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THE EFFECT OF HMB SUPPLEMENTATION ON MUSCLE RECOVERY AND HYPERTROPHY IN STRENGTH-TRAINED ATHLETES: A LITERATURE REVIEW

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ABSTRACT

Background: Post-exercise recovery and effective stimulation of muscle hypertrophy are essential for high performance in strength and strength-endurance sports. Intensive resistance training causes muscle microdamage, metabolic stress, and inflammation, confirming the importance of recovery for adaptation. β -hydroxy- β -methylbutyrate (HMB), a leucine metabolite, has been studied for its possible anti-catabolic and anabolic potential.

Aim: This review evaluates current evidence on HMB supplementation, focusing on muscle recovery, hypertrophy, supplement forms, and athlete populations, with attention to practical uses and research limitations.

Methodology: A narrative literature review was conducted based on searches in PubMed, Scopus, and Web of Science for studies published between 2015 and 2025. Search terms included “HMB,” “ β -hydroxy- β -methylbutyrate,” “muscle recovery,” “hypertrophy,” “resistance training,” “Ca-HMB,” and “HMB-FA.” Only English-language studies involving human participants and reporting outcomes related to muscle recovery, hypertrophy, or strength were included. Data extracted included participant characteristics, HMB form and dosage, supplementation duration, training protocol, and outcomes such as muscle soreness, strength, and biomarkers of muscle damage. Results were synthesized descriptively, with comparisons based on supplement form, training status, and study quality.

Results and Discussion: HMB is endogenously produced in small amounts and is supplemented exogenously as calcium salt (Ca-HMB) or free acid (HMB-FA). Research suggests that HMB reduces muscle-damage biomarkers, supports membrane stability, modulates protein metabolism, and may enhance satellite cell activity. HMB can accelerate recovery, reduce delayed onset muscle soreness (DOMS), and promote hypertrophy, especially in novice or returning athletes. Effects vary by dosage, supplementation duration, form, and individual training status. Evidence indicates greater benefits in early adaptation phases, during high training loads, or during periods of increased risk of muscle loss.

Conclusions: HMB supplementation appears to be beneficial under specific conditions for supporting muscle recovery and hypertrophy. It may accelerate functional restoration, reduce muscle damage, and support fiber remodeling. Benefits are most pronounced in less-trained athletes, individuals returning from breaks, or during high training loads. Effectiveness depends on supplement form, dosage, and individual physiology. HMB is safe and well-tolerated, though additional research is needed to standardize protocols, compare Ca-HMB and HMB-FA, and assess long-term effects across athlete populations.

KEYWORDS

HMB; β -hydroxy- β -methylbutyrate; Muscle Recovery; Hypertrophy; Resistance Training; Supplementation

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Introduction

Post-exercise recovery and effective stimulation of muscle hypertrophy are essential elements for achieving high performance and long-term progression in strength and strength-endurance sports. Intensive resistance training induces microdamage to muscle fibers, elevates metabolic stress, and triggers inflammatory responses, making proper recovery processes critical for physiological adaptation. Alongside the growing popularity of physical activity and the widespread availability of dietary supplements, increasing attention has been directed toward interventions that may enhance training adaptations and accelerate recovery. [1] Athletes and recreationally active individuals frequently seek compounds capable of modulating protein metabolism, nitrogen balance, and catabolic signaling pathways. [1, 2, 3]

One compound that has attracted considerable scientific interest over the past two decades is β -hydroxy- β -methylbutyrate (HMB), a metabolite of leucine, a key amino acid involved in the initiation of muscle protein synthesis. HMB has been investigated for both its anti-catabolic properties and its aptitude to promote increases in muscle mass and strength. A growing body of evidence suggests that HMB supplementation may reduce biomarkers of muscle damage, such as creatine kinase (CK) and lactate dehydrogenase (LDH), while allowing a faster return to functional capacity following intense exercise. [2, 4, 5, 6, 7] However, findings remain

inconsistent, with outcomes affected by factors such as training status, supplementation protocol, dosage, and the chemical form of HMB administered. [2, 6–8] These differences make HMB both a matter of debate and an important area for further research. [2, 8]

From an applied sports-nutrition perspective, HMB is especially interesting because it is positioned at the intersection of performance nutrition and recovery support. Unlike supplements used mainly for acute ergogenic effects, HMB is typically discussed as a compound that may influence the quality of adaptation across repeated training sessions. This makes it relevant not only for athletes attempting to increase muscle mass, but also for those trying to maintain training quality during phases of intensified loading, congested competition schedules, reduced energy intake, or return-to-training periods after illness, injury, or detraining. [1, 8] In this context, the practical value of HMB does not depend solely on whether it produces large absolute gains in muscle size, but also on whether it can preserve training continuity by reducing the magnitude or duration of exercise-induced impairment.

Another reason HMB remains scientifically relevant is that it addresses a recurring issue in strength-training research: the discrepancy between mechanistic plausibility and measurable performance outcomes. Many nutritional compounds show favorable effects on isolated molecular pathways yet fail to translate into meaningful changes in body composition or strength in well-trained participants. HMB is therefore a useful case study for examining how anabolic signaling, proteolysis, membrane integrity, inflammation, and mitochondrial support interact in the real-world setting of resistance training. A careful review of the literature is needed to determine not only whether HMB works, but also under which circumstances its effects are most likely to be practically significant. [2, 8]

The objective of this review is to provide a detailed evaluation of HMB supplementation on muscle recovery and hypertrophy in strength-trained athletes. This review explores both the biochemical basis of HMB action and the findings from major clinical studies, with particular attention to differences between supplement forms. Applied implications, current research limitations, and future research directions are also discussed.

Description of the State of Knowledge

Characteristics of HMB – Structure, Metabolism, Mechanisms of Action

HMB is an organic compound belonging to the class of short-chain hydroxy acids, formed via metabolic pathways of the essential amino acid leucine. Under physiological conditions, only a small fraction of leucine is converted into HMB through the intermediate α -ketoisocaproate (KIC). [2] This process occurs primarily in the liver, with some conversion in skeletal muscle tissue. Endogenous HMB production is estimated at approximately 0.2–0.4 g/day, insufficient to achieve the effects reported in supplementation studies. [2] Therefore, exogenous HMB supplementation is used, most commonly in the form of calcium salt (Ca-HMB) or free acid (HMB-FA), which differ in absorption kinetics and physiological impact. [2, 8]

Biochemically, HMB exhibits multiple functions related to protein metabolism modulation and muscle tissue integrity. Evidence indicates that HMB can attenuate proteolysis, mainly through inhibition of the ubiquitin–proteasome pathway, one of the key mechanisms responsible for muscle protein degradation under metabolic stress. [2, 8] In addition, HMB appears to contribute to membrane stability, potentially via modulation of cholesterol synthesis within the sarcolemma, a structure particularly vulnerable to mechanical stress during high-intensity exercise. [2, 8] It has also been suggested that HMB may indirectly stimulate muscle protein synthesis through activation of the mammalian target of rapamycin (mTOR) signaling pathway, a central regulator of anabolic processes. Moreover, HMB exhibits anti-inflammatory and antioxidant properties, which may aid in reducing exercise-induced cellular stress, including reductions in pro-inflammatory cytokine levels and reactive oxygen species generated during exercise. [2, 8, 9, 10]

In a randomized double-blind study, 6 weeks of HMB-FA supplementation combined with resistance training significantly decreased markers of oxidative stress (malondialdehyde and protein carbonyls) compared to placebo. [9] Moreover, after a single bout of plyometric exercise, acute HMB-FA ingestion attenuated increases in 8-hydroxy-2'-deoxyguanosine, malondialdehyde, and protein carbonyls at 1 hour post-exercise. [10] Finally, at the cellular level, HMB modulates micro ribonucleic acid (microRNA, miRNA) expression in satellite cells exposed to oxidative stress, upregulating miRNAs linked to antioxidant defense and downregulating those associated with pro-catabolic signaling. [11, 12]

Recent research further suggests that HMB may influence satellite cell activity, supporting muscle fiber repair and growth [11, 12] and may modulate gene expression via miRNAs linked to proliferation and differentiation in satellite cells under stress conditions. [11, 12] These various effects position HMB as a supplement with protective, pro-regenerative, and anabolic potential. In animal models of atrophy, HMB has

been shown to preserve satellite cell viability by activating the protein kinase B (PKB)/mTOR pathway and reducing apoptosis. [13] However, the actual effectiveness of such mechanisms is influenced by individual factors, pointing to the need for well-designed clinical studies.

Mechanistically, HMB should not be interpreted as a direct substitute for high-quality dietary protein or leucine-rich meals, but rather as a compound that may modify the balance between muscle damage and repair. This distinction is important. The magnitude of hypertrophy achieved over time depends on repeated elevations in muscle protein synthesis, sufficient amino acid availability, and consistent mechanical overload. HMB may support this process by lowering protein breakdown or preserving myocellular integrity, thereby improving the net anabolic environment over weeks of training rather than dramatically stimulating synthesis in isolation. [3, 8, 14] In this sense, HMB may be especially useful when recovery is constrained or when catabolic pressure is elevated.

A further issue is the interpretation of molecular findings. Activation of anabolic pathways such as mTOR or PKB after supplementation does not automatically translate into visible increases in muscle cross-sectional area or fat-free mass. The relationship between signaling, protein turnover, and measurable hypertrophy is highly dependent on training history, energy intake, total protein consumption, sleep quality, and the duration of follow-up. For this reason, studies assessing HMB should ideally include not only biochemical markers but also direct outcomes such as changes in lean body mass, ultrasound or measures made using dual-energy X-ray absorptiometry (DXA), maximal strength, and restoration of performance capacity. [8, 14]

It is also worth noting that some recent work has challenged earlier assumptions regarding the superiority of one supplemental form over another. Although HMB-FA has commonly been described as the faster-acting form, newer pharmacokinetic data indicate that the calcium salt may exhibit superior bioavailability under some testing conditions. [15, 16] This does not invalidate the practical rationale for pre-exercise HMB-FA use, but it does highlight that differences between forms may be smaller or more context-dependent than previously assumed. Consequently, mechanistic claims about one form being universally superior should be interpreted with caution until more direct head-to-head trials are available in athletic populations. [8, 14–16]

HMB and Muscle Recovery

Muscle recovery following intense exercise is a multifactorial process involving the repair of damaged fibers, restoration of energy balance, and normalization of metabolic homeostasis. The effects of HMB surpass its anti-catabolic properties and include modulation of immune responses and support of intracellular adaptive functions. Evidence suggests that HMB supplementation may influence inflammatory processes, partly through modulation of macrophage activity, which has an essential role in tissue repair and regeneration. [5, 7]

A meta-analysis of randomized controlled trials demonstrated that HMB supplementation substantially reduces circulating markers of muscle damage, including CK and LDH, with greater effects observed in studies lasting ≥ 6 weeks. [6] In a study using a single 3 g dose of HMB-FA in trained young men, work capacity measured after a damaging exercise protocol returned to baseline 24 hours after exercise, whereas in the placebo group full recovery did not occur even by 72 h. [4] Another trial supplementing 3 g/day of HMB for 2 or 4 weeks in previously untrained participants showed that both HMB groups had significantly better recovery of maximal voluntary contraction torque and smaller increases in muscle stiffness after eccentric exercise, compared to placebo. [17]

Intervention studies suggest that HMB supplementation may reduce delayed onset muscle soreness (DOMS) and accelerate strength recovery after sessions causing substantial microdamage. [4, 5, 17] This may be explained by enhanced membrane resilience and improved lipid homeostasis associated with HMB supplementation, which reduce susceptibility to mechanical stress and support more efficient structural repair. [2, 8] HMB also appears to improve oxidative stress management, supporting the neutralization of free radicals produced during high-intensity exercise, consequently minimizing secondary structural damage. [9, 10] Moreover, systematic review evidence supports that HMB supplementation can attenuate exercise-induced muscle damage and improve recovery by lowering oxidative stress markers and inflammatory signaling. [2, 6, 7]

Additionally, HMB may support mitochondrial function, promoting more efficient energy production and recovery between sets, which can be notably beneficial in high-volume or high-frequency training cycles. [18] In older adults subjected to muscle disuse, supplementation with 3 g/day of HMB attenuated declines in mitochondrial content and altered markers of mitochondrial dynamics during bed rest, supporting its protective role in mitochondrial maintenance. [19] The greatest benefits are often observed in less trained athletes, those

returning from a break, or during periods of increased training load, such as preparation phases or energy deficit conditions. [6–8] Overall, the available evidence indicates that HMB may help attenuate muscle damage and support recovery, particularly under conditions of high training stress.

At the same time, the concept of “recovery” in the HMB literature requires careful interpretation. Some studies define recovery primarily through indirect blood biomarkers such as CK or LDH, whereas others emphasize functional restoration, including torque recovery, work capacity, jump performance, or subjective soreness. These outcomes are related but not interchangeable. CK, for example, varies substantially between individuals and may reflect membrane disruption without accurately capturing an athlete’s readiness to perform again. Therefore, a decrease in CK after HMB supplementation should be considered supportive evidence rather than definitive proof of superior practical recovery. [6, 7] The most convincing findings are those showing parallel improvements in biomarkers and functional outcomes after damaging exercise.

This distinction is highly relevant in strength-trained athletes, whose priorities often extend beyond simple soreness reduction. For an experienced athlete, the key question is whether a supplement allows maintenance of training quality across repeated sessions. If HMB reduces the depth of performance decline after eccentric or high-volume loading, even modestly, it may improve the quality of subsequent sessions and indirectly contribute to long-term adaptation. In contrast, if biomarker changes occur without meaningful effects on force output, training volume, or perceived recovery, then the practical value of supplementation becomes less compelling. Future studies should therefore prioritize integrated recovery models that include biochemical, neuromuscular, and perceptual indices. [6–8]

Another important consideration is training phase. Recovery supplements tend to appear more effective when exercise damage is deliberately amplified, such as during intensified training blocks, novel eccentric protocols, or return-to-training periods. This means that null findings in stable, well-adapted training phases do not necessarily indicate that HMB is ineffective; they may simply show that the athletes were already coping successfully with their workload. From a programming standpoint, HMB may therefore be more appropriately viewed as a context-dependent aid rather than a universally necessary supplement for all resistance-trained individuals year-round. [8]

HMB and Muscle Hypertrophy

Muscle hypertrophy results from an anabolic-catabolic balance favoring protein synthesis and the adaptation of fibers to repeated mechanical load. Some evidence suggests that HMB may contribute to hypertrophic adaptations not only by reducing protein degradation but also by modulating growth-regulating factors. [2, 8] HMB has been shown to influence gene expression patterns associated with satellite cell proliferation and differentiation, as evidenced by global transcriptomic shifts induced by HMB in cultured satellite cells. [11, 12] In addition, HMB modulates miRNAs associated with myogenic regulation under oxidative stress conditions in satellite cells. [11] This may facilitate the formation of new myonuclei, an essential component of sustained hypertrophy.

Controlled studies indicate that HMB can increase fiber cross-sectional area in both type I and type II fibers, particularly during early workout phases when adaptive stimuli are strong. Yet, in a 12-week randomized controlled study in resistance-trained combat athletes taking 3 g/day Ca-HMB, fat-free mass significantly increased while fat mass was significantly reduced, supporting that HMB can induce favorable changes in body composition even in highly trained individuals. [20, 21] It has also been proposed that HMB may augment muscle energetics through improved phosphocreatine utilization and upregulation of mitochondrial enzymes, supporting more effective repeated contractions. [18]

The hypertrophic response to HMB is affected by factors such as nutrient availability, training intensity, and volume. In a 12-week double-blind RCT combining 3 g/day Ca-HMB with daily whey protein, untrained men showed a +14.2% increase in leg fat-free mass compared with +7.0% in the protein-only placebo group. [22] Meta-analyses suggest that supplementation is most beneficial under conditions of increased risk for muscle loss or during initial adaptation to training. [23, 24] Related findings from older-adult populations also suggest that HMB may support lean mass retention, muscle quality, and exercise responsiveness when muscle anabolic sensitivity is compromised, although these observations cannot be directly extrapolated to strength-trained athletes. [25–27] In highly trained athletes, hypertrophic gains may be modest, suggesting a potential threshold beyond which additional HMB provides limited benefits. [23, 24] Nonetheless, HMB remains an interesting adjunct during periods focused on muscle mass gains or during post-detraining recovery.

The apparent discrepancy between positive mechanistic data and mixed hypertrophy outcomes in trained athletes is one of the central controversies in the HMB literature. A plausible explanation is that experienced

lifters already operate near a high adaptive ceiling. Their diets often contain sufficient total protein, their training is periodized, and their neuromuscular efficiency is well developed. Under such circumstances, the incremental value of reducing proteolysis may be relatively small compared with beginners, who experience greater muscle disruption and larger early gains in lean mass when exposed to resistance training for the first time. [22–24]

This ceiling effect should not be confused with a complete lack of efficacy. In trained athletes, a supplement does not necessarily need to produce large absolute increases in muscle mass to be worthwhile. Small improvements in body composition, attenuation of muscle loss during demanding phases, or better preservation of training volume may still be meaningful in sports where weight class, physique, or repeated power output matter. Combat sport athletes, for example, may benefit from subtle improvements in lean mass retention during energy-restricted periods, even if the supplement does not dramatically increase muscle size under neutral energy balance. [21]

Methodological differences also complicate the interpretation of hypertrophy outcomes. Some studies use DXA-derived fat-free mass, whereas others use localized muscle thickness, fiber morphology, or whole-body composition changes. These approaches are not equivalent. Fat-free mass can be influenced by hydration and glycogen fluctuations, while short interventions may be too brief to detect robust morphological growth in well-trained participants. As a result, studies that report non-significant changes in hypertrophy should be evaluated in relation to the sensitivity of the measurement method, the duration of intervention, and the training status of participants before concluding that HMB has no anabolic relevance. [23, 24]

To provide a structured overview of the current evidence, key intervention studies investigating the effects of HMB supplementation on muscle recovery and hypertrophy are summarized in Table 1.

Table 1. Summary of key studies on β -hydroxy- β -methylbutyrate (HMB) supplementation and its effects on muscle recovery and hypertrophy

Author (Year)	Participants	Training Status	HMB Form & Dose	Duration	Study Design	Main Outcomes
Shirato et al. (2016) [5]	n = 18 men	Untrained	Ca-HMB + whey protein	approx. 11 days	Randomized Controlled Trial (RCT)	No significant differences between groups in muscle strength loss, soreness, or muscle damage markers
Durkalec-Michalski et al. (2017) [21]	n = 42 athletes	Highly trained	Ca-HMB, 3 g/day	12 weeks	RCT crossover	↑ fat-free mass, ↓ fat mass, ↑ anaerobic performance, ↑ aerobic capacity
Rahimi et al. (2018) [6]	Multiple studies	Mixed	Various (mostly 3 g/day)	≥ 6 weeks	Meta-analysis	↓ CK, ↓ LDH, time-dependent effect (greater in ≥ 6 weeks); reduced muscle damage markers
Correia et al. (2018) [4]	n = 23 young men	Trained	HMB-FA, 3 g (acute)	Single session	RCT, double-blind	Faster recovery of work capacity (24 h vs >72 h placebo)
Arazi et al. (2018) [9]	n = 16 men	Trained	HMB-FA, 3 g/day	6 weeks	RCT	↓ oxidative stress markers (malondialdehyde [MDA], protein carbonyls) in both groups; no additional effect of HMB-FA vs placebo
Standley et al. (2017) [19]	n = 19 older adults	Inactive	Ca-HMB, 3 g/day	10 days bed rest + 8 weeks rehabilitation	RCT	No major changes in mitochondrial content during bed rest; higher mitochondrial oxidative phosphorylation content and mitochondrial dynamics markers during rehabilitation with HMB
Wilkinson et al. (2018) [14]	n = 8 men	Trained	Ca-HMB, 3 g (acute)	Acute (single dose)	Controlled metabolic study	↑ muscle protein synthesis, ↓ muscle protein breakdown

Author (Year)	Participants	Training Status	HMB Form & Dose	Duration	Study Design	Main Outcomes
Sánchez-Martínez et al. (2018) [23]	Multiple studies	Trained	Various	4–12 weeks	Meta-analysis	No significant effects on strength or body composition
Din et al. (2019) [3]	n = 16 older adults	Untrained	HMB-FA, 3 g/day	6 weeks	RCT	Marginal improvement in muscle mass gains; no significant differences vs placebo
Tsuchiya et al. (2019) [17]	n = 28 men	Untrained	Ca-HMB, 3 g/day	2–4 weeks	RCT	↓ muscle damage symptoms, improved torque recovery
Arazi et al. (2019) [10]	n = 16 men	Trained	HMB-FA, 3 g (acute)	Single session	RCT	↓ oxidative stress post-exercise, ↓ leukocyte response
Gepner et al. (2019) [24]	Review	Mixed	Various	Various	Review	Mixed evidence; possibly greater effects in untrained
Stahn et al. (2020) [22]	n = 16 men	Untrained	Ca-HMB (3 g/day) + whey protein	12 weeks	RCT	↑ leg fat-free mass (+14.2% vs +7.0%)
Durkalec-Michalski et al. (2025) [39]	n = 90 men	Mixed	High-dose HMB	6 weeks	RCT	No significant effects of HMB on body mass or body composition

Comparison of Supplement Forms (Ca-HMB vs. HMB-FA)

In practice, HMB is administered as either calcium salt (Ca-HMB) or free acid (HMB-FA). [8, 14–16] These forms differ in their absorption kinetics and practical applications. [14–16] Ca-HMB shows greater chemical stability and slower peak plasma concentrations, offering sustained availability. [14, 15] HMB-FA achieves higher blood concentrations more rapidly, which may be advantageous before intense exercise. [8, 15]

Emerging evidence suggests HMB-FA may enhance acute metabolic mobilization and post-exercise recovery, [4, 9, 10] whereas Ca-HMB could support long-term anabolic adaptations when taken consistently. [21, 22] Future research needs to clarify the effects of these differences in actual athletic settings, including comparisons in bioavailability, acute versus chronic effects, and interactions with various training plans. [8, 15, 16]

In addition to supplement form, practical outcomes may also depend on supplementation timing, dosage strategy, and the broader nutritional context. Available evidence suggests that HMB-FA may be more suitable for acute pre-exercise use because of its faster appearance in circulation, whereas Ca-HMB may be more applicable in chronic supplementation protocols. [8, 15] However, the extent to which higher doses provide additional benefits remains unclear, and dose-response relationships are still insufficiently characterized across athletic populations. [8] It also remains unclear whether HMB efficacy depends on body mass, habitual protein intake, or the intake of leucine-rich protein sources, which may partly overlap with HMB-related anabolic signaling. [8, 24]

The practical distinction between Ca-HMB and HMB-FA should therefore be framed less as “which form is better?” and more as “which form is more appropriate for a specific goal?” If the aim is to maintain chronically elevated exposure during a multi-week training block, Ca-HMB may be entirely sufficient. If the goal is to target an acute pre-exercise window surrounding a particularly damaging session, HMB-FA may offer theoretical advantages because of its faster appearance in plasma. Yet this pharmacokinetic logic still requires stronger translation into repeated demonstrations of superior training outcomes. [14–16]

A second unresolved issue is whether form-specific differences matter once the athlete’s overall nutritional plan is optimized. Athletes consuming high daily protein intakes, distributing protein effectively across the day, and training under well-structured recovery conditions may derive only marginal added value from precise HMB timing. Conversely, athletes under travel stress, competition congestion, or suboptimal dietary conditions may be more sensitive to such timing strategies. For this reason, recommendations about HMB form should be individualized and embedded within the wider nutritional context rather than made in isolation. [8, 24]

HMB in Different Athlete Populations

The effects of HMB appear to extend across multiple athletic disciplines. [8, 24] Strength athletes may benefit most during phases of high-intensity training, where volume and frequency increase the risk of overload. [24] Endurance athletes may use HMB to preserve lean mass during prolonged training or competition phases, especially under high metabolic stress. [28, 29] Mixed-sport athletes, such as team sport players, may find HMB useful for limiting cumulative fatigue and enhancing repeat-effort performance. [24, 30]

Novice athletes or those returning from injury may experience more pronounced benefits due to higher susceptibility to microdamage and faster adaptation to training stimuli. [8, 31] Tailoring HMB use to sport-specific demands, training load, and seasonal context is fundamental, demonstrating the need for comparative research across athlete populations. [8, 28, 30]

For strength-trained athletes specifically, the most realistic application may not be continuous year-round supplementation, but strategic use during phases of elevated recovery demand. These include pre-season hypertrophy blocks, return-to-training after deload or injury, cutting phases with reduced caloric intake, and concentrated periods of eccentric overload. In these situations, the anti-catabolic and recovery-supporting properties of HMB may be more relevant than in a stable maintenance phase with moderate training stress. Such an approach is also more economically rational, as it reserves supplementation for periods when the probability of benefit is highest. [8, 24]

Safety, Side Effects, and Interactions

HMB is generally considered safe when taken at recommended doses of approximately 3 g/day. [2, 8, 32, 33] Toxicological studies report no significant changes in liver, kidney, or hematological parameters over several months of supplementation. [2, 32, 33] Mild gastrointestinal discomfort, such as bloating, may occasionally occur but typically resolves with dose adjustment or taking the supplement with food. [32]

Current evidence suggests minimal interaction with common sports supplements, including creatine, branched-chain amino acids (BCAAs), and beta-alanine. [31, 34] However, the effects of HMB combined with medications that influence protein metabolism or immune function remain insufficiently studied. [32, 35] Quality control of commercial products is important, as contaminants or incorrect dosages can affect safety. [31, 36] HMB is considered low-risk, though long-term studies in elite athletes and populations with comorbidities are warranted. [8, 32–34]

Safety should nevertheless be interpreted within the broader framework of responsible supplementation. A favorable safety profile does not mean that HMB is automatically necessary or effective for every athlete. Supplements can only complement, not replace, fundamental determinants of adaptation such as adequate total energy intake, sufficient daily protein, progressive training, sleep, and recovery management. In practice, HMB should be considered an adjunct with a relatively low risk profile and a moderate, context-dependent probability of benefit rather than a foundational intervention. [1, 8, 32]

Future Research Directions and Controversies

Despite a substantial body of research, several aspects of HMB supplementation remain unresolved. [8, 37] A key point of debate concerns differences in observed effects based on training status – beginners and returning athletes often experience greater benefits than highly trained individuals, although the underlying mechanisms are not fully understood. [2, 8, 23, 24] Additional investigation is needed regarding dosage, supplementation duration, and interactions with nutritional strategies, including macronutrient manipulation and caloric deficits. [37, 38]

Standardized research protocols are also necessary for comparing markers of muscle damage, hypertrophy assessments, and performance measures. [39, 40] Comparative studies of Ca-HMB and HMB-FA in real training scenarios, considering both bioavailability and practical implementation, are required. [8, 15, 16] Additionally, genetic differences, such as leucine metabolism or anabolic signaling sensitivity, may influence individual responses to HMB, pointing to the possibility of personalized supplementation strategies. [38]

Interpretation of current data is also contested: some meta-analyses indicate moderate benefits, while individual studies report non-significant effects. [23, 37, 39, 41] Importantly, inconsistencies across studies may also reflect differences in study design, participant characteristics, and training protocols, which complicate direct comparisons. Active research should integrate molecular mechanisms, structured training interventions, and precise physiological monitoring to clarify the conditions under which HMB provides meaningful performance and recovery advantages. [37, 39, 40]

One major limitation of the field is the frequent mismatch between mechanistic precision and ecological validity. Laboratory studies may tightly control supplementation and exercise damage, but they often use short interventions, small sample sizes, or participants whose training background does not reflect elite or advanced resistance-trained populations. Conversely, applied studies in athletes may capture real-world practice better but sometimes lack direct mechanistic measures. Bridging this gap will require trial designs that combine robust body-composition assessment, standardized resistance-training programs, dietary control, and repeated measures of performance recovery across realistic training cycles. [37, 39, 40]

Another issue concerns outcome prioritization. For some athletes, especially bodybuilders or weight-category competitors, preserving lean mass during energy deficit may be more relevant than maximizing hypertrophy during caloric maintenance or surplus. For others, restoring force output between sessions may be the most important endpoint. Future HMB studies should therefore predefine whether they are primarily targeting recovery, muscle retention, muscle gain, or performance maintenance, because these outcomes may not respond equally to supplementation. Greater conceptual clarity in defining the intended benefit of HMB would substantially improve interpretation of the literature. [37, 41]

Finally, future work should pay closer attention to interaction effects. HMB is rarely used in isolation in athletic settings; it is usually combined with protein supplementation, creatine, periodized resistance training, and sport-specific workloads. Understanding whether HMB provides additive, redundant, or only situational effects alongside these established strategies is essential for evidence-based recommendations. This is particularly important in advanced athletes, where the marginal value of any single supplement is likely to be small and must be justified against cost, practicality, and the already strong influence of total training and nutritional quality. [8, 22, 34, 42]

Beyond the athletic setting, translational work in clinical and rehabilitation models may also help clarify the boundaries of HMB efficacy. Evidence from anabolic support strategies in catabolic or immobilized states suggests that HMB may be particularly relevant when muscle loss risk is high, which strengthens the hypothesis that its effects are condition-dependent rather than universal. [13, 19, 34, 43] At the same time, future sport-specific studies should use validated methods for assessing muscle protein synthesis and remodeling so that mechanistic conclusions are not overstated relative to the quality of the measurement strategy. [14, 44]

Conclusions

HMB supplementation is a promising strategy for improving exercise adaptation, both during muscle recovery and hypertrophy. Evidence suggests HMB may accelerate return to full function after intense exercise, reduce muscle damage, and support satellite cell activity for fiber remodeling. Benefits appear most significant in novice athletes, individuals returning from breaks, and during periods of high training load. From a practical perspective, HMB supplementation may be particularly useful during periods of intensified training, caloric restriction, or return-to-training phases.

Effectiveness depends on supplement form, dosage, and individual physiology, with outcomes in highly trained athletes remaining less conclusive. HMB has a favorable safety profile and high tolerability, making it a viable addition to supplementation strategies. Nevertheless, additional research is required to standardize training protocols, compare Ca-HMB and HMB-FA, and assess long-term effects in various sports populations.

Overall, current evidence does not support viewing HMB as a universally effective hypertrophy supplement. Instead, its effects appear to depend strongly on context. Overall, the current literature suggests that HMB should not be regarded as a universally transformative hypertrophy supplement, but rather as a targeted nutritional tool whose value depends strongly on context. Its most defensible role appears to be in attenuating muscle damage, supporting recovery, and helping preserve or facilitate adaptation when training stress is unusually high or when the athlete is vulnerable to catabolic pressure. In well-trained strength athletes under stable and well-supported conditions, the expected effects on hypertrophy are likely modest, but in strategically chosen phases of training the supplement may still offer meaningful support. Therefore, HMB can be a valuable instrument for improving regenerative and anabolic processes, provided that its use is adjusted to individual needs, training status, and program specificity.

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