



Revisión

# Usefulness of $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) supplementation in different sports: an update and practical implications

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## Abstract

**Introduction:** although  $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) is generally marketed as a supplement for increasing muscle mass and strength, it is still not fully understood how and in which particular sports and conditions HMB can be more effective.

**Aims:** the primary purpose of this review is to update and summarize the current knowledge about the usefulness of HMB and to organize this information by different sports with specific reference to sports with high wear and tear phenomena as soccer, rugby or football.

**Methods:** a search was performed in PubMed database. This review presents the results about HMB use in sport.

**Results:** the articles identified in this review support the notion that HMB could help to attenuate tissue catabolism and initiate muscle anabolism particularly in untrained individuals exposed to strenuous exercise or when trained individual are exposed to periods of high physical stress. HMB could therefore be applied in some specific periods of athlete's season where there are high-intensity training periods, high density of competitions and little recovery time between them, starting recovery phases from an injury period and/or any other different situation where performance or recovery could be affected by a great catabolic environment.

**Conclusion:** this update contributes to clarify and define possible mechanisms and/or effectiveness of HMB supplementation related to endurance sports (i.e. cycling and athletics), strength-power sports (i.e. resistance training, football, rugby, soccer, judo, waterpolo and rowing) and recreational activities.

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Key words: HMB. Recovery. DOMS. Signalling-molecule. mTOR.

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## EFICACIA DE LA SUPLEMENTACIÓN CON $\beta$ -HYDROXY- $\beta$ -METHYLBUTYRATE (HMB) EN EL DEPORTE: ACTUALIZACIÓN E IMPLICACIÓN PRÁCTICA

### Resumen

**Introducción:** aunque el  $\beta$ -hidroxi- $\beta$ -metilbutirato (HMB) se ha empleado generalmente como suplemento para aumentar la masa muscular y la fuerza, es necesario un mejor entendimiento de su función y averiguar en qué deportes es más efectivo.

**Objetivos:** el objetivo principal de esta revisión es actualizar y resumir el conocimiento existente en torno a la utilización del HMB para clasificarla en función de cada modalidad deportiva, con especial mención a aquellas actividades con un alto grado de destrucción muscular, como pueden ser el fútbol, el rugby o el fútbol americano.

**Métodos:** se utilizó la base de datos PubMed para la búsqueda de artículos. Esta revisión presenta los resultados sobre la utilización de HMB clasificados por deportes.

**Resultados:** la mayoría de los artículos seleccionados sugieren que cuando una persona entrenada o no entrenada se somete a un ejercicio intenso o diferente al habitual, el HMB puede atenuar el catabolismo muscular producido e iniciar los procesos anabólicos necesarios para recuperar lo antes posible. De esta forma, el HMB podría aplicarse en algunos momentos concretos de la temporada deportiva en los que hubiera períodos con entrenamientos de alta intensidad, o durante un periodo con alta densidad competitiva y con poca recuperación entre competiciones, o bien durante las primeras fases de la readaptación física después de una lesión y/o durante cualquier otra situación en la que el rendimiento o la recuperación se pueden ver afectados por un entorno altamente catabólico.

**Conclusión:** esta revisión pretende aclarar y definir los posibles mecanismos por los que la suplementación con HMB puede ser efectiva en deportes de resistencia (ciclismo y carreras de fondo), en deportes de fuerza-potencia (fútbol, yudo, waterpolo, remo, fútbol americano y musculación) y en actividades deportivas recreacionales.

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Palabras clave: HMB. Recuperación. DOMS. Molécula de señalización. mTOR.

## Abbreviations

3-MH: 3-methylhistidine.  
AMPK: Adenosine monophosphate protein kinase.  
BCAAs: Branched chain amino acids.  
Ca-HMB:  $\beta$ -hydroxy- $\beta$ -methylbutyrate Calcium Salt.  
CD: Cool Down.  
CK: Creatine Kinase.  
Cr: Creatine.  
CHO: Carbohydrate.  
CRP: C-reactive protein.  
CWI: Cold Water Immersion.  
DOMS: Delayed onset muscle soreness.  
F: Female.  
FM: Fat Mass.  
FML: Fat Mass Lost.  
FFM: Fat Free Mass.  
GH: Growth hormone.  
H: Hamstring.  
HMB:  $\beta$ -hydroxy- $\beta$ -methylbutyrate.  
HMB-FA:  $\beta$ -hydroxy- $\beta$ -methylbutyrate-Free Acid.  
HMG-CoA:  $\beta$ -hydroxy-methylglutaryl-CoA.  
IGF-1: Insulin-like growth factor.  
KIC: Ketoisocaproic Acid.  
LBM: Lean Body Mass.  
LDH: Lactate Dehydrogenase.  
M: Male.  
MAPK/ERK: Mitogen activated protein kinase / extracellular signal regulated kinase.  
MAS: Running speed during an incremental test at which  $\text{VO}_2\text{max}$ . is attained.  
MCV: Maximal Voluntary Contraction.  
N: No.  
NE: No Effect.  
NR: Not Reported.  
Q: Quadriceps.  
OBLA: Onset of Blood Lactate Accumulation.  
PI3K/Akt: Phosphoinositide 3-kinase / Protein kinase B.  
PRS: Perceived Recovery Scale.  
RCP: Respiratory Compensation Point.  
Sirt1: Silent information regulation transcripts.  
Tac: Tactical exercises.  
Tec: Technical exercises.  
TNF $\alpha$ : Tumor Necrosis Factor Alpha.  
TNFR1: Tumor Necrosis Factor Receptor 1.  
V: Velocity.  
 $\text{VO}_2\text{peak}$ : Peak oxygen consumption.  
VT: Ventilatory Threshold.  
WU: Warm-Up.  
Y: Yes.

## Introduction

Limiting the wear and tear process while exercising and adequate recovery afterwards is fundamental for preserving athletes' health and their optimal performance. The two key components of recovery are rest

and supply of adequate nutrients. Essential nutrients are particularly important. The branched chain amino acids (BCAAs) leucine, isoleucine and valine have been widely studied in this context<sup>1</sup>. Leucine has important roles in protein metabolism<sup>2-4</sup>, glucose homeostasis<sup>5</sup>, insulin action<sup>6</sup>. Leucine has anti-catabolic properties<sup>7</sup> and facilitates recovery from exercise<sup>8,9</sup>. In 1996, it was suggested that a plausible candidate responsible for these effects could be its intracellular derived metabolite  $\beta$ -hydroxy- $\beta$ -methylbutyrate widely known as HMB<sup>10</sup>, which is endogenously produced in animals and humans<sup>11</sup>. The first step in HMB production is the reversible transamination of leucine to  $\alpha$ -ketoisocaproate (KIC) by the enzyme branched chain amino acid transferase<sup>12</sup>. Then, KIC is either metabolized into isovaleryl-CoA in the mitochondria, by the enzyme  $\alpha$ -ketoacid dehydrogenase, or into HMB in the cytosol, by the enzyme alpha-ketoisocaproate dioxygenase<sup>12</sup>. KIC is mainly metabolized into isovaleryl-CoA, with only some 5% of leucine being converted into HMB. Isovaleryl-CoA is further metabolized to beta-methyl crotonyl-CoA and then to beta-methyl gluconyl-CoA and  $\beta$ -hydroxy-methylglutaryl-CoA (HMG-CoA). Similarly, HMB can also be converted to beta-hydroxy-methylbutyrate-CoA and then to HMG-CoA. HMG-CoA is a precursor in cholesterol synthesis or alternatively can be degraded to Acetoacetyl-CoA, acetyl CoA and acetoacetate, a ketone body.

Consequently, as precursor of cholesterol it may have structural functions by its incorporation to cell membranes and through acetyl CoA or ketone body may serve as an energy substrate.

Empirically, HMB has been classically proposed and is widely used as a nutritional supplement to limit muscle damage during exercise and to increase muscle gain after strenuous exercise or hard training. The effectiveness of HMB supplementation needs further clarification into how to optimize its administration (dosage and timing) and better specify in which particular conditions its use is recommended and effective. A dose of 3g/day of HMB produces better results on performance markers and has potential health benefits. Since HMB is a metabolite of leucine, the question is why not simply taking proteins, BCAA or leucine instead of its metabolite. To put this into perspective, a subject would need to consume over 600 g of high quality protein to obtain the amount of leucine (60 grams) necessary to produce the typical 3 g daily dosage of HMB used in human studies<sup>13</sup>. Since consumption of this amount of protein is not realistic and perhaps not even healthy either, HMB is typically administered via dietary supplementation<sup>14</sup>.

In athletic context, a number of studies during the last 15 years have indicated that HMB supplementation may elicit several ergogenic benefits, including better recovery<sup>15,16</sup>, increased strength<sup>17-19</sup>, increased lean body mass (LBM)<sup>20</sup>, decreased body fat<sup>3</sup>, increased power<sup>21,22</sup> and improvements in aerobic<sup>23,24</sup> and

anaerobic<sup>25</sup> performance. Moreover, HMB supplementation has been used as a potential strategy in the treatment of patients with muscular atrophy, cachexia<sup>26,27</sup> and sarcopenia<sup>28,29</sup>. While the above mentioned studies supported the efficacy of HMB, other studies do not<sup>30,31</sup>. Part of these discrepancies can be explained by differences in the length of the study, type of training and differences in the participants' previous level of training<sup>13</sup>.

In the present review we focus on the usefulness of HMB in athletic population and special care is taken to assess various influencing variables including exercise modality and type of sport, training loads, training experience, age, and several dependent measures such as markers of muscle damage, strength, and delayed onset muscle soreness (DOMS) in an attempt to explain possible reasons for the reported conflicting results.

Taking into account the studies mentioned above, a primary aim of this review is to update and summarize the current knowledge on the use of HMB and to organize this information by different sports. The output of this review will then have practical implications for sport coaches, nutritionists and/or physicians who want to know the current evidence about the efficacy of HMB in their specific sport discipline.

### Previous reviews on this topic and what this review adds

Existing scientific literature explains the suggested mechanisms of action of HMB. Based on the studies that assessed the mechanisms of action of HMB<sup>32,33,12,34-36</sup>, it is postulated that such supplementation could involve the following mechanisms: 1) increased protein synthesis via mTOR pathway; 2) inhibition of protein degradation via proteasome and decreasing cell apoptosis, leading to a prolonged cell survival; 3) enhancement of sarcolemma integrity via higher availability of cytosolic cholesterol; 4) increased proliferation, differentiation and fusion of satellite muscle cells via the mitogen activated protein kinase/extracellular signal regulated kinase (MAPK/ERK) and phosphoinositide 3-kinase/serine-threonine protein kinase (PI3K/Akt) pathways and enhanced IGF-1 transcription; and, 5) modulation of the autophagic-lysosomal system. The first mechanism underlying the effects of HMB supplementation is the stimulation of the mTOR signalling pathway that enhance the biochemical mechanisms necessary for protein synthesis, leading to increases in strength and fat free mass<sup>37</sup>. Synergy generated by second and fifth mechanisms implies inhibition of the ubiquitin-proteasome system that is involved in skeletal muscle atrophy<sup>12,38</sup> and modulation of the autophagic-lysosomal system<sup>36</sup>, respectively. These actions could explain the positive effects of HMB supplementation in the rate of repair of muscle da-

mage, restoration of muscle functionality, attenuation of the loss in lean mass and shrinkage recovery of the fiber. The third mechanism of action is related to the protective effect of HMB against contractile activity-induced damage that is associated with increased stability of muscle plasma membrane<sup>39</sup>. This effect is the result of several biochemical chain reactions in which  $\beta$ -hydroxy- $\beta$ -methylglutaryl-CoA (HMG-CoA) is synthased in mitochondria and HMG-CoA reductase is inhibited, playing an important role in increasing metabolic efficiency, stimulating lipolysis in adipose tissue and increasing fatty acid oxidation capacity of skeletal muscle<sup>40</sup>. The fourth proposed mechanism is, on one side, the increased expression of insulin-like growth factor 1 (IGF-1) and growth hormone (GH) that could stimulate the mTOR signalling pathway<sup>17,41,42</sup>. On the other hand, the increased proliferation, differentiation and fusion of satellite muscle cells to possibly enhance mitochondrial biogenesis and fat oxidation. This effect could allow to increase metabolic efficiency<sup>43</sup> through improving adenosine monophosphate kinase as sensor of energy balance<sup>44</sup>, Sirt1 (Silent information regulator transcripts) and Sirt3 activity<sup>45</sup> in 3T3-L1 adipocytes and skeletal muscle cells<sup>46</sup>. Summarizing, all these proteins could act improving mitochondrial biogenesis, energy metabolism and the reactive oxygen defense system<sup>44,45</sup>. Exactly how HMB induces changes in Sirt proteins, adenosine monophosphate kinase (AMPK), and mitochondria remains unclear. However, these results could have implications for obesity, insulin resistance, and diabetes, as well as for athletic performance.

When comparing studies, special care should be taken in relation to critical details of each study such as training status, exercise variability, dose, duration of the intervention, magnitude and nature of the effects, overtraining and/or training stimulus. This will help to explain possible reasons for conflicting results and develop well defined training conditions that would help to establish a correct meta-analytical model<sup>13,18</sup>.

The present review has summarized the existing information to this date (April 2015) and classified it into 3 tables (tables I to III), grouping different sport disciplines with specific physiological demands. This approach will contribute to clarify and define possible mechanisms, interactions and/or effectiveness of HMB supplementation (see figure 1 for a summary of the proposed mechanisms) in combination with aerobic, anaerobic, strength and power activities that characterize each sport in order to provide a more practical guide for coaches, nutritionists and/or sport physicians.

We hypothesize that HMB could act as signalling molecule indicating the need of ending catabolic reactions and subsequent activation of anabolic reactions. It is known that an increase in some specific catabolic conditions<sup>16,28,47,48</sup> may promote HMB positive effects on recovery and/or performance<sup>22,49</sup>.



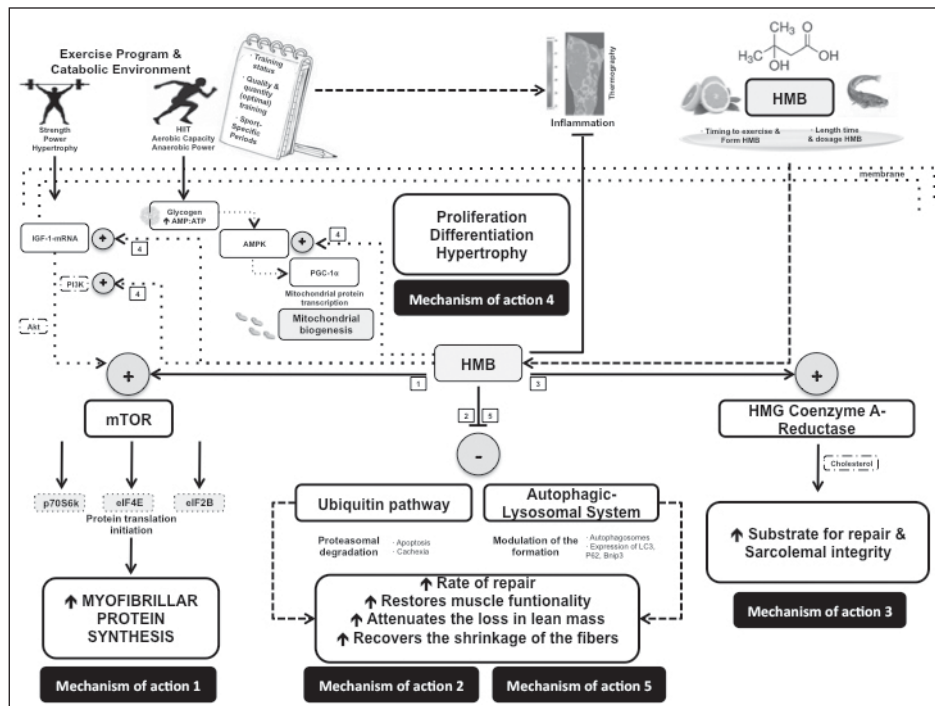


Fig. 1.—Hypothesized metabolism for  $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) with special focus on sports. “+”: promotion; “-”: inhibition. Modified from Hawley et al.<sup>87</sup>

## Practical implications and use of HMB in specific sports

The scientific literature on the effects of HMB on different physiological components evidences that it is population specific and that it depends on the subjects' physical training status, age, and health status (see figure 2 for a summary of HMB reviews in athletic context). The data show that HMB supplementation could assist in increasing strength and decreasing body fat in untrained healthy individuals<sup>50</sup> as well as in elderly individuals<sup>24,51,52</sup>.

Several studies have failed to find statistically significant changes in strength and body composition among those subjects who were already on a physical training regimen<sup>13,19,52</sup>. The lack of significant changes in such articles has been related to the lack of adequate exercise stimulus<sup>14</sup>. When high exercise intensity (>80% 1 repetition maximum [1RM]) or progressive loading periodization programs are used in trained individuals, HMB supplementation has shown similar results to untrained or recreational populations<sup>14,53</sup>. This information is presented in table I. Furthermore, new evidence has shown that HMB supplementation could increase strength, hypertrophy, and power after a 12-week periodized program<sup>53</sup>. Therefore, HMB seems to be more effective during periods of enhanced proteolysis<sup>14</sup>.

Consequently, HMB, at the recommended dose, appears to interact with the training protocol utilized as well as with the experience of the athlete. It is likely that HMB will work ideally if consumed at a dosage of 3g/day for 2 weeks prior a high intensity bout of

HMB Reviews	
Nissen & Abumrad 1997	Nutritional role of the leucine metabolite HMB
Kreider 1999	Dietary Supplementation and the promotion of muscle growth with resistance exercise
Slater & Jenkins 2000	HMB supplementation and the promotion of muscle growth and strength
Slater 2001	HMB as an ergogenic aid in sport
Alon et al. 2002	Supplementing with HMB to build and maintain muscle mass: a review
Nissen & Sharp 2003	Effect of dietary supplements on lean mass and strength gains with resistance exercise: a meta-analysis
Palisin & Stacy 2005	HMB and its use in athletics
Routhier & Stacy 2007	HMB use and its relationship to exercise-induced muscle damage and performance during exercise
Wilson et al. 2008	Effects of beta-hydroxy-beta-methylbutyrate (HMB) on exercise performance and body composition across varying levels of age, sex, and training experience: A review
Rowlands & Thomson 2009	Effects of $\beta$ -hydroxy- $\beta$ -methylbutyrate supplementation during resistance training on strength, body composition, and muscle damage in trained and untrained young men: a meta-analysis
Portal et al. 2010	Effects of body composition, fitness, hormonal profile and muscle damage indices
Zanchi et al. 2011	HMB supplementation: clinical and athletic performance-related effects and mechanisms of action
Fitschen et al. 2013	Efficacy of HMB supplementation in elderly and clinical populations
Molfinio et al. 2013	Beta-hydroxy-beta-methylbutyrate (HMB) Supplementation in health and disease: a systematic review of randomized trials
Ortiz 2013	HMB supplementation in special population
Pinheiro et al. 2013	An Overview on Beta-hydroxy-beta-methylbutyrate (HMB) Supplementation in Skeletal Muscle Function and Sports Performance (Book's chapter)
Manjarrez et al. 2015	$\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) as a dietary supplement (I): metabolism and toxicity $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) as a dietary supplement (II): cell and molecular mechanism of action

Fig. 2.—Reviews on HMB supplementation in physiology biomarkers and sport performance.

**Table 1**

*Studies examining the effect of HMB on performance in recreational sport practitioners*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
Gallagher et al. <sup>65</sup>	USA	NR	37M	Placebo, 38 or 76 mg/kg	CaHMB	Untrained	Greater LBM No effect on FML (independent dose)	CK, no effect on lipid profile, immune system or renal function	Greater isokinetic and isometric torque (independent of dose)	Isometric and Isokinetic testing protocol	8 weeks	Progressive resistance training	Y
Panton et al. <sup>66</sup>	USA	20-40	39M 36F	3 g/day or Placebo	CaHMB	Trained and Untrained	Decreased in Body Fat %	Decreased CK	Greater increase upper body strength	3 days/week 11 exercises 3x3-6 reps 90% 1RM	4 weeks	Weight training	Y
Wilson et al. <sup>67</sup>	USA	23±2	16M	3 g/day or Placebo	HMB	Untrained	NE	Decreased LDH (before exercise)	NE	3xMVC H&Q 55 Maximal Eccentric unilateral knee extension/flexion	Acute (1 day)	Strength Test	Y
Muller <sup>68</sup>	South Africa	19-24	40M	3g/day or Placebo	HMB	Trained	Decreased Total Body Mass Increased LBM	Decreased CK	Increased power output	1h Upper Body Exercises and Lower Body Exercises 3 times/week	8 weeks	Resistance training	Y
Nunan et al. <sup>69</sup>	Great Britain	30±5.5	14M	3 g/day HMB and KIC or Placebo	HMB and KIC	HMB and Recreational	NR	Decreased CK Decreased DOMS	Rapid Recovery Isometric Function and Isokinetic torque 60deg:s-1	Downhill running protocol	14 days	Downhill Running Protocol	Y
Faramarzi et al. <sup>70</sup>	Iran	NR	24M	3g/day or Placebo	HMB	Untrained	Increased LBM Decreased Body Fat	Decreased blood urea nitrogen in urine	Improved strength 1RM	NR	8 weeks	Resistance training	Y
Xing <sup>71</sup>	USA	24,3±2,2	17M 16F	3g/day HMB-FA and 3g/day Ca-HMB or Placebo	HMB-FA and Ca-HMB	Untrained	NE	NE	NE	Single bout eccentric exercise	4 days	Eccentric protocol	N

Abbreviations used in the table. HMB:  $\beta$ -hydroxy- $\beta$ -methylbutyrate; HMB-FA:  $\beta$ -hydroxy- $\beta$ -methylbutyrate-Free Acid; Ca-HMB:  $\beta$ -hydroxy- $\beta$ -methylbutyrate Calcium Salt; NR: Not Reported; OBLA: Onset of Blood Lactate Accumulation; RCP: Respiratory Compensation Point; NE: No Effect; LDH: Lactate Dehydrogenase; CK: Creatine Kinase; TNFa: Tumor Necrosis Factor Alpha; TNFR1: Tumor Necrosis Factor Receptor 1; CRP: C-reactive protein; 3-MH: 3-methylhistidine; VT: Ventilatory Threshold; LBM: Lean Body Mass; FFM: Fat Free Mass; FML: Fat Mass Lost; FM: Fat Mass; Cr: Creatine; PRS: Perceived Recovery Scale; KIC: Ketosiscaproic Acid; CHO: Carbohydrate; CWI: Cold Water Immersion; M: Male; F: Female; Y: Yes; N: No; MAS: Running speed during an incremental test at which VO<sub>2</sub>max. is attained; MCV: Maximal Voluntary Contraction; H: Hamstring; Q: Quadriceps; WU: Warm-Up; Tec: Technical exercises; CD: Cool Down; V: Velocity.

exercise able to induce muscle damage<sup>49</sup>. Supplements should be taken at a dose of 1-2 g, 30-60 minutes prior to exercise if consuming HMB-FA and 60-120 minutes prior to exercise if consuming HMB-Ca. Many of the earlier studies used HMB formulated as a calcium salt (HMB-Ca); however, a new free acid form of HMB (HMB-FA) has been shown to yield higher plasma concentrations in shorter amount of time compared to the calcium salt form<sup>54</sup>. These results offer the theoretical advantages of achieving a greater bioavailability of HMB and providing potential benefits to improve training adaptations<sup>54,55</sup>.

### Effects of HMB in Endurance Sports

Cardiorespiratory endurance refers to the ability of performing activity for prolonged periods of time<sup>56</sup>. Previous studies have demonstrated the potential benefits of HMB for aerobic athletes. This information is shown in table II. Vukovich and Dreifort<sup>24</sup> investigated the effects of HMB supplementation on peak oxygen consumption ( $VO_{2peak}$ ) and the onset of blood lactate accumulation (OBLA) in eight endurance-trained master-level competitive cyclist with an average training volume of 300 miles per week. Participants performed a graded cycle ergometer test until exhaustion. Results from the graded exercise test indicated that HMB supplementation increased by 8% the time to reach ( $VO_{2peak}$ ) while leucine and the placebo did not have any effect. The  $VO_{2peak}$  at 2 mM blood lactate (OBLA) increased with HMB (9.1%) and leucine (2.1%) supplementation, but did not change with placebo supplementation. The discrepancy with other endurance training studies<sup>23,24</sup> could be due to training experience of the participants in the investigation. It has been suggested that active men and women not used to high intensity interval training may benefit more from HMB-Ca supplementation than trained athletes who are used to high intensity interval training<sup>57</sup>. Individualized high intensity interval training (HIIT) programs were applied based on each participant's baseline fitness level and monitored throughout the 28 days of training. It should be taken into account that the training stimulus to stimulate physiological adaptation<sup>12,13,16</sup> can be insufficient in some studies<sup>15,24</sup>.

The results obtained from high intensity interval training studies<sup>23</sup> shows that a four-week HIIT program in combination with HMB-FA is an effective training stimulus for improving aerobic performance. In addition, the use of HMB-FA supplementation, in combination with HIIT, resulted in greater changes in  $VO_{2peak}$ , power output at ventilatory threshold (PVT) and ventilatory threshold (VT) than HIIT alone. These results are in accordance with other studies that used HMB supplementation with aerobic training methods for augmenting the beneficial effects on aerobic performance by increasing fatigue thresh-

old measures that reflect the physiological response to moderate and/or severe intensity exercise<sup>23,24,57</sup>.

The mechanism for these benefits of HMB on aerobic performance and fat loss are poorly understood. However, recent evidence demonstrated that HMB supplementation could improve fatty acid oxidation as has been previously described in HMB's mechanisms of action<sup>46</sup>.

### Effects of HMB on Strength and Power Sports

Strength and power are two of the most critical attributes of success in sport<sup>58,59</sup>. Strength training increases muscle fiber size and maximal tension output. These adaptations are attained by positive muscle protein balance and satellite cell addition to pre-existing fibers<sup>60</sup>. Also, the activation of mTOR signalling pathway appears to be very important for contraction induced increases in muscle protein synthesis<sup>14,61</sup>.

Several research groups in this area<sup>19,52,62</sup> reported conflicting results when men and women were supplemented with HMB during a resistance training programme. Among the outcome variables analyzed in these studies were 1RM bench press, 1RM deadlifts, 1RM rowing, 1RM shoulder press, 1 RM chin up, 1RM leg extension, 1RM squats, and 1RM biceps curl. In addition, other physiological variables, such as body composition, power production, creatine kinase levels, and lactate dehydrogenase, were also evaluated. This information is presented in table III together with studies that showed strength and power benefits in sport-specific movements, i.e. squat, bench press and vertical jump<sup>10,19,21,22</sup>. In contrast, researchers have found small treatment effect when using non-specific, isolated movements<sup>19,62</sup>. Furthermore, as previously mentioned, the lack of significant changes in performance could be attributed to the absence of periodized and progressive exercise programs. Finally, benefits of HMB supplementation are more marked when exercise involves multi-joint movement that stresses a greater total amount of the skeletal muscle system.

The results of several studies<sup>22,63</sup> suggest that changes in strength and power following HMB supplementation are optimized within a context of a periodized as compared to a non periodized training program<sup>19</sup>. Furthermore, those findings suggest that supplementation with  $\beta$ -hydroxy- $\beta$ -methylbutyrate plus Adenosine Triphosphate (HMB/ATP) in combination with a high intensity undulating periodization-training model results in increases in LBM, muscle hypertrophy, strength and power. Translated into athletes and coaches' languages, this means that when facing periods of high training frequencies (overreaching cycle of training) HMB and/or HMB/ATP supplementation may not only prevent typical declines in performance (power, strength and perceived recovery) that are characteristic of overreaching but might also results in additional gains in strength<sup>22</sup>.

**Table II**  
*Studies examining the effect of HMB on performance stratified by endurance sports*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
<b>Cycling</b>													
Vukovich & Adams <sup>72</sup>	USA	NR	8M	3 g/day HMB, Leucine or Placebo	CaHMB	Trained	NR	NR	HMB increased time to reach VO2 peak and VO2 at OBLA	NR	2 weeks	Specific Endurance exercise condition	Y
Vukovich & Dreifort <sup>24</sup>	USA	NR	8M	Placebo, Leucine or 3g/day HMB	CaHMB	Trained	NR	NR	HMB increased time to reach VO2 peak and VO2 at OBLA	NR	2 weeks	Specific endurance exercise condition	Y
<b>Athletics</b>													
Knitter et al. <sup>15</sup>	USA	20-50	16F 16M	Placebo or 3 g/day	CaHMB	Trained	NR	Lowered LDH and CK	NR	Prolonged run	1 week	Specific exercise condition	Y
Byrd et al. <sup>73</sup>	USA	NR	28M	3 g/day HMB, Creatine or Placebo	CaHMB	Trained	NR	NR	HMB lowered soreness	Downhill running protocol	1 week	Specific exercise condition	Y
Robinson et al. <sup>23</sup>	USA	21±2,4	21M 19F	3 g/day or Placebo	HMB-FA	Trained	NE	NR	Greater increased in VO2max and Power VT and VT	3 times/week 5x2min (1minRec) %VO2max	4 weeks	HIIT	Y
Lamboley et al. <sup>58</sup>	Canada	23±1	16F 16M	3 g/day or Placebo	CaHMB	Untrained	No effect on LBM or FM	NR	Greater increase in VO2max and RCP	5x100% MAS	5 weeks	Interval training	Y

**Table III**

*Studies examining the effect of HMB on performance stratified by strength and power sports*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
<b>Resistance Training</b>													
Nissen et al. <sup>10</sup>	USA	19-29	41M	0, 1.5 or 3 g/day	CaHMB	Untrained	Decreased LBM	Decrease CK and 3-MH	Increased Total weight lift (Dose dependent) Increased IRM biceps curl and ROM Decreased DOMS	3 times/week during 3 weeks 3x5 reps 90% IRM	7 Weeks	Weight training	Y
Nissen et al. <sup>74</sup>	USA	19-22	32M	0, 1.5 or 3 g/day	CaHMB and Nutrient Powder	Trained	Increased FFM	NR	Increased IRM Bench and Squat lift	6 times/week during 3 weeks 3x4 reps 90% IRM	7 weeks	Weight training	Y
Panton et al. <sup>66</sup>	USA	20-40	36F 39M	Placebo or 3 g/day	CaHMB	Trained and Untrained	Greater LBM and FFM	NR	Greater upper body strength (3-15%)	Monitored High Intensity progressive resistance training	4 weeks	High Intensity resistance training	Y
Jowko et al. <sup>75</sup>	USA	19-23	40M	Placebo, 3 g HMB, HMB and Creatine or Creatine	CaHMB	Untrained	Positive effect on LBM (additive effect HMB and Ct)	Only HMB lowered CK, urine urea nitrogen, and plasma urea	HMB and Creatine additive effect on weight lifted	1-4 set x 5-8 reps 45-75% IRM	3 weeks	Weight training	Y
Paddon-Jones et al. <sup>30</sup>	Australia	21-22	17M	0 or 3 g/day	CaHMB	Untrained	NR	NR	No effect on strength	NR	6 days	Test Eccentric Exercise	N
Van Someren et al. <sup>76</sup>	Great Britain	20-24	8M	3 g/day HMB 3 g/day KIC	CaHMB	Untrained	NR	Decreased CK	Greater IRM biceps curl and ROM Lower DOMS	3x10 reps 70% IRM	2 weeks	Weight training Eccentric Exercise	Y
Thomson <sup>77</sup>	New Zealand	24±4	34M	Placebo or 3 g/day	CaHMB	Trained	NR	NR	Greater leg extension strength	3times/week 9 exercises/session 2-3 set 5-15 reps 30-90s recovery	9 weeks	Weight training	Y



**Table III (cont.)**

*Studies examining the effect of HMB on performance stratified by strength and power sports*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
Van Someren et al. <sup>78</sup>	Great Britain	23±4	8M	3 g/day HMB 3 g/day KIC	CaHMB	Untrained	NR	Decreased CK	Greater IRM biceps curl and ROM, lower DOMS	Single bout of eccentric resistance exercise	2 weeks	Eccentric Exercise	Y
Thomson et al. <sup>19</sup>	New Zealand	24±4	34M	3g/day or Placebo	HMB	Trained	Decreased FM	NR	Increased Strength lower body	3 times/week 9 exercises/session 2-3 set 5-15 reps 30-90s recovery	9 weeks	Weight training	Y
Kruszewski <sup>79</sup>	Poland	NR	182M	2g/day HMB, 900mg L-Carnitine, 20mg Creatine or Placebo	HMB	Trained	Increased LBM Decreased water content	NR	Improve muscle torque	Weightlifting: 5days/week 60-100%RM 3 exercises Bodybuilding: 3 times/week 3x12reps 50%RM Isometric: 5 times/week 3 exercises 3x3reps or 3x4 reps 80%RM	4 weeks	Weight training	Y
Townsend et al. <sup>80</sup>	USA	22,3±2,4	40M	3 g/day HMB-FA or Placebo Additive effect of CWI	HMB-FA	Trained	NR	Attenuated TNFa and TNFR1	NR	4 sets 10reps 70-80% IRM 3 exercises	4 days	Resistance training	Y
Gonzalez et al. <sup>63</sup>	USA	23.8±3	40M	3 g/day HMB-FA or Placebo Additive effect of CWI	HMB-FA	Trained	NR	Attenuated CRP (HMB-FA+CWI)	Maintained average power/repetition	4 sets 10reps 70-80% IRM 3 exercises	4 days	Resistance training	Y

**Table III (cont.)**

*Studies examining the effect of HMB on performance stratified by strength and power sports*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
Lowery et al. <sup>22</sup>	USA	21,7±0,4	17M	3 g/day HMB-FA and ATP 400mg ATP or Placebo	HMB-FA and ATP	Trained	Increased LBM	Attenuated CK and Cortisol	Increased strength + power Improved Recovery (PRS)	Phase1: Undulation Periodization 3x8-12RM 5x5maxV 3x3-5RM Phase2: Overreaching 3x8-12RM Phase 3: 5x5maxV 1x3-5RM	12 weeks	Resistance training	Y
Wilson et al. <sup>49</sup>	USA	21,6±0,5	20M	3 g/day or Placebo	HMB-FA	Trained	Increased LBM Decreased Body Fat	Attenuated CK and LDH	Increased total strength and power (vertical jump and Wingate) Improved Recovery (PRS)	Phase1: Undulation Periodization 3x8-12RM 5x5maxV 3x3-5RM Phase2: Overreaching 3x8-12RM Phase 3: 5x5maxV 1x3-5RM	12 weeks	Resistance training	Y
<b>Football</b>													
Kreider et al. <sup>81</sup>	USA	20-22	40M	0, 3 or 6 g/day	CaHMB	Trained	No effect on LBM or FM	No effect markers of muscle damage	No effect on strength	NR	4 weeks	Weight training	N
Kreider et al. <sup>82</sup>	USA	20-22	18M	0, 3 g/day	CaHMB	Trained	No effect on LBM or FM	No effect markers of muscle damage	No effect on strength or Intermittent High Intensity exercise performance	5 hours/week 1-3sets x 2-8 reps · 60-95% 1RM	4 weeks	Off-Season Weight training and Agility training	N

**Table III (cont.)**  
*Studies examining the effect of HMB on performance stratified by strength and power sports*

Reference	Country	Age	N (Sex)	Dosage	Form	Training Experience	Body Composition	Biochemistry	Sport Performance	Training Load	Duration	Training Modality	Efficacy
Ransone et al. <sup>83</sup>	USA	20-22	35M	Placebo or 3 g/day	CaHMB	Trained	No effect on body composition	NR	No effect on weight lifting strength	4 days/week 4 hours/day Strength: 10 exercises/session 8-12 sets x 2-10 reps 70-90% 1RM Endurance exercises (V) Endurance exercises (tempo):	4 weeks + 1 week + 4 weeks	Weight + Endurance Training	N
Jay Hoffman et al. <sup>84</sup>	USA	20-22	26M	0 or 3 g/day	CaHMB	Trained	No effect on LBM or FM	No effect markers of muscle damage	No effect on performance	Pre-Season specific training	4 weeks	Football camp specific training	N
<b>Soccer</b>													
Faramarzi et al. <sup>25</sup>	Iran	20±0,7	24M	3 g/day, P or HMB and Creatine (HMBCr)	CaHMB	Trained	NR	Decreased LDH and CK	Increased peak power Increased anaerobic performance	Team training program (10'WU + 15' Tec + 30'Tac + 25'Game + 10'CD)	6 days	Specific training	Y
<b>Rugby</b>													
O'Connor & Crowe <sup>85</sup>	Australia	25±1	27M	3 g/day HMB or HMB and Creatine	CaHMB	Trained	NR	NR	No effect on soreness, ROM, or elbow flexor strength	NR	6 weeks	Weight training	N
O'Connor & Crowe <sup>53</sup>	Australia	25±1	30M	3g HMB 3g Creatine 6g CHO	CaHMB	Trained	NE	NR	NE	NR	6 weeks	Weight training	N
<b>Judo</b>													
Hung et al. <sup>86</sup>	Taiwan	21,8±1,1	8F	3 g/day or Placebo	HMB	Trained	No effect on LBM Increased Fat Loss;	NR	Attenuates decreases in power	Regular Judo Training	3 days	Specific Training	Y
<b>Waterpolo and Rowing</b>													
Slater et al. <sup>31</sup>	Australia	24-26	27M	0 or 3 g/day	CaHMB	Trained	No effect on LBM or FM	No effect markers of muscle damage	No effect on strength	2-3 days/week 3-5sets x 4-6 reps	6 weeks	Weight training	N

When a long-term (12 weeks) periodized training program is used in trained individuals, HMB has been found to increase strength, power, and muscle mass in major upper and lower muscle groups<sup>53</sup>. Moreover, when similar outcome variables were evaluated in healthy untrained individuals after a supervised resistance-training program 3 times per week for 8 weeks, torque generation, creatine phosphokinase and body composition significantly improved among those supplemented with HMB, as compared with those not supplemented<sup>64</sup>.

Collectively, these studies provide evidence supporting the usefulness of HMB supplementation specifically in conditions of high proteolysis, which is frequent in phases of the competition with high intensity exercise done at a high frequency rate. Therefore, it seems appropriate to hypothesize that HMB could help in increasing cardiorespiratory fitness, strength, power and physical function in those experiencing the effects of negative protein turnover in specific catabolic environments.

## Conclusions

Within the sports context, the evidence shows that HMB could have positive effects on several catabolic conditions such as attenuation of the characteristic rise in catabolic biomarkers, limitation of rise in stress hormone response (overreaching) and decreases in power in athletes facing periods of high-density competitions, high-intensity training, first stages of injury recovery and/or any other different situations in which muscle adaptations could be affected by the catabolic environment.

Therefore, since adequate balance between the training stimulus and the subsequent recovery is a great challenge for exercise physiology, HMB supplementation could be of interest as a signalling molecule that may convey specific information to optimize recovery. Future research will additionally contribute to elucidate the underlying mechanisms by which HMB acts improving high-intensity training adaptations.

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