



Original research

Effect of 6-week HMB (beta-hydroxy-beta methylbutyrate) supplementation on muscle strength and body composition in sedentary overweight women

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ABSTRACT

Aim: Today, the role of some nutritional supplements maintaining soft lean mass and obesity treatment has been proven. Among these supplements, beta-hydroxy-beta-methyl butyrate (HMB), has become popular recently. The aim of the present study was to investigate the effect of 6-week HMB supplementation on muscle strength and body composition of overweight sedentary women.

Methods: Forty 20-45-year-old female were recruited to the study. The subjects were randomized to an HMB supplement (n = 20) or placebo (n = 20) group. Body composition was measured by body impedance analyzer. Strength was evaluated by one repetition maximum (1RM) measurements for upper and lower body using body solid leg press and chest press machines.

Results: Thirty-five participants were analyzed at the end of the study. Changes in the 1RM strength tests in the upper and lower body were significant between the two groups after 6 weeks (p = 0.01 and p = 0.04 respectively). The changes in body composition indices were not significant between the two groups (p > 0.05).

Conclusions: Based on the results of the present study, six weeks of HMB supplementation in overweight women increased the muscle strength compared to the control group.

1. Introduction

In today's world, the prevalence of obesity – both in developed and developing countries-is increasing and endanger the general health of humans (Eshtiaghi et al., 2015). In 2014, 600 million suffered from obesity all over the world (Obesity and overweight, 2016). Due to the high prevalence of obesity, interventions such as diet therapy, exercise therapy, supplementary therapies or medications have become increasingly important in reducing weight and decreasing morbidity rate in the general population (Azizi et al., 2005; Barnes, 2012; Bertisch et al., 2008; Lo Presti et al., 2010). However, while low-calorie diets prescribed for weight loss leads to a reduction in FM,¹ SLM² is also reduced. And as a result, the ability to do physical and sports activities decrease greatly (Neff et al., 2015). This can also have a negative effect on the body's metabolism (Wilson et al., 2013).

Today, the role of some nutritional supplements in maintaining

muscle mass during calorie-restricted diets, improving metabolic rate and decreasing fat mass has been proven. Among these supplements, HMB,³ has become popular recently. HMB is a metabolite of the branched-chain amino acid, leucine, which stimulate the synthesis of protein and also prevent protein degradation in skeletal muscle. Therefore, some evidence shows that consuming HMB as a supplement during exercise or low-calorie diets, can be effective in maintaining LMB⁴ (Neff et al., 2015; Arciero et al., 2016). Moreover, it has been effective in reducing adipose tissue by increasing fatty acid oxidation in skeletal muscles (Albert et al., 2015).

However, in most of the studies that have been done so far, the potential effects of taking HMB as a dietary supplement, has been assessed in association with prescribed exercise program especially strength training (Stancliffe et al., 2011; Jówko et al., 2001; Nissen et al., 1996; Panton et al., 2000). Also, limited studies have been conducted in sedentary individuals or people with chronic disabilities (May

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¹ fat mass.

² soft lean mass.

³ beta-hydroxy-beta-methyl butyrate.

⁴ lean body mass.

et al., 2002). Therefore, the main hypothesis of the study was: HMB supplementation could affect muscle strength due to decrease in a catabolic state. However, in some previous studies, HMB supplementation had positive effects on body composition without a difference in exercise or dietary plan between intervention groups (Durkalec-Michalski and Jeszka, 2015). Subsequently, the secondary outcome was: HMB supplementation could change body composition in overweight women.

2. Materials and methods

The study was a double-blinded randomized controlled clinical trial that was performed on human specimens and examined the effect of six weeks of HMB supplementation on body composition and muscle strength in sedentary overweight women.

2.1. Subjects

Forty 20-45-year-old female with a BMI between 25 and 29.9 kg/m² participated in this study and divided into 2 experimental groups of twenty.

Subjects were excluded if they were pregnant or at the post-menopausal stage, suffered from diabetes, musculoskeletal and neurological disorders, cardiovascular disease or any other restrictive disease which might affect exercise performance. Moreover, the volunteers who used appetite suppressant or any drugs which had a significant influence on weight, heart rate, and physical performance were excluded. The subjects were randomized to an intervention (n = 20) and a control (n = 20) group using a 1:1 randomization ratio.

2.2. Assessments

A Body Impedance Analyzer (AVIS33 body composition analyzer, Jawon Medical Co. Ltd, South Korea) was used for analyzing body composition including weight, FM, PBF⁵ and SLM. Height was measured by using a standard tape at the first visit while subjects stood up barefoot. The waist (immediately above the bony prominence of the iliac crest (and hip circumference) around the pelvis in the biggest posterior extension of the buttocks (were measured in a standing position with light clothing (Health and Obesity, 2000). Each measurement was repeated for two times and if the difference was more than 0.5 cm, the third measurement was done for each region.

A Slim Guide Caliper was used for measuring skin thickness on the right side of the body in two regions: abdominal point (5 cm to the umbilicus) and Supra iliac point (intersection of the mid-axillary line and supra-iliac line), while subjects stood up with the naked upper body. Each area was measured two or three times and when the difference was further than 3 mm, subjects underwent another measurement. All measurements were done by a one trained examiner.

At the same session, a trained nutritionist completed a 24-h food record for each subject and at the end of the study, the daily food intake was assessed again. Dietary intakes were analyzed by the University of Minnesota Nutrition Data System for Research, version 5.0–3.5.

In order to investigate the upper and lower limb muscle strength, 1RM⁶ was performed at baseline and 6-week follow-up visit. 1RM defined as the maximal weight that any person can lift just for one time with accurate lifting method (Kraemer et al., 1995). Body Solid Leg Press and Chest Press Machines were used. 1RM for chest press and leg press were recorded under the supervision of a sports medicine specialist. After a short warm-up, subjects were asked to lift a load which examiner estimated that it could not be lifted more than 10 times. The rest time was 1–2 min Between each attempt and finally, the maximum

number of repetitions was recorded (Medicine, 2012). The final result was calculated using the formula: $1RM = (\text{weight lifted}) / (1 - 0.02 \times \text{RTF} \times \text{repetitions to failure})$ (Desgorces et al., 2010).

In the first visit, patients were educated about healthy nutrition principles such as greater consumption of whole grains, low-fat dairy, white meat and vegetables, and lesser consumption of fast foods or Junk foods. They were encouraged to follow normal physical activity during the intervention.

The study period was six weeks and the participants were followed up by telephone at 3rd week, and any vagueness or question was resolved through telephone counseling by a sports medicine specialist.

At the end of the study period, the participants were re-visited and they were analyzed by Bio-Impedance device again. Also, anthropometric measurements were repeated.

2.3. Supplement prescription

The intervention group received HMB supplement in the form of 1250 mg calcium salt capsules (the Olimp Pharmacy Company) two pills per day (equal to 2.5 g daily) and placebo was given to the control group two times per day. The participants were requested to use the pills with morning and evening snacks. The placebo pills contained a neutral substance (glycerine) produced by Kharazmi Co. All subjects were required to fill logbook if they take their supplement and if did not consume the pills, the exact cause should be mentioned.

Informed consent was obtained from each patient included in the study. This research has been approved by the Tehran University of Medical Sciences and Health Services (IRCT registration ID: IRCT201703177903N9).

2.4. Statistical analysis

The statistical software SPSS 19.0.0 (SPSS Inc. Chicago, IL, USA) was used for all data analyses.

Descriptive baseline characteristics for two group's comparisons were tabulated as means and SD or as percentages. Comparing baseline characteristics was done with *t*-test and chi-square test. All analyses comparing the efficacy of our primary outcomes (strength parameters) were by intention-to-treat principles. Using General Linear Model (GLM) score of those parameters between the two groups were compared by repeated measures ANOVA test. Compound symmetry assumption was tested using Mauchly's Sphericity test. The time groups cross-product (interaction term) was considered as group differences in their response over time with the baseline values (age and height) as a covariate in this model. A significance level of 5% (alpha = 0.05) was used for all statistical tests.

3. Results

Forty subjects participated in the study, and 35 subjects (including 17 in control and 18 in the HMB group) analyzed at the end of the study (Fig. 1). Four subjects were excluded because lack of interest to continue and have no time for participating in the test sessions and one was excluded because of pregnancy planning. The mean (SD) age of HMB and control group was 35.65 (7.83) and 35.11 (5.69) years respectively, but the difference between the two groups was not statistically significant ($p = 0.82$). The mean (SD) of height in HMB and control group was 161.47 (3.49) and 159.61 (4.92) cm, respectively, and the difference between the two groups was not statistically significant ($P = 0.21$). The mean (SD) of BMI in HMB and control group was 27.33 (1.27) and 27.72 (1.39) kg/m², respectively, and the difference between the two groups was not statistically significant ($P = 0.39$).

The supplement consumption logbooks were assessed. The mean (SD) number of the capsule which was taken by subjects was 81 (5.2) and the lowest was 70 out of 84 for 6 weeks.

⁵ percentage of body fat.

⁶ one-repetition maximum test.

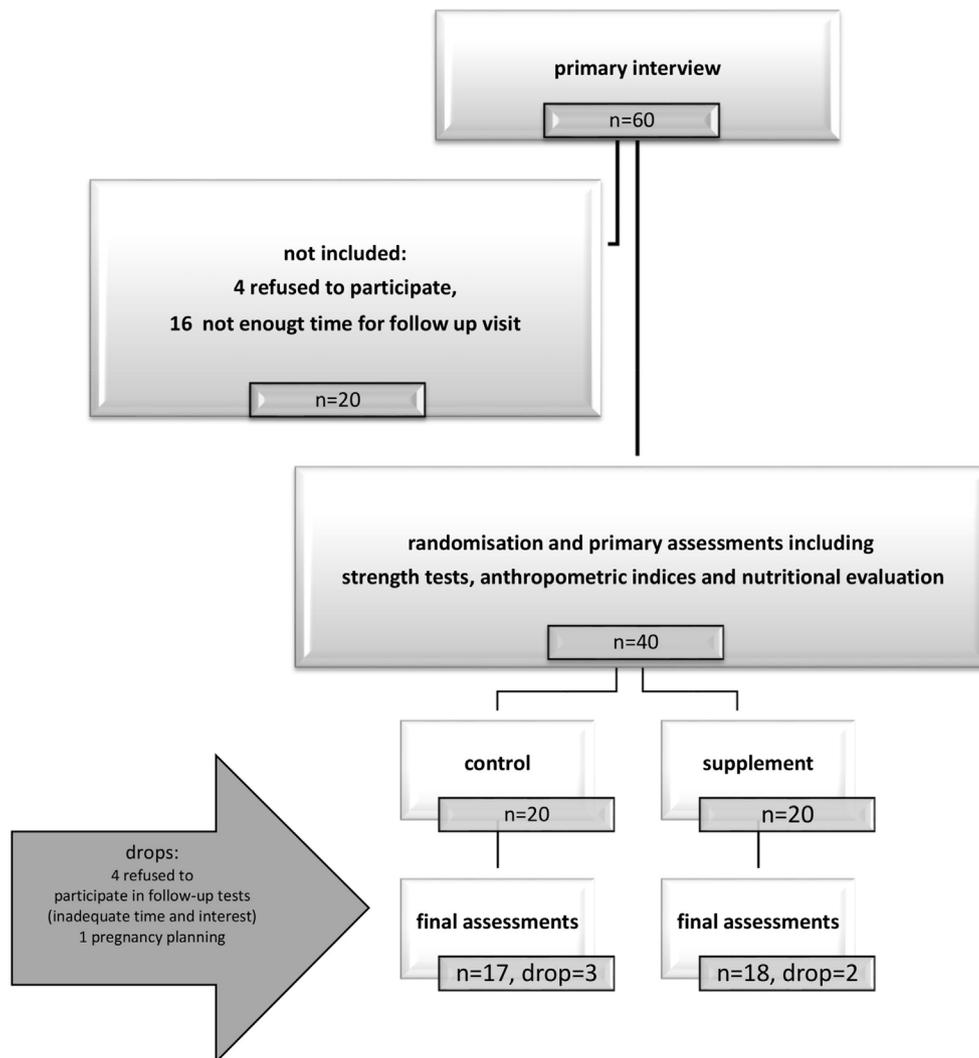


Fig. 1. Flow chart of how participants progressed through the study, and how many contributors completed each stage.

3.1. Anthropometric indices

Anthropometric indices and the changes over 6 weeks in both groups were presented in Table 1.

As listed in Table 1, there was no significant difference in the anthropometric indices at the baseline ($P > 0.05$). Reduction in weight, fat percentage, fat mass, waist and hip circumference, abdominal and supra-iliac skin fold in HMB group were significant during 6 weeks, but in control group, only the waist circumference and Abdominal skinfold were reduced significantly during 6 weeks ($P < 0.05$). However, no significant difference was seen between the two groups after 6 weeks. In terms of SLM and BMI, there were no significant changes intra-group or inter-group.

3.2. Strength indices

Upper and lower 1RM tests and related indices at the beginning of the study and the changes over 6 weeks in both groups were presented in Table 2.

In terms of upper and lower body strength tests, there were no significant differences in the baseline measurements ($P > 0.05$). After 6 weeks, the increase in upper and lower body 1RM was significant in the supplement group ($P < 0.05$). Furthermore, the differences in upper and lower body 1RM were significant between the two groups ($P < 0.05$). The details of changes in a number of repetitions of chest

or leg press and amount of lifted weights were presented at Table 2.

3.3. Results of 24-h food records

According to the analysis, calorie intake at the baseline was not significant between the two groups ($P = 0.21$). After the intervention, the changes in the recall items (total calorie, carbohydrate, and protein intake) from baseline were calculated in each group and the differences between groups were compared and analyzed. The results showed that changes in calorie intake ($p = 0.21$), received protein ($p = 0.45$) and consumed carbohydrate ($p = 0.42$) were not statistically significant between the two groups.

4. Discussion

The present study was a double-blinded, randomized, placebo-controlled trial in order to evaluate the Effects of 6-week supplementation of HMB (beta-hydroxy-beta methylbutyrate) on body composition and muscle strength in sedentary overweight women. Forty female subjects entered the study, data from 35 subjects were analyzed at the end. (Fig. 1).

4.1. The effect of HMB on anthropometric indices

It was shown that consuming HMB supplements had a positive effect

Table 1
Baseline and changes in anthropometric measurements over time in the groups.

Variable	Group	Before	After	P-value*	P-value**		
					Time	Group	Interaction
Weight (kg)	HMB	69.9 ± 4.7	68.78 ± 4.79	0.01	0.002	0.13	0.87
	Control	72.27 ± 4.25	71.25 ± 5.11	0.07			
BMI (kg/m ²)	HMB	27.33 ± 1.27	27.01 ± 1.59	0.15	0.03	0.45	0.9
	Control	27.72 ± 1.39	27.37 ± 1.73	0.11			
FAT%	HMB	35.49 ± 1.51	34.72 ± 2.20	0.007	0.006	0.71	0.31
	Control	35.55 ± 2.38	35.18 ± 2.46	0.24			
SLM (kg)	HMB	41.16 ± 2.91	41.01 ± 2.99	0.44	0.67	0.25	0.84
	Control	42.12 ± 1.80	42.07 ± 2.58	0.91			
FM (kg)	HMB	24.83 ± 2.06	23.93 ± 2.46	0.005	0.004	0.22	0.53
	Control	25.75 ± 2.79	25.15 ± 3.09	0.15			
Waist C (cm)	HMB	96.44 ± 5.41	94.86 ± 5.11	0.002	< 0.001	0.18	0.87
	Control	98.87 ± 5.09	97.16 ± 5.23	0.01			
Hip C (cm)	HMB	103.41 ± 4.63	101.46 ± 4.69	0.002	< 0.001	0.11	0.28
	Control	105.14 ± 2.95	104.05 ± 3.38	0.08			
Abdomen SF (mm)	HMB	32.12 ± 5.46	30.13 ± 5.71	< 0.001	< 0.001	0.76	0.61
	Control	32.64 ± 7.90	31.05 ± 9.01	0.04			
Supra iliac SF (mm)	HMB	28.11 ± 6.04	25.88 ± 5.56	< 0.001	< 0.001	0.1	0.55
	Control	30.85 ± 5.43	29.20 ± 4.58	0.07			

• The values are expressed as mean (SD), Statistical difference: p < 0.05, BMI: body mass index, FAT%: fat percent, SLM: soft lean mass, FM: fat mass, C: circumference, SF: skin fold, * within group, ** between group.

on anthropometric indices in the intervention group, but there was no significant difference between the two groups at the end of the study (Table 1).

In the study of Vukovich et al. consuming 3 g of HMB-Ca (Calcium salt) per day along with a resistance exercise program for 8 weeks, lead to an increase in muscle mass and reduction of fat mass (Vukovich et al., 2001). Durkalec-Michalski et al. observed the effects of HMB on the body composition of 16 elite rowers. In this crossover study, athletes were given 3 g of HMB per day for 12 weeks. After a 10-day washout period, placebo was given to athletes for another 12 weeks and at the end of the study, a significant decrease in fat mass with preservation of lean mass was observed in the athletes during supplementation period (Durkalec-Michalski and Jeszka, 2015). Furthermore, a significant reduction in weight and fat mass was seen in the HMB group aligned with preservation of lean mass. Maintaining lean mass is clinically important for obese or overweight subjects who undergo weight loss diets. In 2013, Deutz et al. reported that HMB supplementation helped elderly adults in a bed rest condition to preserve lean mass (Deutz et al., 2013). The result was in consist of the study of Vukovich et al., which showed that 8-week supplementation with HMB increased gains in fat-free mass in older adults. However, their participants were healthy people and participated in a specific exercise

program (Vukovich et al., 2001).

Although the anthropometric and body composition changes in our study were significant in the supplement group, no differences between the two groups were seen which may be due to the short duration of the study or the lack of resistance exercise program during the supplementation period. Most studies which reported a significant difference between HMB supplement and control group emphasized on exercises during the study period or were done on athletes (Durkalec-Michalski and Jeszka, 2015; Vukovich et al., 2001; Holecek, 2017). Though a number of studies did not support these findings (Kreider et al. 1999, 2000). The discrepancy in results of the mentioned studies could be explained by study duration, experimental design and finally type of evaluated participants in terms of having sports history. Additionally, in previous studies, the effect of dietary intake, especially daily calorie consumption has not been properly investigated.

In this regard, 6 weeks of HMB supplementation in sedentary overweight women, may have a positive effect on body composition indices and it seems that in order to increase the positive outcomes, it would be better to use supplementation with a specific resistance training.

Table 2
Baseline and changes in 1RM test indices over time in the groups.

Variable	Group	Before	After	P-value*	P-value**		
					Time	Group	Interaction
Rep U (Number)	HMB	4.50 ± 1.79	4.05 ± 1.86	0.39	0.82	0.73	0.28
	Control	4.35 ± 2.34	4.64 ± 2.52	0.05			
Weight U (kg)	HMB	15.83 ± 7.12	20.00 ± 8.04	0.001	0.05	0.69	0.005
	Control	17.05 ± 5.60	17.05 ± 5.01	0.99			
1RM U (kg)	HMB	17.32 ± 7.77	21.59 ± 8.11	0.001	0.007	0.77	0.01
	Control	18.72 ± 6.13	18.88 ± 5.80	0.88			
Rep L (Number)	HMB	3.38 ± 1.71	4.16 ± 2.09	0.08	0.04	0.17	0.04
	Control	5.05 ± 2.63	4.41 ± 2.56	0.26			
Weight L (kg)	HMB	45.83 ± 13.20	53.61 ± 15.41	< 0.001	0.002	0.99	0.08
	Control	48.52 ± 12.47	50.88 ± 11.75	0.41			
1RM L (kg)	HMB	49.32 ± 14.55	58.68 ± 17.28	< 0.001	0.002	0.84	0.04
	Control	53.81 ± 12.66	56.11 ± 14.38	0.47			

• The values are expressed as mean (SD); Statistical difference: p < 0.05, REP: number of repetitions of chest or leg press, 1RM:1 repetition maximum, U: Upper limbs L: Lower limbs, * within group, ** between group.

4.2. Effect of HMB supplementation on strength performance testing

Results of the present study showed that HMB supplementation could lead to an increase in muscle strength in sedentary subjects.

In some *in vivo* studies, the role of HMB in inhibiting starvation-induced myofibrillar protein degradation with or without insulin was observed (Duan et al., 2018).

In the most of the human studies the effect of HMB supplementation were evaluated in addition to resistance training. There are studies available on the effects of HMB supplementation on athletes' strength, which are in line with the results of the present study. Wilson et al. evaluated the effect of HMB supplementation with strength training on amateur male athletes. After 12 weeks, they observed an increase in LBM accompanied by a significant increase in strength in Bench Press, Squat, and Deadlift tests (Wilson et al., 2008). Also, Lowery et al. reported an increase in LBM and strength in trained individual within 12 weeks of supplementation with HMB and Adenosine triphosphate (ATP) (Lowery et al., 2016).

In some studies, with shorter time of intervention, the same results were obtained. In a review article, it has been reported that HMB consumption with strength training for 3 weeks, had a positive effect on LBM and strength enhancement (Nissen and Sharp, 2003). In non-athletic subjects, the effect of HMB supplementation with strength training has been studied too. Gallagher et al. evaluated 1RM and FFM after 8 weeks supplementation with different doses of HMB (0, 38 and 76 mg/kg/day) in addition to resistance exercise in the non-athletic individuals. While the 1RM strength gains were not different between groups, results showed an increase in peak isometric and various isokinetic torque values in supplement groups. In addition, the 38 mg/kg group exhibited a greater increase in FFM (Gallagher et al., 2000).

Achieving greater muscular strength is not only important for athletic performance (Suchomel et al., 2016) but also has a principal role in the life of sedentary population or patients with chronic disease (Loprinzi, 2016; Gianoudis et al., 2015; Li et al., 2018). Nevertheless, protein degradation is equally as important as protein synthesis. Under conditions of starvation, uremia, sepsis, and acidosis, muscle protein degradation results in loss of protein stores and a reduction in muscle mass thus increasing morbidity and mortality (Wang et al., 2006). The protein degradation of skeletal muscle under all of the mentioned catabolic circumstances has been proven to be associated with the activation of muscular ubiquitin-proteasome proteolytic (UPP) pathway (Sheriff et al., 2012; Goodman et al., 2011). Recently, Holeček reviewed the effect of HMB supplementation on athletes and chronic cachectic patients and concluded that HMB could affect muscle mass in both groups. However, the results of the mentioned study did not support the positive effect of HMB supplementation on healthy subjects (Holeček, 2017). In 2016, Loprinzi suggested that lower extremity muscle strength could be considered as predictive of mortality among people with a sedentary lifestyle (Loprinzi, 2016). Muscle strength plays an important role in functional daily activities such as the speed of walking or climbing up and down stairs (Barbat-Artigas et al., 2014; Lerner et al., 2014). Moreover, muscle strength is a key factor for those who underwent weight loss programs. Generally, an obese population especially females may have lower muscle strength (Carvalho et al., 2015; Miller et al., 2013). So, calorie restriction for losing weight leads to a reduction in muscle mass and strength, and finally functional capacity (Miller et al., 2013; Marks and Rippe, 1996; Weiss et al., 2007). Due to the vital role of being physically active for maintaining metabolic rate and losing fat mass, the effect of HMB supplementation on muscle strength is noticeable.

Since sedentary individuals were evaluated in the present study, the use of HMB may have reduced catabolic state with daily routine activities, which improved their ability for general activity and consequently, increased 1RM.

In sum, the use of six weeks of HMB supplementation without strength training in the sedentary overweight female could increase

muscle strength.

4.3. Limitations and strengths

The results of the present study are not generalizable to postmenopausal female and male subjects due to the limitation of our inclusion criteria. Body composition analysis method that used in the study, was another limitation, which may have errors in the report of the fat mass/or lean mass measures. The period of the study was short. Considering that, most HMB studies have been conducted on the athlete's population, it is recommended to study non-athletic obese and/or overweight populations, with concurrent exercise in a longer period.

5. Conclusions

According to the results, 6 weeks of HMB supplementation in sedentary overweight women, may have a positive effect on body composition indices such as weight, waist and abdominal circumferences and some skin fold points. An important finding of the present study was the effect of HMB supplementation without resistance training on the increasing strength of sedentary overweight women without changes in SLM.

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Declarations of interest

None.

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References

- Albert, F.J., Morente-Sánchez, J., Ortega, F.B., Castillo, M.J., Gutiérrez, Á., 2015. Usefulness of β -hydroxy- β -methylbutyrate (HMB) supplementation in different sports: an update and practical implications. *Nutr. Hosp.* 32 (1), 20–33.
- Arciero, P.J., Edmonds, R., He, F., Ward, E., Gumprich, E., Mohr, A., Ormsbee, M.J., Astrup, A., 2016. Protein-pacing caloric-restriction enhances body composition similarly in obese men and women during weight loss and sustains efficacy during long-term weight maintenance. *Nutrients* 8 (8), 476.
- Azizi, F., Azadbakht, L., Mirmiran, P., 2005. Trends in overweight, obesity and central fat accumulation among Tehranian adults between 1998–1999 and 2001–2002: Tehran lipid and glucose study. *Ann. Nutr. Metab.* 49 (1), 3–8.
- Barbat-Artigas, S., Pion, C.H., Leduc-Gaudet, J.-P., Rolland, Y., Aubertin-Leheudre, M., 2014. Exploring the role of muscle mass, obesity, and age in the relationship between muscle quality and physical function. *J. Am. Med. Dir. Assoc.* 15 (4) 303. e313-303. e320.
- Barnes, A.S., 2012. Obesity and sedentary lifestyles: risk for cardiovascular disease in women. *Tex. Heart Inst. J.* 39 (2), 224.
- Bertisch, S.M., Wee, C.C., McCarthy, E.P., 2008. Use of complementary and alternative therapies by overweight and obese adults. *Obesity* 16 (7), 1610–1615.
- Carvalho, L.P., Di Thommazo-Luporini, L., Aubertin-Leheudre, M., Junior, J.C.B., De Oliveira, C.R., Luporini, R.L., Mendes, R.G., Zangrando, K.T.L., Trimer, R., Arena, R., 2015. Prediction of cardiorespiratory fitness by the six-minute step test and its association with muscle strength and power in sedentary obese and lean young women: a cross-sectional study. *PLoS One* 10 (12) e0145960.
- Desgorges, F.D., Berthelot, G., Dietrich, G., Testa, M.S., 2010. Local muscular endurance and prediction of 1 repetition maximum for bench in 4 athletic populations. *J. Strength Cond. Res.* 24 (2), 394–400.
- Deutz, N.E., Pereira, S.L., Hays, N.P., Oliver, J.S., Edens, N.K., Evans, C.M., Wolfe, R.R., 2013. Effect of β -hydroxy- β -methylbutyrate (HMB) on lean body mass during 10 days of bed rest in older adults. *Clin. Nutr.* 32 (5), 704–712.
- Duan, Y., Li, F., Guo, Q., Wang, W., Zhang, L., Wen, C., Chen, X., Yin, Y., 2018. Beta-hydroxy-beta-methyl butyrate is more potent than leucine in inhibiting starvation-induced protein degradation in C2C12 myotubes. *J. Agric. Food Chem.* 66 (1), 170–176.

- Durkalec-Michalski, K., Jeszka, J., 2015. The efficacy of a β -hydroxy- β -methylbutyrate supplementation on physical capacity, body composition and biochemical markers in elite rowers: a randomised, double-blind, placebo-controlled crossover study. *J. Int. Soc. Sport. Nutr.* 12 (1), 31.
- Eshtiagh, R., Keihani, S., Hosseini, F., Barzin, M., Azizi, F., 2015. Natural course of metabolically healthy abdominal obese adults after 10 years of follow-up: the Tehran Lipid and Glucose Study. *Int. J. Obes.* 39 (3), 514.
- Gallagher, P.M., Carrithers, J.A., Godard, M.P., Schulze, K.E., Trappe, S.W., 2000. β -hydroxy- β -methylbutyrate ingestion, part I: effects on strength and fat free mass. *Med. Sci. Sport. Exerc.* 32 (12), 2109–2115.
- Gianoudis, J., Bailey, C., Daly, R., 2015. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. *Osteoporos. Int.* 26 (2), 571–579.
- Goodman, C.A., Mayhew, D.L., Hornberger, T.A., 2011. Recent progress toward understanding the molecular mechanisms that regulate skeletal muscle mass. *Cell. Signal.* 23 (12), 1896–1906.
- Health, N.I.O., N.A. A. f. t. s. o. Obesity, 2000. **The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults.** NIH Publication Number 00-4084. http://www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf.
- Holeczek, M., 2017. Beta-hydroxy-beta-methylbutyrate supplementation and skeletal muscle in healthy and muscle-wasting conditions. *J. Cachexia Sarcop. Muscle* 8 (4), 529–541.
- Jówo, E., Ostaszewski, P., Jank, M., Sacharuk, J., Zieniewicz, A., Wilczak, J., Nissen, S., 2001. Creatine and β -hydroxy- β -methylbutyrate (HMB) additively increase lean body mass and muscle strength during a weight-training program. *Nutrition* 17 (7–8), 558–566.
- Kraemer, W., Fry, A., Ratamess, N., French, D., 1995. Strength testing: development and evaluation of methodology. *Physiol. Assess. Hum. Fit.* 2, 119–150.
- Kreider, R., Ferreira, M., Wilson, M., Almada, A., 1999. Effects of calcium β -hydroxy- β -methylbutyrate (HMB) supplementation during resistance-training on markers of catabolism, body composition and strength. *Int. J. Sports Med.* 20 (08), 503–509.
- Kreider, R.B., Ferreira, M.P., Greenwood, M., Wilson, M., Grindstaff, P., Plisk, S., Reinardy, J., Cantler, E., Amalda, A.L., 2000. Effects of calcium β -HMB supplementation during training on markers of catabolism, body composition, strength and sprint performance.
- Lerner, Z.F., Board, W.J., Browning, R.C., 2014. Effects of obesity on lower extremity muscle function during walking at two speeds. *Gait Posture* 39 (3), 978–984.
- Li, R., Xia, J., Zhang, X., Gathirua-Mwangi, W.G., Guo, J., Li, Y., Mckenzie, S., Song, Y., 2018. Associations of muscle mass and strength with all-cause mortality among US older adults. *Med. Sci. Sport. Exerc.* 50 (3), 458–467.
- Lo Presti, R., Lai, J., Hildebrandt, T., Loeb, K.L., 2010. Psychological treatments for obesity in youth and adults. *Mt. Sinai J. Med.* 77 (5), 472–487.
- Loprinzi, P.D., 2016. Lower extremity muscular strength, sedentary behavior, and mortality. *Age* 38 (2), 32.
- Lowery, R.P., Joy, J.M., Rathmacher, J.A., Baier, S.M., Fuller, J.C., Shelley, M.C., Jäger, R., Purpura, M., Wilson, S., Wilson, J.M., 2016. Interaction of beta-hydroxy-beta-methylbutyrate free acid and adenosine triphosphate on muscle mass, strength, and power in resistance trained individuals. *J. Strength Cond. Res.* 30 (7), 1843–1854.
- Marks, B.L., Rippe, J.M., 1996. The importance of fat free mass maintenance in weight loss programmes. *Sport. Med.* 22 (5), 273–281.
- May, P.E., Barber, A., T D'Olimpio, J., Hourihane, A., Abumrad, N.N., 2002. Reversal of cancer-related wasting using oral supplementation with a combination of β -hydroxy- β -methylbutyrate, arginine, and glutamine. *Am. J. Surg.* 183 (4), 471–479.
- Medicine, A.C. o. S., 2012. **ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription.** Lippincott Williams & Wilkins.
- Miller, C.T., Fraser, S.F., Levinger, I., Straznicki, N.E., Dixon, J.B., Reynolds, J., Selig, S.E., 2013. The effects of exercise training in addition to energy restriction on functional capacities and body composition in obese adults during weight loss: a systematic review. *PLoS One* 8 (11) e81692.
- Neff, K.J., Ferrannini, E., le Roux, C.W., 2015. Treatment of obesity: bariatric surgery. In: *International Textbook of Diabetes Mellitus*, pp. 505–518.
- Nissen, S., Sharp, R., Ray, M., Rathmacher, J., Rice, D., Fuller Jr., J., Connelly, A., Abumrad, N., 1996. Effect of leucine metabolite β -hydroxy- β -methylbutyrate on muscle metabolism during resistance-exercise training. *J. Appl. Physiol.* 81 (5), 2095–2104.
- Nissen, S.L., Sharp, R.L., 2003. Effect of dietary supplements on lean mass and strength gains with resistance exercise: a meta-analysis. *J. Appl. Physiol.* 94 (2), 651–659.
- Obesity and Overweight.** World Health Organization 2018. 2018 2016 [cited 2018]. Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/>.
- Panton, L.B., Rathmacher, J.A., Baier, S., Nissen, S., 2000. Nutritional supplementation of the leucine metabolite β -hydroxy- β -methylbutyrate (hmb) during resistance training. *Nutrition* 16 (9), 734–739.
- Sheriff, S., Kadeer, N., Joshi, R., Friend, L.A., James, J.H., Balasubramaniam, A., 2012. Des-acyl ghrelin exhibits pro-anabolic and anti-catabolic effects on C2C12 myotubes exposed to cytokines and reduces burn-induced muscle proteolysis in rats. *Mol. Cell. Endocrinol.* 351 (2), 286–295.
- Stancliffe, R.A., Eades, M., Smart, K., Zemel, M.B., 2011. Role of mTOR and β -hydroxy- β -methylbutyrate (HMB) in Leucine Stimulation of Muscle Mitochondrial Biogenesis and Fatty Acid Oxidation: Federation of American Societies for Experimental Biology.
- Suchomel, T.J., Nimphius, S., Stone, M.H., 2016. The importance of muscular strength in athletic performance. *Sport. Med.* 46 (10), 1419–1449.
- Vukovich, M.D., Stubbs, N.B., Bohlken, R.M., 2001. Body composition in 70-year-old adults responds to dietary β -hydroxy- β -methylbutyrate similarly to that of young adults. *J. Nutr.* 131 (7), 2049–2052.
- Wang, X., Hu, Z., Hu, J., Du, J., Mitch, W.E., 2006. Insulin resistance accelerates muscle protein degradation: activation of the ubiquitin-proteasome pathway by defects in muscle cell signaling. *Endocrinology* 147 (9), 4160–4168.
- Weiss, E.P., Racette, S.B., Villareal, D.T., Fontana, L., Steger-May, K., Schechtman, K.B., Klein, S., Ehsani, A.A., Holloszy, J.O., S. o. M. C. Group, W.U., 2007. Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss. *J. Appl. Physiol.* 102 (2), 634–640.
- Wilson, G.J., Wilson, J.M., Manninen, A.H., 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. *Nutr. Metab.* 5 (1), 1.
- Wilson, J.M., Fitschen, P.J., Campbell, B., Wilson, G.J., Zanchi, N., Taylor, L., Wilborn, C., Kalman, D.S., Stout, J.R., Hoffman, J.R., 2013. International society of sports nutrition position stand: beta-hydroxy-beta-methylbutyrate (HMB). *J. Int. Soc. Sport. Nutr.* 10 (1), 6.