



## REVIEW ARTICLE

# The anabolic role of plant-based proteins in response to chronic resistance exercise

*O papel anabólico das proteínas de origem vegetal em resposta ao exercício físico resistido crônico*

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### KEYWORDS

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### ABSTRACT

Proper maintenance of skeletal muscle mass is essential to prevent sarcopenia and ensure health and quality of life as aging progress. The two determinants of muscle protein synthesis are the increased load on skeletal muscle through resistance exercise and protein intake. For an effective result of maintaining or increasing muscle mass, it is relevant to consider the quantitative and adequate intake of protein, and the dietary source of protein since the plant-based protein has differences in comparison to animals that limit its anabolic capacity. Given the increase in vegetarianism and the elderly population, which consumes fewer food sources of animal protein, the importance of understanding how protein of plant-based protein can sustain muscle protein synthesis in the long term when associated with resistance exercise is justified, as well as the possibilities of dietary adequacy in the face of this demand.

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**PALAVRAS-CHAVE**

Exercício  
 Massa muscular  
 esquelética  
 Proteínas de origem  
 animal  
 Proteínas de origem  
 vegetal  
 Síntese da proteína  
 muscular

**RESUMO**

A manutenção adequada da massa muscular esquelética é essencial para prevenir a sarcopenia e garantir a saúde e qualidade de vida à medida que se envelhece. Os dois determinantes da síntese de proteína muscular são o aumento de carga no músculo por meio do exercício físico resistido e a ingestão de proteínas. Para um resultado efetivo de manutenção ou aumento da massa muscular, deve-se considerar a ingestão quantitativa e adequada de proteína e a fonte alimentar, visto que a proteína de origem vegetal possui diferenças em comparação a animal que limitam sua capacidade anabólica. Em virtude do aumento do vegetarianismo e da população idosa, que consome menos alimentos fontes de proteína animal, justifica-se a importância de compreender como a proteína de origem vegetal pode sustentar em longo prazo a síntese de proteína muscular quando associada ao exercício físico resistido, bem como, as possibilidades de adequação dietética frente à esta demanda.

**INTRODUCTION**

Adequate maintenance of strength and skeletal muscle mass (MM) is essential to ensure the quality of life of an individual as they age. It is associated with independence from performing routine activities such as locomotion, getting up from a chair, maintaining posture, and reducing the risk of metabolic diseases - as skeletal muscle is the central tissue responsible for maintaining insulin sensitivity. The strength and MM decrease with aging. It has been reported that, over the age of 50 years, the loss of strength is 1.5%-5%/year, and the loss of MM is 1%-2%/year<sup>1,2</sup>. Low MM has been associated with increased morbidity and mortality, whereas low muscle strength is a significant and independent predictor of mortality risk<sup>3,4</sup>.

The two main determinants of muscle protein synthesis (MPS), which independently and synergistically exert a positive influence on the net protein balance and which in the long-term lead to increased MM, are the increased load on the skeletal muscle through resistance exercise (RE), and adequate protein intake<sup>5-7</sup>. Protein supplementation (higher-than-usual protein intake) maximizes the MPS associated with RE. However, current recommendations do not distinguish between the source, whether animal origin (PAO) or plant-based protein (PBP). By extension, PBP has specific differences compared to PAO that limit its anabolic muscle capacity<sup>8,9</sup>.

Recently, changing demographics and dietary patterns have demonstrated the growing need to understand the implications of these differences for MPS. An increase in population aging<sup>10</sup> characterizes the change in the demographic scenario, and this stage of life is marked by changes that can impair the proper maintenance of muscle tissue. With advancing age, there is an increase in muscle anabolic resistance, leading to the need for greater protein intake to stimulate MPS both at rest and after RE<sup>11,12</sup>. However, older individuals consume less protein-rich foods due to several physiological, pathological, and social factors inherent in the phase itself<sup>13</sup>. The change in dietary pattern, on the other hand, has

been marked by increased consumption of plant foods. In Brazil, in 2018, 14% of the population declared adopting some vegan and vegetarian diet (total or partial exclusion of animal foods), showing a 75% growth of this public compared to 8% in 2012<sup>14</sup>.

Thus, given this context, which is due to the association: (a) of the importance of adequate protein intake associated with the RE to attenuate the reduction in strength and MM<sup>1,7</sup>; (b) the increase in veganism and vegetarianism<sup>14</sup> and the increase in the elderly population<sup>10</sup> who consumes more minor food sources of protein<sup>11,13</sup>; and (c) the fact that PBP has specific differences compared to animal proteins that limit its anabolic muscle capacity<sup>8,9</sup> - the importance of understanding how PBP can sustain MPS in the long term when associated with RE is justified. Therefore, the objective of this paper is, from the perspective of primary health science (physiology) and applied (nutrition), to present a review and synthesis of current evidence on the role of PBP in increasing MM and strength in response to chronic RE and possibilities of dietary adequacy. It is expected that this review, synthesized and made available in the virtual environment, will facilitate the use by health professionals and decision-makers in the prescription of conduct based on scientific evidence.

**METHODS**

A bibliographic search was performed until June 15, 2021, independently by the authors, of articles published in peer-reviewed journals using PubMed, Web of Science, and Google Scholar databases. It was used three blocks of concepts with keywords combined with the Boolean operators AND, OR and NOT. The first survey looked at current protein intake recommendations to maximize MPS associated with RE, and it looked for a specific recommendation for PBP intake using the descriptors "consensus statement", "position stand", "recommendations", "muscle protein synthesis", "hypertrophy, resistance exercise", "protein dose", "dietary protein". The second research looked for the difference in quality between PBP and PAO and a

possible impact for MPS according to the descriptors “vegetable protein”, “plant-based protein”, “animal-based protein”, “quality”. The third research was related to the search for evidence regarding the effect of PBP supplementation compared to PAO when associated with long-term RE on MM and muscle strength outcomes: “meta-analysis”, “randomized controlled trials”, “protein supplementation”, “protein source”, “resistance exercise”, “muscle strength”, “muscle mass”. Two reviewers (CSS and ESOJ) selected the articles initially based on the reading of the title, followed by the reading of abstracts and, later, the full text of the articles. In case of disagreement between the two reviewers, a third reviewer (EAE) decided on the inclusion. The bibliographic references of the studies found in these databases were also reviewed. In the first and second surveys, relevant studies were analyzed and combined to overview the subject. In the third survey, to synthesize the available evidence, the authors included studies from meta-analyses published to date and relevant clinical trials that were not analyzed by such studies.

## DEVELOPMENT

### *Protein intake recommendations to maximize MPS in response to RE*

MPS depends on the balance between the degradation and synthesis of new proteins. In summary, there is a net loss of protein in the post-absorptive state, and degradation exceeds synthesis. In the postprandial state, protein intake and the resulting hyperaminoacidemia, a positive net protein balance occurs, and synthesis exceeds degradation. The role of RE for MPS is to sensitize the muscle to hyperaminoacidemia and provide a more extended period of positive net protein balance than that caused by food alone<sup>5-7</sup>. In this sense, a recent meta-analysis showed that protein supplementation in the absence of metabolic stressors, such as RE and calorie restriction, does not increase MM over time<sup>15</sup>.

The recommended protein intake to maximize MPS associated with RE is the intake of complete sources (with all 20 amino acids) in 1.4 - 2.0 g protein/kg body weight/day. It is recommended that the amount be distributed throughout the day (every 3 - 4 h with 20 - 40 g of protein/meal or 0.25 - 0.55 g/kg of body weight/meal), prioritizing an intake after the exercise and another close to sleep. It is also recommended that the protein source provide all the essential amino acids in 6 - 15 g/meal, being 0.7 - 3 g of leucine<sup>16,17</sup>. In calorie-restricted diets, the increase in protein intake between 2.3 and 3.1 g/kg of fat-free mass associated with RE is effective in helping to preserve MM<sup>18</sup>.

Of the indispensable amino acids, leucine is most important as it is responsible for independently activating MPS. Leucine binds to Sestrin2, a protein

that functions as an activation sensor for the mechanistic target of rapamycin complex 1 (mTORC1), which is the key signaling protein of MPS<sup>6</sup>. This effect, called the “threshold or trigger” of leucine, promotes a rapid increase in leukemia (intracellular concentration) after an RE session, the most anabolic stimulus for MPS. In the short term, it triggers an increase in MPS and the long term, when associated with RE, it promotes an increase in MM<sup>6,7,19</sup>. One difference between PBP and PAO is in the amount of leucine; therefore, it is essential to understand the impact of this and other differences in MPS.

### *Plant-based protein quality*

The quality of dietary protein is evaluated about human needs, considering the protein's ability to be digested and, consequently, its amino acids to be absorbed and retained by the body to support the renewal of body proteins<sup>20,21</sup>. When comparing gram for gram, the quality of PBP differs from PAO (Table 1). PBP is less digestible due to structural differences in the protein itself and antinutritional factors in their food sources (in the food matrix). The secondary structure of PBP is characterized by low  $\alpha$ -helix and high  $\beta$ -sheet conformation that facilitates aggregation and resistance to proteolysis. By extension, PBP food sources contain non-starch, non-amylase-digestible polysaccharides, which prevent access to proteolytic enzymes. They also have antinutritional factors such as phytic acid, hemagglutinins, glucosinolates and tannins that interfere with digestibility and absorption<sup>8,9</sup>.

In addition to being more difficult to digest compared to PAO, PBP have a smaller amount of indispensable amino acids such as leucine, lysine and methionine and the conditionally indispensable amino acid cysteine<sup>22</sup>. This difference can directly impact MPS. Studies in humans have already documented how the same absolute amount of milk protein and isolated soy protein (equivalent in nitrogen content) were directed differently to the splanchnic and peripheral tissues. Soy protein amino acids were directed to more remarkable splanchnic protein synthesis, greater tissue oxidation in this region and converted to urea to a greater extent than milk protein amino acids. As a result, soy protein amino acids were less available for protein synthesis in skeletal muscle. When soy protein is isolated, its digestibility is similar to that of milk protein. Therefore, when comparing gram for gram, the reason may be related to the difference in the content of essential amino acids<sup>23-25</sup>.

Since the limiting factor for MPS is the availability of all essential amino acids (especially leucine) and the lack of one or more amino acids can compromise the anabolic response<sup>5</sup>, the need for nutritional adjustments to correctly adjust the replacement of PAO by PBP is recognized.

**Table 1** – Food sources of animal and vegetable protein: the amount of protein, EAA, leucine and quality indicators.

Source	Protein/100g	EAA (g)	Leucine (g)	PDCAAS	DIAAS
<b>Source animal</b>					
Whey protein isolate	90 <sup>2</sup>	56.5 <sup>2</sup>	14.4 <sup>2</sup>	100 <sup>6</sup>	109 <sup>6</sup>
Egg, whole	12.6 <sup>1</sup>	5.5 <sup>1</sup>	1.1 <sup>1</sup>	100 <sup>7</sup>	113 <sup>7</sup>
Milk, whole	3.2 <sup>1</sup>	1.4 <sup>1</sup>	0.3 <sup>1</sup>	100 <sup>7</sup>	114 <sup>7</sup>
Ckicken breast grilled	31.0 <sup>1</sup>	12.9 <sup>1</sup>	2.3 <sup>1</sup>	100 <sup>7</sup>	108 <sup>7</sup>
Bovine meat	27.7 <sup>1</sup>	11.6 <sup>1</sup>	2.2 <sup>1</sup>	92 <sup>7</sup>	99 Boiled <sup>8</sup> 91 Roasted 80 Grilled
<b>Source vegetable</b>					
Soy protein isolate	90 <sup>3</sup>	38.6 <sup>3</sup>	8.2 <sup>3</sup>	100 <sup>6</sup>	90 <sup>6</sup>
Pea protein isolate	85 <sup>4</sup>	38.9 <sup>4</sup>	8.2 <sup>4</sup>	89 <sup>6</sup>	82 <sup>6</sup>
Chickpeas, boiled	8.9 <sup>1</sup>	3.2 <sup>1</sup>	0.6 <sup>1</sup>	74 <sup>7</sup>	83 <sup>7</sup>
Cooked rolled oats (porridge)	2.5 <sup>1</sup>	1.0 <sup>1</sup>	0.2 <sup>1</sup>	67 <sup>6</sup>	54 <sup>6</sup>
Pea, boiled	7.1 <sup>1</sup>	2.3 <sup>1</sup>	0.5 <sup>1</sup>	60 <sup>6</sup>	58 <sup>6</sup>
Baked beans	4.8 <sup>1</sup>	1.8 <sup>1</sup>	0.4 <sup>1</sup>	60 <sup>7</sup>	56 <sup>7</sup>
Soy-based tofu	17.3 <sup>1</sup>	6.5 <sup>1</sup>	1.4 <sup>1</sup>	56 <sup>7</sup>	52 <sup>7</sup>
Baked rice	2.7 <sup>1</sup>	1.0 <sup>1</sup>	0.2 <sup>1</sup>	56 <sup>7</sup>	57 <sup>7</sup>
Roasted peanut	23.7 <sup>1</sup>	7.4 <sup>1</sup>	1.5 <sup>1</sup>	51 <sup>6</sup>	43 <sup>6</sup>
Rice protein isolate	90 <sup>5</sup>	28.2 <sup>5</sup>	6.3 <sup>5</sup>	42 <sup>6</sup>	37 <sup>6</sup>
Wheat bread	12.0 <sup>1</sup>	3.5 <sup>1</sup>	0.8 <sup>1</sup>	28 <sup>7</sup>	29 <sup>7</sup>

**EAA:** Essential Amino Acids. The most used indicators to assess protein quality are **PDCAAS** and **DIAAS**. The **PDCAAS** (Protein Digestibility Corrected Amino Acid Score) is determined by calculating the ratio between the concentration of the limiting amino acid (smallest amount) in the test protein and the concentration of the same amino acid in a reference protein. This ratio is adjusted for true protein digestibility, representing the difference between ingested nitrogen and fecal nitrogen excreted<sup>20</sup>. The **DIAAS** (Digestible Indispensable Amino Acid Score), a more recent and considered superior method, uses the true ileal digestibility coefficient (determined at the end of the small intestine where amino acids are absorbed) rather than the true digestibility of fecal nitrogen. The DIAAS values are not truncated to the upper limit of 100<sup>21</sup>. Values less than 100 characterize a protein that cannot fully meet the body's indispensable amino acid needs. Protein sources of animals are highly digestible, with digestibility greater than 90%. Protein sources of vegetable origin have lower scores, ranging from 45 to 80% (except for isolated soy protein, considered a reference). Thus, fewer amino acids from a plant source are absorbed by the small intestine resulting in less availability in the blood. **References:** 1.USDA<sup>22</sup>; 2. *Whey protein isolate* (8855®, Fonterra); 3.*Soy protein isolate* (Supro 670®, Solae); 4.*Pea protein isolate* (Nutralys S85®, Roquette); 5.*Rice protein isolate* (Oryzatein 90®, Axiom Foods); 6.Rutherford et al.<sup>26</sup>; 7.Marinangeli et al.<sup>27</sup>; 8.Hodgkinson et al.<sup>28</sup>.

### Plant-based protein and MPS

As the current paper presents a review and synthesis of current evidence, Table 2 summarizes the only three meta-analysis studies of randomized clinical trials published until June 2021 that investigated the effect of PBP supplementation compared to PAO when combined with RE in MM and muscle strength outcomes. The meta-analyses only included studies with intervention time above six weeks, as the increase in MM is defined as the result of chronic stimulation of the MPS through repeated sessions of RE and positive net protein balance<sup>5,7</sup>.

In the meta-analysis by Morton et al.<sup>29</sup>, the most significant published to date on the topic, the primary objective was to determine the effect of protein supplementation associated with prolonged RE on body composition and muscle strength. The evaluation of the effect of the protein source was conducted in the secondary analyses. The meta-analysis included a total of 1,863 healthy, trained and untrained individuals. The authors found that protein supplementation, to raise the average initial intake from 1.4 ± 0.4 g/kg to 1.8 ± 0.7 g/kg body mass/day,

increased MM and muscle strength during prolonged RE independent of food source (whey protein vs. isolated soy and byproducts). However, this effect was influenced by age and physical training status, and these results are essential to be highlighted. Regardless of food source, protein supplementation led to more significant MM gain in trained individuals than untrained individuals and had no effect in older individuals (> 45 years). Regarding the status of physical training, it has been shown that in beginners RE is a determinant of a more significant impact for the MM gain compared to the amount and source of protein<sup>30,31</sup>. Physical training, over time, attenuates post-exercise protein turnover and limits muscle growth potential<sup>32</sup>. About the lack of protein supplementation in older individuals (> 45 years) - for the authors, the reason may be related to the dose of supplemented protein. The dose was lower in studies with older subjects (~20 g/day) than those with younger subjects (~40 g/day). In this sense, even though the RE sensitizes the muscles to hyperaminoacidemia, it is essential to consider each individual's inherent specificity. Trained and older individuals are resistant to anabolic stimuli and have

**Table 2** – Summary of meta-analysis studies that evaluated the effect of plant-based protein supplementation compared to animal protein supplementation when associated with resistance exercise on muscle mass and strength outcomes.

Author	Study	Inclusion criteria	Characteristics of the clinical trials included in the meta-analysis	Main results
Morton et al. <sup>29</sup>	<p><b>Study:</b> systematic review, meta-analysis and meta-regression of randomized clinical trials</p> <p><b>Objective:</b> To determine whether dietary protein supplementation increases MM and strength RE-induced</p> <p><b>Secondary analysis</b> Determine the difference/effect between:</p> <ul style="list-style-type: none"> <li>▪ food source of supplementation (whey vs. soy)</li> <li>▪ trained vs. untrained</li> <li>▪ &lt; 45 vs. &gt; 45 years old</li> <li>▪ supplementation vs. RE</li> </ul>	<p>Healthy trained and untrained adults</p> <p>Dietary protein supplementation</p> <p><b>Weekly RE frequency:</b> ≥ 2 x/week</p> <p><b>RE duration:</b> ≥ 6 weeks</p>	<p>49 studies between 1962 and 2016</p> <p>1,863 individuals</p> <p><b>Dietary protein supplementation:</b> whey, casein, isolated soy and derivatives, peas, milk, beef</p> <p><b>Weekly RE frequency:</b> 2 to 5 x/week</p> <p><b>RE duration:</b> 6 to 52 weeks</p> <p><b>Initial protein intake:</b> 1.4 ± 0.4 g/kg body weight/day</p>	<p>Protein supplementation, to raise the intake to 1.8 ± 0.7 g/kg body mass/day (-1.6 g; 95%CI 1.03 - 2.2 g):</p> <ul style="list-style-type: none"> <li>▪ ↑ MM and muscle strength regardless of food source (whey vs. soy)</li> <li>▪ ↑ MM in trained compared to untrained individuals and had no effect in older individuals (&gt; 45 years)</li> </ul>
Messina et al. <sup>33</sup>	<p><b>Study:</b> meta-analysis of randomized clinical trials</p> <p><b>Objective:</b> to compare soy protein supplementation with animal protein on increases MM and strength RE-induced</p> <p><b>Secondary analysis</b> Determine the difference/effect between:</p> <ul style="list-style-type: none"> <li>▪ soy protein vs. whey</li> <li>▪ soy protein vs. other animal proteins</li> </ul>	<p>Healthy trained and untrained adults</p> <p><b>Dietary protein supplementation:</b> adding soy protein to the diet compared to adding non-soy protein</p> <p><b>Weekly RE frequency:</b> ≥ 2 x/week</p> <p><b>RE duration:</b> ≥ 6 weeks</p>	<p>9 studies until November 2017</p> <p>351 individuals</p> <p><b>Dietary protein supplementation:</b> isolated soy and by-products, whey, beef, milk</p> <p><b>Weekly RE frequency:</b> 2 to 5 x/week</p> <p><b>RE duration:</b> 6 to 36 weeks</p> <p><b>Initial protein intake:</b> 1.0 g/kg body weight/day</p>	<p>Protein supplementation, to raise intake to -1.8 g/kg body mass/day, resulted in ↑ MM and muscle strength regardless of food source.</p>

RE, resistance exercise; MM, muscle mass; vs., versus.

**Table 2** – Summary of meta-analysis studies that evaluated the effect of plant-based protein supplementation compared to animal protein supplementation when associated with resistance exercise on muscle mass and strength outcomes (cont.).

Author	Study	Inclusion criteria	Characteristics of the clinical trials included in the meta-analysis	Main results
Lim et al. <sup>34</sup>	<p><b>Study:</b> systematic review and meta-analysis of randomized clinical trials</p> <p><b>Objective:</b> to evaluate the differences in the effect of animal and plant-based protein in increasing MM and muscle strength</p> <p><b>Secondary analysis</b> Determine the difference between:</p> <ul style="list-style-type: none"> <li>▪ &lt; 50 vs. &gt; 50 years old</li> <li>▪ RE and no RE</li> </ul>	Adults, healthy and unhealthy, trained and untrained, who evaluated the effect of plant-based protein supplementation compared to other proteins, regardless of whether there were other interventions such as a calorie-restricted diet	<p>16 studies until June/2020 with 788 individuals, as follows:</p> <ul style="list-style-type: none"> <li>▪ 11 studies with RE lasting between 6 weeks and 9 months (345 subjects)</li> <li>▪ 2 studies with trained individuals (39 individuals - 21 to 38 years)</li> <li>▪ 3 studies with ER over 50 years (97 individuals - 61 to 67 years)</li> </ul> <p>▪</p> <p><b>Dietary protein supplementation:</b> soy and by-products, isolated peas and rice, whey, milk and by-products, beef</p> <p><b>Initial protein intake:</b> 0.9 g/kg body weight/day</p>	<p>Results of analyzes of RE studies:</p> <ul style="list-style-type: none"> <li>▪ the highest reported protein supplementation increased intake to 3.1 g/kg body mass/day</li> <li>▪ the protein source did not affect MM gain and muscle strength - other variables were not considered (age, physical training status, disease)</li> </ul>

RE, resistance exercise; MM, muscle mass; vs., *versus*.

a higher leucine threshold<sup>11,12</sup>. Therefore, according to Morton et al.<sup>29</sup>, they are the ones who will benefit the most from higher protein intake to respond optimally to the increase in MM to supplementation.

Messina et al.<sup>33</sup> performed a meta-analysis to compare soy protein supplementation vs. animal proteins in MM gain and muscle strength in response to RE. The meta-analysis included 351 healthy, trained, and untrained individuals. The authors found that protein supplementation, to raise the average initial intake from ~1.0 g/kg to ~1.8 g/kg body mass/day - regardless of the food source (isolated soy and derivatives vs. whey protein; isolated soy and derivatives vs. other proteins - beef and milk), increased MM and strength. The relatively small number of individuals did not provide the appropriate power to analyze the influence of age and physical training status on the results. For clarification, of the nine studies analyzed, seven were with untrained individuals, totaling 304 participants (out of 351).

The most recent meta-analysis extended the study by Messina et al.<sup>33</sup> beyond soy protein. Lim et al.<sup>34</sup> investigated the difference between the supplementation of various PBP (soy - isolated, protein drinks and bars, pea, rice isolated) vs. PAO (whey, casein, milk and dairy products, beef) in MM gain and strength in response to RE. In addition to studies with healthy individuals, trained and untrained, the authors included studies with unhealthy individuals and those that did not associate RE. Of the 16 studies evaluated from the meta-analysis, 11 studies evaluated the effect of protein supplementation associated with RE (345 individuals, 306 untrained individuals, the lowest reported initial intake was 0.9 g/kg body mass/day and the highest reported intake with supplementation it was 3.1 g/kg body mass/day). In this group, found no difference between PBP and PAO supplementation in MM and strength outcomes. This analysis did not take the age of individuals, physical training status and disease into account.

The three meta-analyses<sup>29,33,34</sup> show essential answers about the effect of PBP supplementation associated with RE on the increase of MM and muscle strength: no differences were found between soy protein vs. whey; between soy protein vs. beef and milk; and between pea and rice vs. whey, casein, milk and dairy products and beef. But there are still questions to be answered. Trained and older individuals need greater protein intake to optimize MM gain and muscle strength associated with RE<sup>11,12,29,32</sup>. However, the two meta-analyses that assessed the effect of PBP on these outcomes did not perform this analysis due to the low number of studies.

Another critical issue to be highlighted is that the randomized clinical trials available in the literature, included in the meta-analyses<sup>29,33,34</sup>, evaluated the supplementation of PBP to the omnivorous diet. These studies did not evaluate the effect of a diet with exclusive intake of plant foods.

In fact, clinical trials did not assess dietary patterns. They assumed that subjects randomized to the PAO and PBP-supplemented group consumed richer diet in animal and plant protein, respectively. Collectively, protein supplementation increased daily protein intake (~1.8g/kg body mass/day - regardless of PAO or PBP) by current optimal intake recommendations to stimulate RE-associated MPS<sup>16,17</sup>. However, the lack of difference in the effect between PBP and PAO on MM gain and muscle strength cannot be generalized because the addition of a vegetable protein to the omnivorous diet does not provide a complete understanding of the role that the food source plays in mediating muscle anabolism in response to exercise.

This issue is essential because it should not make adaptations in a vegan diet from absolute exchanges between foods as some short- and long-term trials have shown that MPS stimulation with PBP is dose-dependent. In the short term, the MPS response to acute PBP supplementation after RE (3 to 5 h) was of less magnitude than the same absolute amount of PAO, that is, when combined according to nitrogen content<sup>25,35,36</sup>. This result partially contributes to PBP amino acids being more directed toward splanchnic protein synthesis and oxidation instead of MPS<sup>23,24</sup>. However, Gorissen et al.<sup>37</sup> demonstrated that acute supplementation of a larger amount of hydrolyzed wheat protein (60 g protein with 4.4 g leucine) equally increased MPS after RE (up to 4 h) compared to casein dose (35 g protein and 3.2 g leucine). The study by Joy et al.<sup>37</sup> showed that it was necessary to ingest a bigger amount of isolated rice protein during eight weeks of RE to ensure a minimum dose of leucine to stimulate MPS and MM gain similar to whey. Thus, when replacing PAO with PBP, it is essential to seek not the equivalence of the absolute amount of protein, but the supplementation of amounts that guarantee the equivalence of indispensable amino acids, especially leucine, since the intracellular increase in this amino acid is the primary driver of the MPS<sup>6,19</sup>.

This methodological gap in the studies was identified by Brazilian researchers who published this year (2021) the first clinical trial in the scientific literature to assess the effect of the protein source in a vegan diet versus an omnivorous diet on MM gain and strength in response to 12 weeks of RE<sup>39</sup>. The trial was not randomized. Participants: healthy individuals who already had a diet exclusively in vegetables or omnivorous for at least one year, physically active, but without RE practice for at least one year, without using protein supplements and nutritional ergogenic resources (caffeine, creatine, and others) and no history of anabolic steroid use. The participants' usual diet was assessed for four weeks before the start of the study to adjust their daily protein intake. Over the 12 weeks, every day, twice a day (breakfast and at night snack), the individuals consumed powdered protein supplements (isolated whey or soy isolated) to complement the protein in the usual diet

(whole foods) until reaching 1.6 g/kg body weight/day. As a result, individuals on a vegan diet (whole foods and supplemental soy protein isolate) showed an increase in MM and strength similar to those on an omnivorous diet. The study is the first with evidence that the dietary source of protein does not affect ER adaptations in young, untrained men who consume the amount of protein recommended in the literature (1.6 g/kg body mass/day). The study is promising and launches a series of observations to be considered in future investigations. The initial intake of individuals on the vegan diet was lower than that of individuals on the omnivorous diet. Therefore, needed a higher absolute dose of supplemental soy protein to reach 1.6 g/kg body mass/day (~ 58 g of protein isolated from soy versus ~41 g whey protein isolate). Supplementing the diet with a processed and isolated protein powder also contributed to increasing the intake of essential amino acids, especially leucine, but not enough to equal the intake of individuals with an omnivorous diet (respectively: indispensable amino acids ~ 21g versus ~ 26 g /meal; leucine ~ 2.25 g versus ~ 2.75 g/meal). However, it was enough to reach the intake range recommended by international nutrition societies to maximize muscle anabolism in response to RE: indispensable amino acids from 6 to 15 g/meal, with 0.7-3 g of leucine<sup>16,17</sup>. Another critical issue is that the vegan diet has twice as much fiber as the omnivorous diet, increasing the intake of antinutritional factors and decreasing protein digestibility. Thus, the authors point out the need for a longer-term study to assess the long-term impact of these specific issues and expand the investigation with other individuals, especially trained and older ones.

#### *Adequacy of plant-based protein intake to stimulate MPS*

Generally, the adequacy of protein intake in a diet with whole-plant foods does not seem to be so simple when the objective is to optimize adaptations by RE of MM and muscle strength. Considering that PBP has less indispensable amino acids, has lower digestibility and still differs from each other in these characteristics (Table 1), we list three challenges for the adequacy of protein in a vegan diet to maximize MPS in response to RE. The first challenge is to adjust the total amount of protein to guarantee the equivalence of essential amino acids, especially leucine<sup>6,8</sup>. The second challenge is to achieve this adequacy for trained and older individuals who benefit from a higher protein intake<sup>11,29</sup>. The third and most significant challenge is the dietary adequacy for athletes who, by themselves, need a greater

caloric intake to supply the energy expenditure of the intense physical training routine<sup>40</sup>.

The first strategy is to use vegetable food sources that have undergone processing to isolate proteins sold in powder form. Powder processed PBP offers the advantage of being devoid of antinutritional factors and can help optimize the energy density of the diet. Attempting to consume only whole foods to reach the recommended amounts of protein, essential amino acids, and leucine can increase the intake of calories and antinutritional factors. Among the PBP sources, the quality of isolated soy protein is superior to that of other PBP and relatively similar to that of PAO<sup>8,9</sup>. This strategy can be helpful for the elderly who have a decreased appetite and other factors inherent to aging, which by themselves decrease food intake<sup>13</sup>.

The second strategy is to prioritize different plant foods with protein sources to achieve the proper amount of essential amino acids. For example, combine foods with less lysine and more methionine (wheat, rice and corn) with more lysine and less methionine (beans, oats, soybeans and peas). It is currently possible to find combinations of powdered processed proteins, for example, peas and rice. A third strategy is using preparation techniques such as immersion in water and cooking to increase the kinetics of amino acid digestion and absorption<sup>8,9</sup>. It is essential to highlight that in a diet with an exclusive intake of plant foods, it is necessary to adjust the amount of protein and vitamin B12, iron, calcium, and creatine, which are found in PAO and contribute directly and indirectly to MPS<sup>40</sup>.

#### CONCLUSION

In an omnivorous diet, there is solid evidence that PBP supplementation, to the point of raising intake to ~1.8 g/kg body mass/day, has a similar ability to PAO supplementation in increasing muscle mass and strength exercise-associated young and untrained individuals. In a diet with exclusive intake of plant foods, the only clinical trial found with young and untrained, presents promising evidence that the dietary source of protein does not affect the adaptations induced by resistance exercise with adequate protein intake of ~ 1.6 g/kg body weight/day. For now, in a vegan diet, to achieve protein recommendations to support muscle anabolism, strategies should be used, such as increasing the absolute amount of protein, combining different food sources, and using processed supplements.

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