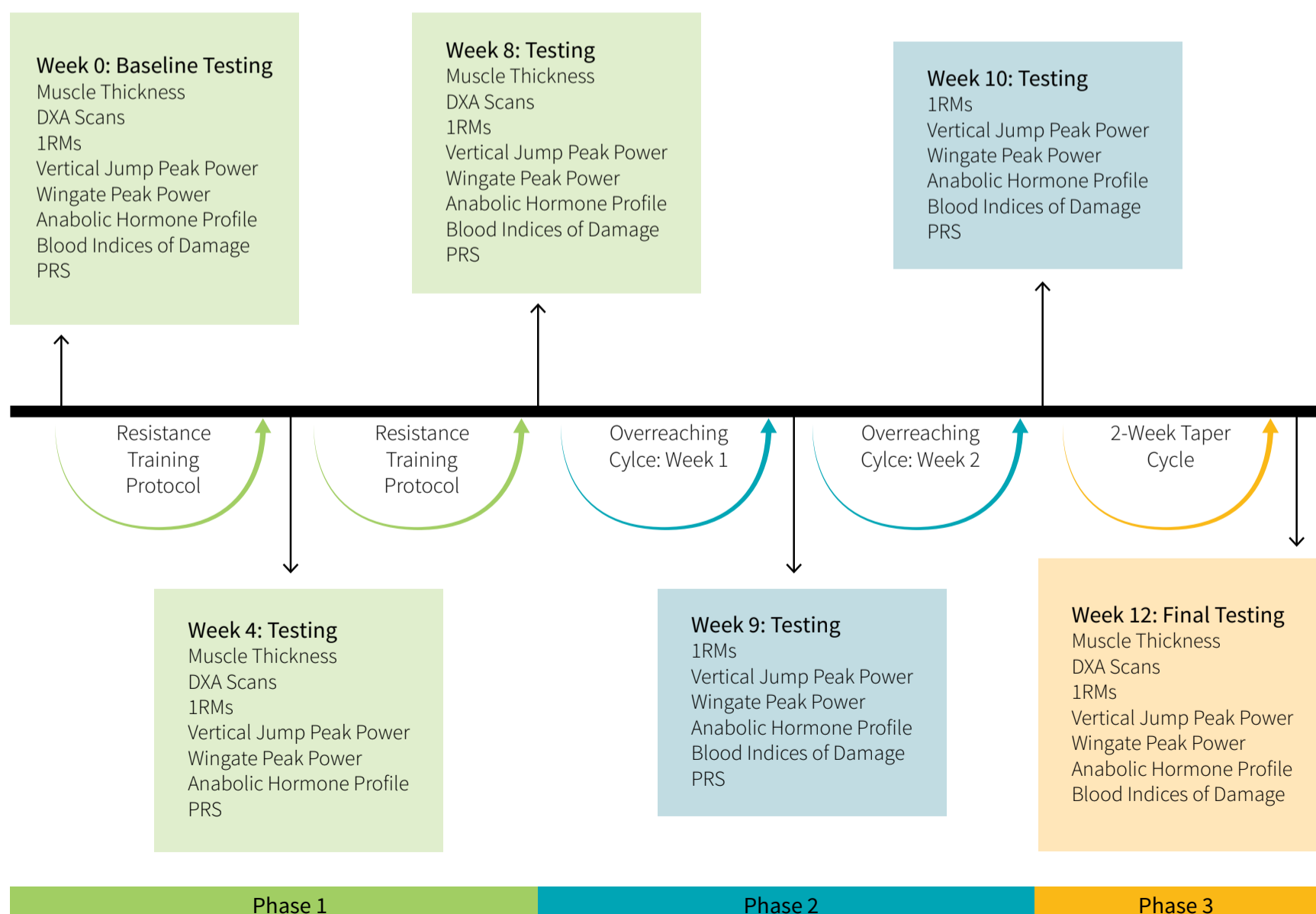
(n=9) and the intervention group (n=8) at the beginning of the study. Participants were instructed and coached by a registered dietitian on how to keep their diets at 25% protein, 50% carbohydrates, and 25% fat throughout the trial.

The primary purpose of the study was to test if supplementing with HMB free acid (HMB-FA) and ATP would improve measures of muscle mass, strength, or power over a 12-week period of resistance training. Participants supplementing with HMB-FA/ATP were taking three grams of HMB-FA and 400 milligrams of ATP per day. Of this dose, one gram of HMB-FA and all 400 milligrams of ATP were consumed 30 minutes prior to a workout session. The ATP and HMB-FA were provided by TSI, Inc. and Metabolic Technologies, Inc, respectively. Both products were tested for purity and for the steroid hormone DHEA by Metabolic

Technologies, Inc. Each of these companies provided grants to help fund this study and three of the researchers were employed by Metabolic Technologies. An independent laboratory tested HMB-FA for microbes and heavy metals. Both products came back as nearly 100% pure and free of contaminants.

The 12-week resistance training protocol was made up of three phases, as outlined in Figure 2. Phase one was an eight-week nonlinear periodized resistance training program (daily undulating periodization). In this phase, sets and reps for exercises are modified from workout to workout. Participants exercised three times a week during this phase. Phase two was a two-week overreaching cycle, where participants exercised at very high volumes, six days a week. Overreaching is defined as “an accumulation of training and/or non-training stress resulting in *short-term* decrement in performance

Figure 2: Study Design



capacity...in which restoration of performance capacity may take from *several days to several weeks*.” The purpose of this overreaching phase was to determine if the HMB-FA/ATP combo could help inhibit any performance decreases. Phase three was a two-week deload, in which volume of work was cut back drastically in order to allow the participants to recover.

Seventeen resistance trained young men completed this RCT. The study aimed to investigate if HMB-FA/ATP could improve muscle mass, strength, or power over a 12-week three-phase training cycle. Phase one was a three-day per week periodized exercise program, phase two was a six day per week overreaching program, and phase three was a deload that allowed participants to recover. The phase two overreaching cycle was designed to see if HMB-FA/ATP could offset performance decreases.

What were the findings?

Some of the main study results are shown in Figure 3. The HMB-FA/ATP group saw significant increases in all measures of muscle strength (measured as one rep max for bench press, squat, deadlift), power (vertical jump, Wingate), lean body mass (DXA scan) and mus-

cle hypertrophy (ultrasonography). At the end of the trial, lean body mass had increased by 4.6 pounds (2.1 kilograms) in the placebo group and the HMB-FA/ATP group gained 18.7 pounds (8.5 kilograms). Percentage of fat mass dropped 2.4% in placebo and 8.5% in HMB-FA/ATP. Hypertrophy was gauged by measuring the increase in quadriceps thickness, showing a significant treatment effect of HMB-FA/ATP-treated participants (7.8 millimeters) when compared to placebo-treated participants (2.4 millimeters) over the 12 week period.

Blood levels of creatine kinase, an indicator of levels of muscle damage, remained significantly lower in the HMB-FA/ATP group throughout phase one and two. Once the phase two overreaching training began, the placebo group experienced a 153% increase while the HMB-FA/ATP condition only went up by 35%. Cortisol levels were significantly lower with HMB-FA/ATP throughout the entire trial. Inflammation measured via C-reactive protein and free and total testosterone levels did not differ between groups. Participants also gave a subjective evaluation of their own muscle recovery and readiness to train again via a perceived recovery status score (PRS). The HMB-FA/ATP group maintained better PRS scores over the entire study, but even more so during the overreaching phase.

HMB free acid vs. calcium HMB

HMB supplements typically come in two forms: the calcium salt form, referred to as calcium HMB, and the HMB free acid form (HMB without the calcium salt attached).

Calcium HBM is the more commonly available (and studied) form. When timing HMB around your workout, calcium HMB [is not absorbed as quickly or as well](#) as HMB-FA. It takes 1.5 to two or more hours before calcium HMB peaks in the bloodstream, compared to just 30 minutes with HMB-FA. The absorption of HMB-FA is also greater, resulting in almost twice the concentration in the bloodstream when comparing respective peaks. However, it is not yet known if timing for either supplement form plays a critical role in its effect on exercise performance. While calcium HBM has more research studies using it, [three publications](#) (including the [study under review](#)) have used HBM-FA and observed striking results in trained individuals.

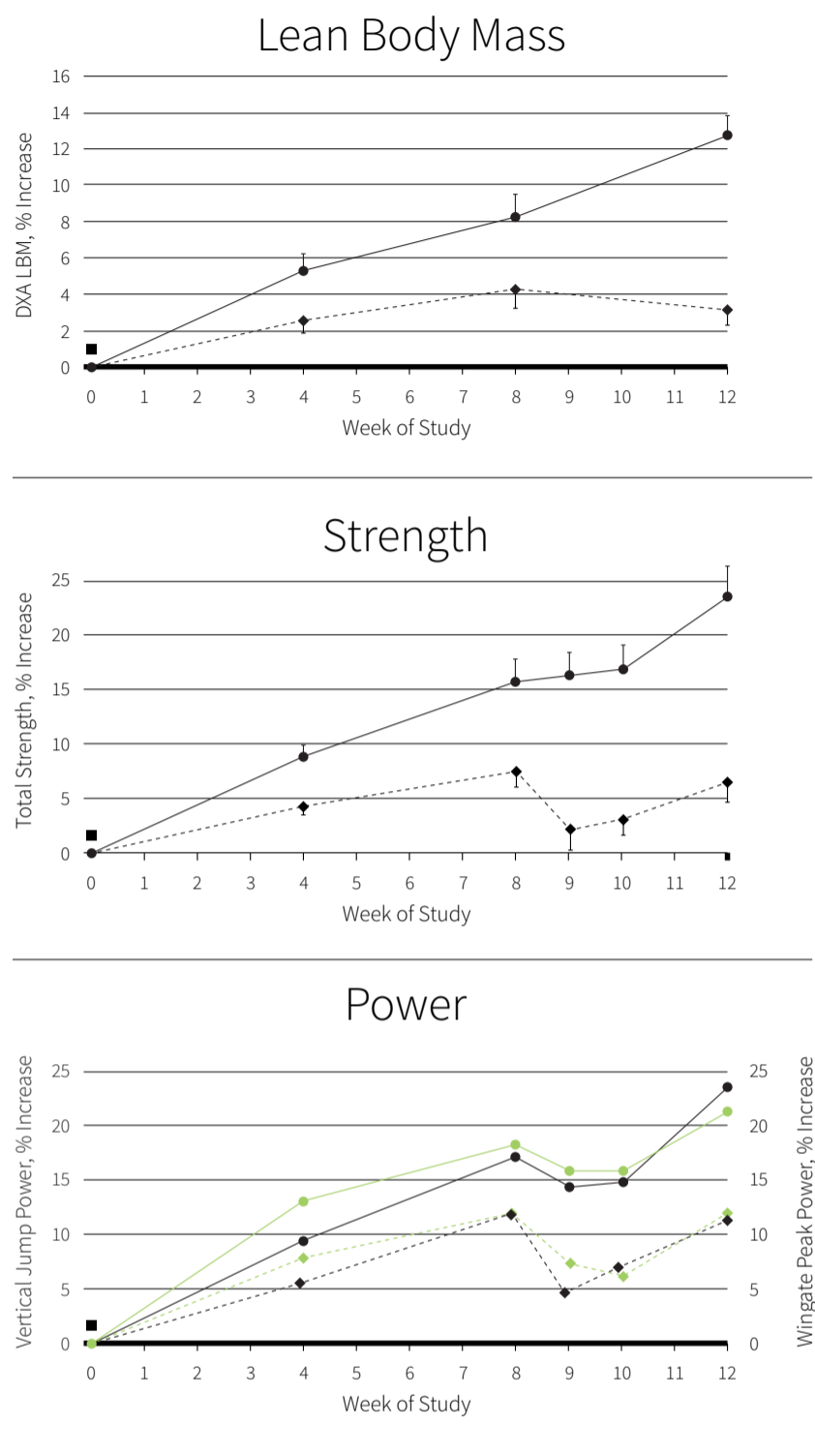
Participants supplementing with HMB-FA/ATP significantly improved muscle mass, power, lean body mass, and strength. The HMB-FA/ATP group increased lean mass by 18.7 pounds (8.5 kilograms) compared to the placebo group's 4.6 pounds (2.1 kilograms). Measures of muscle damage were much lower with HMB-FA/ATP during the overreaching in phase two.

What does the study really tell us?

An HMB-FA/ATP supplement combination appears to improve muscle recovery time. It is thought that [HMB primarily works through](#) decreasing protein degradation and that it may stimulate protein synthesis. Decreasing protein breakdown in muscle would allow for people undertaking exercise to put in more total work, leading to increased muscle adaptations. It is important to note that there is an exercise volume interaction occurring here. HMB supplementation does appear to aid muscle recovery in both well-trained and untrained individuals, but only if the training stimulus is high enough. Well-trained persons would have to train at high intensities or volumes to see the greatest benefit of an HMB-FA/ATP supplement. For untrained individuals, the very nature of going from mostly sedentary starting an exercise program will initially be enough of a stimulus to reap HMB's muscle recovery effects.

The benefits of preventing muscle breakdown are illustrated by the placebo group, when those subjects began their phase two overreaching sessions in weeks 9 and 10. As seen in Figure 3, during this period measures of lean body mass, strength, and power either regressed or flat-lined. In contrast, the HMB-FA/ATP group kept progressing. The HMB-FA/ATP essentially “protected” the athletes from the excessive damage incurred through the overreaching phase, allowing them to do more total work, thus achieving greater results.

Figure 3: Study results



Many have expressed amazement at how much lean body mass the HMB-FA/ATP group was able to put on in 12 weeks (18.7 pounds/8.5 kilograms) compared to placebo (4.6 pounds/2.1 kilograms). These are the kind of gains usually reserved for those on anabolic steroids, and caution is warranted when translating these trial results to individuals. If the overreaching portion of the trial had not occurred, it's very likely these differences would not have been so divergent. Lean body mass, which decreased in placebo group after the overreaching began, would probably have continued to increase. Another factor that could have contributed to the lean mass gains was the incredibly high amount of total

volume of work these participants were doing and the periodized nature of the workouts. The research group conducting this study has used a similar exercise protocol in prior studies, a sample of which [can be viewed here](#). It's also possible that the spectacular results seen were due to a "perfect storm" of factors: well-trained athletes given a periodized program designed to maximize hypertrophy alongside a supplement that helps them recover more quickly from exercise.

However, there were many notable limitations of the study. One potential limitation of the study was the number of calories being consumed by the participants and the ratio of carb, fat, and protein. While counseled weekly by a registered dietitian who specializes in sports nutrition, it is unknown if total calories or macronutrient ratios remained constant throughout the duration of the study. This too could have contributed to the spectacular results seen in the HMB-FA/ATP group. Additionally, while all participants completed the trial, the sample size of 17 is relatively small and limits the generalizability of the results. It is also unknown how well the effects seen in this study would translate to a female population.

This study was [pre-registered at ClinicalTrials.gov](#), which is considered good practice when conducting an RCT as it prevents researcher from going back and altering their primary outcome. Altering your primary outcome after a trial has begun can bias the results. The primary outcome listed for this study was measuring "Increased muscle strength, force, and power after intense weight training" which is actually multiple things. Thus, the problem of multiple comparisons pops up. Ideally, a single clear primary outcome is selected and all other measures are else secondary. However, the effect sizes of the primary endpoints they measured are fairly large, so there's likely something to them. But to confirm these results, the study would need to be replicated with a larger sample size, and with a prespecified clear primary outcome to see if the large effect size would hold up.

For individuals doing moderate to high volumes of exercise, a combination of HMB-FA/ATP seems to be able to protect against fatigue and decrease recovery times. This would allow for the ability to do more total work, which translates into greater muscle adaptations.

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The big picture

The authors conclude that “when faced with greater training frequencies...HMB/ATP may not only prevent typical declines in performance that are characteristic of over-reaching but may also result in additional gains in strength.”

People training consistently at high levels, such as athletes, or untrained individuals beginning an exercise program may benefit the most from the ergogenic effects of HMB-FA/ATP. The ability to train at high intensities as much as possible without sustaining injury is key for attaining optimal performance. During periods of frequent high-intensity resistance training, this supplement combo may reduce recovery times, which can be inferred from the higher perceived recovery status scores seen in the HMB-FA/ATP group along with their significant improvements in muscle adaptations. A [prior review by the ISSN has noted that](#) “HMB appears to be most effective at augmenting gains in lean mass during early stages of training in untrained individuals and at improving strength over longer training periods in trained individuals.” Despite this, it's hard to ignore that the present trial showed almost unbelievably positive results. That isn't to say that the results are definitively false, but the methods (such as the lack of dietary control) may have skewed the results, or there could possibly have been other issues that led to these steroid-like results. Thus, replication of this trial is essential.

A combo of HMB-FA/ATP is likely to be most advantageous for well-trained individuals undertaking high and frequent volumes of training over long periods and novice lifters who are pushing themselves.

Frequently asked questions

Since HMB is just a leucine metabolite, why not just consume foods or supplements high in leucine?

You could increase your intake of foods containing leucine, but only a [very small percentage](#) of leucine is oxidized

into HMB. It's much more efficient to use supplemental HMB to get an effective dose.

If I'm going to supplement with HMB, which is more effective - HMB free acid or calcium HMB?

There has not yet been a direct comparison of HMB-FA to calcium HMB and there is currently not enough research to declare one form “superior” to the other. There is research showing that HMB-FA gets absorbed better and peaks faster in the bloodstream but it is unknown whether supplement timing plays a critical role in the performance enhancing benefits. When supplementing with any form of HMB, note that it may take up to two weeks of regular supplementation for the full effects to kick in.

Are there any side effects I should know about?

Using a dose of up to three grams daily has not demonstrated any negative side effects in those who are already fairly healthy. Higher doses of up to six grams daily are suspected to be safe but this dose has not undergone as much testing. No consistent side effects have been observed at a [three gram a day dose](#).

What should I know?

A combination of HMB-FA and ATP may aid in shortening the recovery window, allowing for more total volume of work to be done and preserving a more linear improvement in muscle strength, power, and hypertrophy in well-trained and untrained individuals starting a rigorous training program.

Bonus - If you want to dive into more about this study, there was a [letter to the editor](#) submitted about this trial and a [response by the authors](#). ♦

This trial was controversial due to the tremendous results. Huge effect sizes don't disqualify a trial though, so we wait with bated breath for the next HMB trial to see if the results can be replicated. Discuss this study at the [ERD Facebook forum](#).