Whey protein (WP) is a highly nutritious, commercially available alternative food source that is used primarily as a food supplement by athletes and physically active individuals to provide them with essential amino acids and bioactive peptides, and additional benefits have been attributed to WP consumption. In this context, the objective of this review was to explore current evidence regarding the consumption of different WP supplements in sports nutrition to elucidate their efficiency in affecting muscle hypertrophy, physical performance, response to muscle injury, weight loss, and body composition changes. Furthermore, these effects were assessed by comparing whey protein hydrolysate (WPH), whey protein concentrate (WPC), and whey protein isolate (WPI) supplementation. Supplementation with WPI or WPC was related to increased muscle protein synthesis (MPS), and WPH caused muscle hypertrophy and improved physical performance. Compared to WPC and WPI, WPH improved peak torque associated with strength training without reducing the creatine kinase (CK) and tumor necrosis factor alpha (TNF-α) levels in this type of physical activity, and the decreases in CK and lactate dehydrogenase (LDH) associated with aerobic exercise were significant. Supplementation with WPC resulted in weight loss, satiety, and improved body composition, without compromising whole-body lean mass loss. WPH was more effective than WPC and WPI regarding improved peak torque and muscle hypertrophy associated with strength training, and WPH reduced muscle damage associated with aerobic exercise via decreased CK levels.

**LIST OF ABBREVIATIONS**


**INTRODUCTION**

The search for nutrients in alternative food sources has been widely explored [Oliveira et al., 2012]. Accordingly, whey, a product of cheese manufacture, has a significant commercial value due to its wide availability, low production cost, and a high nutritional value [Kankananme et al., 2015]. Its use in the production of fruit-flavored dairy drinks, with fruit pulps such as acerola [Cappato et al., 2018] and chocolate [Monteiro et al., 2018] has increased, constituting an alternative to yogurt. It has also increased in the processing of dairy foods such as whey-grape juice [Amaral et al., 2018] and even in probiotic dairy drink formulations, added with inulin [Guimarães et al., 2018]. Whey accounts for approximately 20 to 30% of the total protein content of bovine milk [Devries & Phillips, 2015]; β-lactoglobulin (BLG) (45–57%) is the most abundant protein, followed by α-lactoalbumin (ALA) (15–25%), immunoglobulins (10–15%), glycomacropeptide (10–15%), bovine serum albumin (10%), lactofermin (~1%), and lactoperoxidase (<1%) [Bendtsen et al., 2013].

BLG is composed of approximately 26% of branched-chain amino acids (BCAAs) (L-leucine, L-valine, and L-isoleucine) [Pal & Radavelli-Bagatini, 2013], which are among...
the nine essential amino acids (isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, and histidine) [Waitzberg & Logullo, 2006], which are essential for muscle protein synthesis (MPS) [Burd et al., 2017] and, therefore, for muscle hypertrophy [Aoi et al., 2011]. Hypertrophy, increased lean body mass [Volek et al., 2013], and reduced muscle fatigue [Babault et al., 2014] are observed when strength training is followed by BCAA supplementation ingestion because BCAs minimize lean body mass loss and promote muscle regeneration [Aoi et al., 2011] after injuries caused by exhaustive exercise [Burd et al., 2017]. However, these processes occur as long as they are combined with a positive nitrogen balance [McArdle et al., 2014]; although all 20 different types of amino acids are essential to protein synthesis, the organism needs a dietary intake of the nine essential amino acids, including BCAs. The absence or inadequate intake of any of these amino acids leads to a negative nitrogen balance, and might cause weight loss and hinder growth, which does not benefit the MPS process and muscle hypertrophy [Mahan & Escott-Stump, 1998].

Using different technologies for production [Biocatalysts, 2014], whey proteins are sold as sports supplements termed whey protein (WP) [Haraguchi et al., 2006]. These products are available as whey protein concentrate (WPC), isolate (WPI), and hydrolysate (WPH) varieties [Pal & Radavelli-Bagatini, 2013]. WPC contains approximately 25–89% protein, with or without lactose; WPI has approximately 90–95% protein, usually without carbohydrates; and WPH has higher peptide fractions [Marshall, 2004].

WP is a complete protein containing all the essential amino acids [Aoi et al., 2011] required for MPS [Stark et al., 2012], enabling muscle hypertrophy [Devries & Philips, 2015] and improved strength performance [Chen et al., 2014]. Furthermore, essential amino acids improve body composition [Devries & Phillips, 2015], reduce immunosuppression and inflammation caused by muscle injury during physical training, and attenuate oxidative stress induced by exercise because they have antioxidant effects, and comprise a nutritional supplement also referred to as immune-nutrient [Cruzat et al., 2014]. In addition, other amino acids such as L-glutamine and L-arginine might also play these roles. Therefore, protein and amino acid supply is required for optimal synthesis and concentrations of immune-related proteins, including cytokines and antibodies. Amino acids will help regulate the main metabolic pathways of immune cells, from cell response to oxidative stress, and anti-inflammatory response, all of which are essential for an optimal immune function and for recovery from intense periods of physical training [Cruzat et al., 2014]. For athletes, WPH provides greater advantages over WPC and WPI [Biocatalysts, 2014] (Figure 1) because WP hydrolysis releases biologically active amino acids and peptides [Madureira et al., 2010].

However, for athletes and physically active people, the issue of whether to supplement remains controversial due to inconsistent data on WP varieties. Several factors, including dosage, mode of administration, intake time(s), duration of use, and integration into a specific physical training program, affect protein supplementation effects [Naclerio & Larumbe-Zabala, 2016].

These factors highlight the need to review studies related to WP to elucidate its effects on hypertrophy, physical performance, response to muscle injury, weight loss, and change in body composition and to compare the effects of WPH, WPC, and WPI supplementation.

**EFFECTS OF WHEY PROTEIN CONCENTRATE, WHEY PROTEIN ISOLATE, AND WHEY PROTEIN HYDROLYSATE CONSUMPTION ON MUSCLE HYPERTROPHY AND PHYSICAL PERFORMANCE**

Muscle hypertrophy is the main objective of individuals seeking improved athletic performance. Muscle mass gain requires adequate nutrient intake and primarily requires protein [Rigon & Rossi, 2012]. The recommended dietary allowance (RDA) of protein established by the Dietary References Intakes (DRI) of the Food and Nutrition Board of the Institute of Medicine (IOM) of the United States is 0.8 g/kg weight/day [IOM, 2002/2005]. However, protein intake greater than the RDA is required for individuals to optimize their adaptation to strength training [Chen et al., 2014]. These individuals should maintain moderate protein consumption ranging from 1.4 to 2.0 g protein/kg body weight/day [Jäger et al., 2017; Roberts et al., 2017].

Accordingly, the high-quality proteins and essential amino acids found in WP make this supplement one of the most widely used for MPS, ensuring good physical performance [Monteyne et al., 2018; Morton et al., 2018]. Table 1 outlines the results on muscle hypertrophy and physical performance from studies of supplementation with WPC, WPI, and WPH.

Muscle hypertrophy associated with WP supplementation can improve the performance of strength athletes and athletes who perform aerobic sports, such as marathons, cycling, and swimming [Chen et al., 2014]. Several studies on WP supplementation before and immediately after each workout involving different physical exercises showed muscle hypertrophy [Farup et al., 2014b; Rahbek et al., 2014; Stefanetti et al., 2014].

Athletes who supplement with WPH before and after each running session in a combined daily intake of 1.8 g protein/kg weight per day showed improved functional strength and physical performance [Hansen et al., 2015]. Conversely, supplementation with WPH or WPC immediately before and after the daily workout in a combined daily intake of 1.3 g protein/kg weight per day failed to improve physical performance, and only WPC consumption increased muscle mass
TABLE 1. Effects of supplementation with WPC, WPI, and WPH on muscle hypertrophy and physical performance.

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Groups</th>
<th>Type of study</th>
<th>Supplementation</th>
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<th>Type of exercise</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen et al. [2015]</td>
<td>18 elite runners (men and women) divided into 2 similar groups in number, age, height, weight, and %BF</td>
<td>2 groups: WPH (n=9) and CHO (n=9)</td>
<td>randomized, controlled intervention</td>
<td>0.3 g/kg weight WPH 10 minutes before and 0.3 g WPH/kg weight + 1 g CHO/kg weight 15 minutes after each workout; 1.3 g/kg weight CHO 10 minutes before and 15 minutes after each workout diluted in non-caloric iced tea, ingesting anything except water up to 2 h after each workout</td>
<td>with controlled diet: 15% PTN (1.8 g/kg weight), 63% CHO and 22% LIP</td>
<td>1 week</td>
<td>13 aerobic workouts with a 4-km run</td>
<td>WPH increased physical performance</td>
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<td>Lillo et al. [2014]</td>
<td>24 elite soccer players (18 ± 0.8 years, 73.95 ± 4.87 kg, and 178.5 ± 0.48 cm)</td>
<td>3 groups: WPH (n=8), WPC (n=8), and CHO (n=8)</td>
<td>double-blind regarding dietary supplementation</td>
<td>0.5 g WPH, WPC, or CHO/kg weight, immediately before and immediately after the daily training or soccer league matches, including rest days</td>
<td>with controlled diet by a nutritionist: 2.3 g/kg weight PTN (1.3 g food and 1.0 g supplement), totaling 10 to 15% total energy (diet + supplement)</td>
<td>12 weeks</td>
<td>aerobic activity between training and soccer league matches</td>
<td>WPC increased LBM</td>
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<td>Macnaughton et al. [2016]</td>
<td>30 men subjected to strength training allocated to 2 groups: lower LBM (≤65 kg) (21.3 ± 2.2 years, 1.78 ± 0.05 m, 76.8 ± 4.8 kg, 18.8 ± 3.7% BF) and higher LBM (≥70 kg) (23.2 ± 3.5 years, 1.84 ± 0.05 m, 98.8 ± 7.8 kg, 17.3 ± 4.9% BF)</td>
<td>2 groups: lower LBM (n=15) and higher LBM (n=15)</td>
<td>randomized, double-blind, cross-sectional</td>
<td>20 g WPI or 40 g WPI; diluted in 500 mL water; immediately after the workout</td>
<td>without controlled diet</td>
<td>2 weeks</td>
<td>2 strength training interventions on upper and lower limbs</td>
<td>WPI caused MPS 3 h after ingesting 40 g WPI</td>
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<td>Mitchell et al. [2017]</td>
<td>16 healthy, physically active men divided into 2 groups: WPC (52.6 ± 3.9 years, 26.7 ± 2.5 kg/m²) or mWPC (51.0 ± 3.5 years, 26.5 ± 3.1 kg/m²)</td>
<td>2 groups: WPC (n=8) and mWPC (n=8)</td>
<td>randomized, double-blind, parallel</td>
<td>20 g WPC or 20 g mWPC and containing less than 2 g LIP and approximately 2 g CHO; diluted in 350 mL of water</td>
<td>without controlled diet</td>
<td>8 h</td>
<td>without physical exercise intervention</td>
<td>mWPC and WPC caused MPS 1.0 h after their ingestion</td>
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<td>Atherton et al. [2010]</td>
<td>8 healthy, untrained but physically active men (21 ± 2 years; 22.9 ± 0.9 kg/m² BMI)</td>
<td>1 group: WPI (n=8)</td>
<td>controlled intervention</td>
<td>0.7 mg/kg weight/h leucine in continuous infusion + 48 g WPI diluted in 500 mL water, equivalent to 20 g EAA; after 2.5 h intravenous administration of leucine</td>
<td>without controlled diet</td>
<td>8.5 h</td>
<td>72 h after the last high-intensity strength training session (usual)</td>
<td>WPI caused MPS 45–90 minutes after ingesting 48 g WPI</td>
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<td>Areta et al. [2013]</td>
<td>24 trained healthy men (minimum of 2 years of high-intensity resistance training more than 2 times per week) matched by body mass</td>
<td>3 groups: PULSO (n=8), INT (n=8), and BOLUS (n=8)</td>
<td>controlled intervention</td>
<td>80 g WPI over 12 h of recovery according to the following protocols: 8 × 10 g every 1.5 h (PULSE), 4 × 20 g every 3 h (INT), or 2 × 40 g in 6-h intervals (BOLUS)</td>
<td>with controlled diet 3 days before the experimental test: 45 kcal/kg LBM, 1.5 g PTN/kg weight and 4 g CHO/kg weight, LIP (remaining energy)</td>
<td>12 h</td>
<td>single strength training session: bilateral leg extension</td>
<td>PULSO, INT and BOLUS increased MPS between 1 and 12 h, but INT caused higher MPS than PULSO and BOLUS</td>
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<tr>
<td>Study</td>
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<td>West et al. [2011]</td>
<td>8 healthy, untrained but physically active men (21.5 ± 1 years, 1.81 ± 0.02 m, 80.1 ± 3.5 kg, 24.3 ± 0.8 kg/m² BMI)</td>
<td>2 groups: PULSO (n=8) and BOLUS (n=8) for both sessions</td>
<td>randomized, cross-sectional</td>
<td>25 g WPC (BOLUS) or 10 drinks of 2.5 g WPC every 20 min (PULSO); diluted in water, after the workout</td>
<td>without controlled diet</td>
<td>5 h per intervention</td>
<td>2 strength training interventions: bilateral leg extension; 30-day interval between interventions</td>
<td>BOLUS improved MPS and anabolic signaling and increased the concentration of EAA 60 min 1 to 3 h and 3 to 5 h after the workout</td>
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<td>Volek et al. [2013]</td>
<td>63 healthy men divided into 3 groups: WPC (22.8 ± 3.7 years, 171.8 ± 10.3 cm, 74.1 ± 15.7 kg and 25.3 ± 12.0% BF); CHO (22.3 ± 3.1 years, 172.0 ± 8.7 cm, 72.4 ± 14.9 kg and 26.4 ± 8.7% BF); and SOY (24.0 ± 2.9 years, 170.5 ± 2.9 cm, 72.0 ± 8.4 kg and 27.3 ± 11.0% BF)</td>
<td>3 groups: WPC (n=19), isocaloric CHO (n=22) and isonitrogenous soy protein isolate, free isoflavone (SOY) (n=22)</td>
<td>double-blind, prospective, parallel</td>
<td>1.4, 1.1, and 1.4 g/kg weight WPC, CHO, and SOY, respectively; CHO contained 0.8 g PTN, WPC 21.6 g PTN, and SOY 20.0 g PTN; diluted in 240 mL water; ingested after training and on non-training days, in the morning with breakfast</td>
<td>with diet controlled by a nutritionist</td>
<td>9 months</td>
<td>strength training program with 96 exercises for upper and lower muscles from 30 to 75 minutes</td>
<td>WPC increased LBM</td>
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<td>Stefanetti et al. [2014]</td>
<td>24 healthy, untrained men (181.5 ± 1.5 cm; 78.1 ± 1.8 kg; 23.9 ± 0.8 years and 16 ± 0.9% BF)</td>
<td>2 groups: WPH (n=12) and CHO (n=12)</td>
<td>randomized, double-blind</td>
<td>0.3 g WPH + 0.3 g CHO/kg LBM, totaling 19.5 g WPH + 19.5 g CHO, or 0.6 g isocaloric CHO/kg LBM, totaling 39 g CHO, diluted in artificially flavored water; half of the solution ingested before and the other half immediately after each workout, without ingesting calories 1½ h before and 1 h after the workout</td>
<td>without controlled diet</td>
<td>12 weeks</td>
<td>strength training; ECC and CONC unilateral leg contraction</td>
<td>WPH combined with ECC and CONC increased LBM</td>
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<td>Farup et al. [2014b]</td>
<td>22 healthy men (23.9 ± 0.8 years, 181.5 ± 1.5 cm, 78.1 ± 1.8 kg; 16.0 ± 0.9% BF)</td>
<td>2 groups: WPH + CHO (n=11) and CHO (placebo) (n=11), subdivided into 4 subgroups: WPH-ECC, Placebo-ECC, WPH-CONC, and Placebo-CONC</td>
<td>double-blinded regarding dietary supplementation</td>
<td>solution with 19.5 g WPH + 19.5 g CHO or 39 g CHO on workout days, ingesting half of the supplement immediately before the workout and the other half immediately after</td>
<td>without controlled diet</td>
<td>12 weeks</td>
<td>strength training, including ECC and CONC lower-limb strength</td>
<td>WPH-CONC showed greater muscle hypertrophy</td>
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<td>Rahbek et al. [2014]</td>
<td>24 healthy men (23.9 ± 0.8 years, 1.82 ± 0.015 m, 78.1 ± 1.8 kg and 16 ± 0.9% BF)</td>
<td>2 groups: WPH + CHO (n=12) and CHO (n=12), subdivided into 4 subgroups: WPH + CHO-ecc, CHO-ecc, WPH + CHO-conc, and CHO-conc</td>
<td>double-blinded regarding dietary supplementation</td>
<td>500 mL drink containing 0.30 g WPH + 0.30 g CHO/kg weight, totaling 19.5 g WPH and 19.5 g CHO or 500 mL with 0.60 g CHO/kg weight, totaling 39 g CHO on workout days, ingesting half immediately before the workout and the other half immediately after</td>
<td>without controlled diet</td>
<td>12 weeks</td>
<td>strength training, including ECC and CONC lower-limb strength</td>
<td>WPH + CHO showed higher muscle hypertrophy than CHO; the mode of muscle contraction had a weaker effect on muscle hypertrophy</td>
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<td>Study</td>
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<td>Hamarsland et al. [2017]</td>
<td>22 trained men and women allocated to 2 groups: WPC or NWP (25 ± 2 years; 700 ± 11.6 kg; 52.9 ± 9.6 kg MM; 21.5 ± 6.4 BF) and MP (25 ± 5 years; 72.8 ± 12.4 kg; 57.1 ± 13.5 kg MM; 19.1 ± 7.2 BF)</td>
<td>2 groups: WPC or MP (n = 10)</td>
<td>double-blind, randomized, placebo-controlled, partial crossover trial</td>
<td>20 g of WPC or NWP diluted in water and 20 g of MP (30% whey and 60% casein) immediately and 2 hours after strength training with diet guided by a nutritionist on the day before the experiment and during the rest of the trial period (2.5 days in total): 40 kcal/kg and 1.5 PTN g/kg/day. breakfast: 23 kJ, 0.11 g PTN, 0.30 g LIP and 0.58 g CHO/kg</td>
<td>2.5 days</td>
<td>lower-limb strength training</td>
<td>NWP increased the plasma leucine concentration in relation to WPC and MP. WPC increased MPS faster (within 1–3 hours post-workout) than NWP (within 1–3 hours post-workout). NWP increased MPS (1–5 h post-workout) more than MP.</td>
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</table>

BF: body fat; CHO: carbohydrates; PTN: protein; LIP: lipids; LBM: lean body mass; MPS: muscle protein synthesis; PULSO: supplemented group name; INT: intermediate (supplemented group name); BOLUS: supplemented group name; EAA: essential amino acids; ECC: eccentric exercise; CONC: concentric exercise; NWP: native whey protein; MP: milk protein.
workout period improved MPS and anabolic signaling when the protein was administered more frequently and in smaller quantities. On the other hand, Areta et al. [2013], who administered WPI gradually, 20 g every 3 h after strength training for a 12-h period, suggest that more frequent and smaller quantity supplementation may be an optimal intervention. These results suggest that increased WP intake, e.g., 20 to 25 g, in one single ingestion stimulates MPS more than repeated protein supplementation in small portions [West et al., 2011] and that the effect of modulating the distribution of protein intake on anabolic responses in the skeletal muscle has the potential to maximize training results, reaching the peak of muscle mass [Areta et al., 2013].

Furthermore, leucine consumption through WP varieties helps MPS. In a recent study by Mitchell et al. [2017], improved muscle synthesis was observed 1 h after consuming WPC microparticles (mWPC) or WPC, both with similar leucine concentrations, in physically active, healthy young men. Similarly, supplementation with WPI and leucine shortens MPS compared with supplementation exclusively with WPI [Macnaughton et al., 2016]. Atherton et al. [2010] observed increased MPS after 45–90 min when WPI intake was combined with the intravenous injection of 0.7 mg leucine/kg weight/h for 8.5 h.

Furthermore, native WP, produced by raw, unprocessed milk filtration, which is a production method that maintains milk proteins intact, has a higher leucine content than WPC, which is derived from whey [Hamarsland et al., 2017]. These authors also compared MPS in response to two 20-g doses of WPC or native WP ingested immediately and two hours after strength training and observed that native WP increased blood leucine concentrations more than WPC, although the MPS rates increased faster with WPC (within 1–3 hours post-workout), whereas native WP increased MPS rates within 1–5 hours post-workout. These results suggest that WP supplementation with leucine maximizes its effect on MPS and that leucine in connection with exercise plays a unique role in the regulation of MPS [Moberg et al., 2014]. Previous studies also suggest that leucine, composition of the protein, and rapidly ingested amino acids in the bloodstream are the major factors that determine MPS response [West et al., 2011].

According to the Food and Agriculture Organization [FAO, 2013], protein quality varies according to its amino acid content, digestibility, and bioavailability. Plant protein sources are frequently inferior in one or more essential amino acids and thus fail to meet the requirements of complete proteins, such as those contained in whey [Joy et al., 2013]. Therefore, WP quality is related to its high biological value and the content of essential amino acids [Aoi et al., 2011; Atherton et al., 2017]. Increased gains in lean body mass were observed in individuals who consumed daily isocaloric WP supplements compared with those who consumed soy protein isolate and carbohydrates, thus highlighting the importance of protein quality in strength training [Volek et al., 2013]. This discrepancy occurs because strength training combined with WP supplementation is associated with increased lean body mass compared with other isoenergetic supplements containing carbohydrates or other sources of protein [Naclerio & Larumbe-Zabala, 2016].

However, in addition to type, the effects of protein supplementation on the concentration of blood amino acids will depend on quantity [Mitchell et al., 2015] and state (whether solid or liquid) required to increase the concentration of blood amino acids, i.e., cause aminoacidemia [Baer et al., 2011], as well as absorption time and kinetics of plasma amino acids [Burd et al., 2012]. That is why consuming protein supplementation within 1 h after strength training is ideal for promoting hypertrophy and gains in muscle strength [Stark et al., 2012].

As mentioned above, protein intake regulates muscle protein synthesis in response to repeated anabolic stimuli to maintain and promote MPS, which should be considered in the development of nutritional strategies [Areta et al., 2013]. According to Devries & Phillips [2015], although protein intake is the strongest predictor of muscle hypertrophy after strength training, diets with a 20 to 35% higher protein content of total daily energy consumption maximize muscle hypertrophy compared with protein intake only a few hours before and/or after strength training. Furthermore, the quantity of muscle mass may also affect MPS, given the increased demand for amino acids, which may be met by exogenous sources [Macnaughton et al., 2016]. However, a protein intake higher than 2.0 g/kg weight/day is unlikely to provide additional gains in lean body mass [Pasiakos et al., 2013].

Protein supplements, essential amino acids, and leucine increase MPS rates while decreasing muscle protein degradation and possibly enhancing recovery after exercise [Jäger et al., 2017], although whether protein supplementation promotes hypertrophy and increases muscle strength gain remains unclear [Erskine et al., 2012] because studies have limitations, including small sample size, inaccurate measures of muscle size and strength, lack of control over previous training programs or regular protein intake, and issues with the study period or number of study variables [Nogiec & Kasif, 2013]. Furthermore, the individual response to strength training may vary between subjects [Erskine et al., 2010], and this effect may be reduced by the increased experimental control of physical activity and protein intake [Erskine et al., 2012]. The lack of studies measuring MPS also prevents the establishment of an RDA of protein during the muscle recovery period [Areta et al., 2013].

**EFFECT OF SUPPLEMENTATION WITH WHEY PROTEIN CONCENTRATE, WHEY PROTEIN ISOLATE, OR WHEY PROTEIN HYDROLYSATE ON MUSCLE INJURY**

The inflammation that occurs in response to muscle damage is induced and aggravated by the increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) [Cruzat & Tirapugli, 2009]. Although physical training stimulates ROS production, the intracellular ROS concentration may not reach harmful levels due to the increase in and adaptations of antioxidant system responses [Cruzat et al., 2014]. However, inadequate physical training and a single, high-intensity training session or excessive physical training may cause changes in the redox states, oxidative stress [Petry et al., 2014], muscle fatigue, and muscle injury [Cruzat et al., 2010].
A significant release of hemoglobin-derived Fe$^{2+}$ ions occurs during specific types of exercise, particularly those involving eccentric contractions [Welch et al., 2002]. Therefore, damage to erythrocyte membranes [Koury & Donangelo, 2003] may enhance oxidative stress, leading to fatigue and muscle damage [Niess & Simon, 2007] and thereby impairing athletic performance [Koury & Donangelo, 2003].

Moreover, ROS and RNS production may induce an increase in intracellular Ca$^{2+}$ concentrations and inactivate several enzymes involved in anaerobic and aerobic metabolism, leading to muscle fatigue [Duhamel et al., 2005].

Muscle injury, neutrophil infiltration, and ROS generation are directly related to the initiation of the inflammatory response and depend on the intensity, type, and duration of physical exercise [Niess & Simon, 2007; Petry et al., 2014]. Furthermore, during the recovery period, immunity may become compromised, thereby contributing to chronic inflammation [Cruzat et al., 2014] through considerable changes in the immune function.

The effects of exercise on the immune system are mediated by changes in the production of hormones, such as adrenaline, cortisol, and growth hormone, and pro- and anti-inflammatory cytokines [Cannon, 2000]. The increase in circulating proinflammatory cytokines induces edema and pain and worsens inflammation until this increase is reversed and recovery from muscle injury is established [Cruzat & Tirapegui, 2009].

Among the pro-inflammatory cytokines, tumor necrosis factor alpha (TNF-α) stands out [Rohde et al., 1997]. TNF-α induces inflammatory responses involving the release of cytokines that persist for up to 5 days, resulting in the pronounced accumulation of neutrophils and macrophages in the damaged tissue, where these cytokines perform key functions for damaged tissue repair [Tsivitse et al., 2003]. Circulating TNF-α levels increase one- to two-fold after strenuous and prolonged training [Ostrowski et al., 1999], and their pro-inflammatory effect decreases during moderate exercise due to the increase in anti-inflammatory cytokines [Cruzat et al., 2014], as the effects of exercise-induced cytokines depend on the type of mediator involved and on the balance between pro-inflammatory cytokines (IL-1, TNF-α, IFNα, IFNγ, TNF-β, IL-2, IL-12 e MCP-1) and anti-inflammatory cytokines (IL-4, IL-10, IL-13, IL-12p40, IL-1ra). While performing moderate exercises, the production of pro-inflammatory cytokines is negatively regulated and that of anti-inflammatory cytokines is positively regulated [Rohde et al., 1997]. During strenuous and prolonged exercises, there is an increase in the levels of circulating pro-inflammatory cytokines, such as TNF-α, counterbalanced by the production of the anti-inflammatory cytokine IL-10 [Ostrowski et al., 1999]. Therefore, plasma IL-1 and TNF-α concentrations increase one- to two-fold, while IL-6 might increase over 100 times in the skeletal muscle after the practice of prolonged physical exercises, causing IL-6 to stimulate the circulation of anti-inflammatory cytokines IL-1ra and IL-10, thus inhibiting the production of the pro-inflammatory cytokine TNF-α [Ostrowski et al., 1999].

Intense and prolonged physical training [Brancaccio et al., 2008] also increases the serum levels of creatine kinase (CK) [Brancaccio et al., 2007] due to cell membrane rupture [Wal-lace, 2011], which damages the sarcomere of skeletal muscle cells [Brancaccio et al., 2007]. The CK levels tend to peak 16–24 h after the workout and remain high for approximately 72 h [Uchida et al., 2009]. Increased lactate dehydrogenase (LDH) activity, indicative of muscle cell injury, is also seen when mechanical tension is applied to muscle fibers during exercises due to the increased sarcolemma permeability, which releases LDH into the bloodstream and increases its concentration [Van De Vyver & Myburgh, 2012].

Nutritional supplements that contain proteins and amino acids, such as WP, may contribute to reduced immunosuppression and excessive inflammation [Cruzat et al., 2014], accelerating muscle function recovery after strength training, although the evidence for this assumption remains unclear [Kim et al., 2017]. A systematic review made by Davies et al. [2018] demonstrated a mild-to-moderate ergogenic effect of WP use on the acceleration of muscle function recovery after strength training. Table 2 outlines the effects of supplementation with WPC, WPI, or WPH on the response to muscle injury induced by strenuous physical training.

The repair of damaged muscle tissue can be shown by assessing the activity levels of LDH [Brancaccio et al., 2008] and CK because they are indicators of muscle injury [Soares et al., 2012]. Significant decreases in CK and LDH were observed by Lollo et al. [2014] when WPH was provided to soccer players before and after aerobic training. The study by Brown et al. [2018] found that in physically active women, WPH supplementation immediately and 2 h after muscle damage induced by repeated sprint exercises also promoted greater reductions in CK. Similarly, WPH intake before and after each aerobic workout, as proposed by Hansen et al. [2015], attenuated the increase in CK, thus indicating that protein supplementation facilitates recovery from strenuous training among elite runners, despite the increase in LDH and the failure to alter TNF-α levels.

The reductions in muscle damage and acceleration of recovery from muscle injury caused by strenuous physical exercise may be related to the use of WPH supplementation [Brown et al., 2018]. These findings are in line with the study by Lollo et al. [2014], in which supplementation with WP immediately before and after daily training sessions or soccer league matches showed a trend toward increased CK and LDH levels, and with the study by Hamarsland et al. [2017], in which CK levels increased upon intake of two 20-g doses of WPC-80, native WP or milk protein (20% whey and 80% casein), both immediately and two hours after strength training. Furthermore, other authors found no improvement in muscle damage markers (CK and TNF-α) or muscle pain in individuals supplemented with a 0.4 g/kg mixture of WPC with WPI 30 min before and after exercise, both with the short-term diet with high protein content (2.9 g protein/kg/day) and with diet with moderate protein content (1.8 g protein/kg/day), after repeated days of intensive training [Roberts et al., 2017].

Supplementation with WPH decreased the muscle damage indicators CK and LDH but failed to improve physical performance, increase muscle mass, or decrease body fat compared with supplementation with WPC among soccer players undergoing aerobic training [Lollo et al., 2014].
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Groups</th>
<th>Type of study</th>
<th>Supplementation</th>
<th>Diet</th>
<th>Length</th>
<th>Type of exercise</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buckley et al. [2010]</td>
<td>28 sedentary men (18 and 30 year old)</td>
<td>WPH (n=6), WPI (n=11), and placebo (n=11)</td>
<td>randomized, double-blind, parallel</td>
<td>25 g WPH, WPI (supplemented with 3.75 g vanilla scent + 1.25 g skim milk powder) or placebo (7.5 g vanilla scent + 2.5 g skim milk powder) diluted in 250 mL flavored water at 3 different times: 2 minutes and 6 h after the ECC assessments and 2 h before the ECC assessments at 24 h</td>
<td>without controlled diet</td>
<td>24 h</td>
<td>single session of 100 maximum ECC knee extensor contractions, in fasting, in the morning</td>
<td>WPH improved IPT; WPH, WPI and placebo failed to decrease CK or TNF-α</td>
</tr>
<tr>
<td>Blacker et al. [2010]</td>
<td>10 healthy, physically active men, experienced in backpack load carriage (28 ± 9 years, 81.5 ± 10.5 kg, 1.82 ± 0.07 m; 16.4 ± 3.2% BF)</td>
<td>3 groups: placebo (n=10), CHO (n=10) + WPI (n=10)</td>
<td>Three-way randomized, cross-sectional</td>
<td>500 mL (490 mL water + 10 mL sugar-free orange flavor) for placebo; 500 mL (44 g CHO) (490 mL water + 10 mL sugar-free orange flavor) for CHO; 500 mL water + 44 g (WPI + WPH) (3 g CHO; 36 g PTN; 3 g LIP) orange flavor; 250 mL at the beginning and 250 mL after a 60-min walk</td>
<td>without controlled diet</td>
<td>5.9 ± 4.1 weeks</td>
<td>Mixed exercise program (aerobic + strength training): 3 treadmill walking tests (2 h at 6.5 km/h), carrying a 25-kg backpack; 2-week recovery period between each test</td>
<td>WPI + WPH increased IPT similarly</td>
</tr>
<tr>
<td>Lollo et al. [2014]</td>
<td>24 elite soccer players (18 ± 0.8 years, 73.95 ± 4.87 kg and 178.5 ± 0.48 cm)</td>
<td>3 groups: WPH (n=8), WPC (n=8) + CHO (n=8)</td>
<td>double-blinded regarding dietary supplementation</td>
<td>0.5 g WPH, WPC, or CHO/kg weight, immediately before and immediate after the daily workout or soccer league matches, including rest days</td>
<td>with diet controlled by a nutritionist: 2.3 g/kg weight PTN (1.3 g food and 1.0 g supplement), totaling 10 to 15% total energy (diet + supplement)</td>
<td>12 weeks</td>
<td>aerobic activity between training and soccer league matches</td>
<td>WPH decreased CK and LDH; WPC increased CK and LDH, albeit nonsignificantly</td>
</tr>
<tr>
<td>Hansen et al. [2015]</td>
<td>18 elite runners (men and women) divided into 2 number-, age-, height-, weight-, and %BF-matched groups</td>
<td>2 groups: WPH (n=9) + CHO (n=9)</td>
<td>randomized, controlled intervention</td>
<td>0.3 g/kg weight WPH 10 minutes before and 0.3 g after WPH/kg weight + 1 g CHO/kg weight 15 minutes after each workout; 1.3 g/kg weight CHO 10 minutes before and 15 minutes after each workout diluted in non-caloric iced tea, ingesting no food until 2 h after each workout, except water</td>
<td>with controlled diet: 15% PTN, 63% CHO and 22% LIP</td>
<td>1 week</td>
<td>13 aerobic workouts with a 4-km run</td>
<td>WPH reduced the increase in CK; WPH and CHO increased LDH; WPH and CHO caused no changes in TNF-α levels</td>
</tr>
<tr>
<td>Burnley et al. [2010]</td>
<td>21 healthy, untrained, young men (23 ± 2 years, 79.2 ± 10.1 kg, 179.6 ± 5.4 cm, 24.6 ± 3.0 BMI, 16.2 ± 5.0 BF)</td>
<td>3 groups: WPI (n=21), CHO (n=21) + placebo (n=21)</td>
<td>double-blind, cross-sectional</td>
<td>0.4 g/kg WPI with cherry flavoring, 0.4 g/kg sugar (CHO) with cherry flavoring or 0.0485 g/kg weight artificial sweetener with cherry flavoring (placebo) dissolved in 240 mL water immediately after training; without ingesting calories after 45 min</td>
<td>without controlled diet</td>
<td>3 days</td>
<td>10 sets of 10 repetitions of ECC knee extensions every day</td>
<td>WPI and CHO failed to decrease CK</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Groups</td>
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<td>Lockwood et al. [2017]</td>
<td>56 trained men (21.4 ± 0.4 years, 179 ± 1 cm, 79.5 ± 1 kg, 18.9% ± 0.7 BF)</td>
<td>4 groups: CHO (n=15), WPC (n=13), WPC-L (n=15) and WPH (n=13)</td>
<td>double-blind</td>
<td>30 g CHO, 30 g 80% WPC, 30 g WPC containing high lactoferrin (WPC-L) or 30 g WPH, diluted in 500 mL water; immediately before and after training and between mean on non-training days</td>
<td>without controlled diet</td>
<td>8 weeks</td>
<td>upper- and lower-limb strength training</td>
<td>WPH increased BF loss but not CK</td>
</tr>
<tr>
<td>Brown et al. [2018]</td>
<td>20 physically active women (20 ± 1 years, 165.9 ± 5.6 cm, 61.8 ± 7.9 kg)</td>
<td>2 groups: WPH (n=10) and CHO (n=10)</td>
<td>randomized, double-blind</td>
<td>2 doses of 20 g WPH or 20 g CHO per day; on exercise days immediately and 2 hours after exercise; two days after exercise in the morning, 30 to 60 minutes prior to laboratory visits, and before the evening meal; on the third day in the morning, fasting</td>
<td>with controlled diet: 5 to 7 g/kg of weight CHO and 1.2 to 1.7 g/kg of weight PTN, in all the experimental periods; standardized meal offer 24 h before the initial test and lasting for ≥10 h, except for water, which was consumed ad libitum</td>
<td>4 days</td>
<td>repeated sprint exercise</td>
<td>WPH promoted greater reduction of CK 48 h after EIMD</td>
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<tr>
<td>Hamarsland et al. [2017]</td>
<td>22 trained men and women allocated to 2 groups: WPC or NWP (25 ± 2 years; 70.0 ± 11.6 kg; 52.9 ± 9.6 kg MM; 21.5 ± 6.4% BF) and MP (25 ± 5 years; 72.8 ± 12.4 kg; 57.1 ± 13.5 kg MM; 19.1 ± 7.2% BF)</td>
<td>2 groups: WPC or NWP (n=10) and MP (n=12)</td>
<td>double-blind, randomized, placebo-controlled, partial crossover trial</td>
<td>20 g of WPC or NWP diluted in water and 20 g of MP (20% whey and 80% casein) immediately and 2 h after strength training</td>
<td>Diet guided by a nutritionist on the day before and during the trial period (2.5 days in total): 40 kcal/kg and 1.5 PTN g/kg/day; breakfast: 23 kcal, 0.11 g PTN, 0.30 g LIP and 0.58 g CHO/kg</td>
<td>2.5 days</td>
<td>lower limb strength training</td>
<td>WPC or NWP and MP increased the CK levels at 180 min, 300 min and 24 h, without significant differences</td>
</tr>
<tr>
<td>Roberts et al. [2017]</td>
<td>14 trained men and women (31 ± 6 years; 1.71 ± 0.12 m; 78.45 ± 24.72 kg; 64.32 ± 18.42 MM; 17.47 ± 3.99% BF)</td>
<td>2 groups: PROMOD (1.8 g PTN/kg/day) and PROHIGH (2.9 g PTN/kg/day)</td>
<td>randomized crossover trail</td>
<td>0.4 g/kg of a mixture of WPC + WPI diluted in water 30 min before and after exercise sessions</td>
<td>With controlled diet: PROMOD (1.8 g PTN/kg/day) and PROHIGH (2.9 g PTN/kg/day)</td>
<td>10 days</td>
<td>strength training</td>
<td>PROMOD and PROHIGH with WPI increased the pre- and post-workout CK levels with no significant differences in TNF-α or muscle pain</td>
</tr>
</tbody>
</table>

ECC: eccentric exercise; IPT: isometric peak torque; BF: body fat; CHO: carbohydrates; PTN: protein; LIP: lipids; BMI: body mass index; CK: creatine kinase; LDH: lactate dehydrogenase; TNF-α: tumor necrosis factor; EIMD: exercise-induced muscle damage; NWP: native whey protein; MP: milk protein.
When comparing WPH and WPI intake, Buckley et al. [2010] noted that WPH intake accelerated the recovery of strength capacity and muscle regeneration after a single session of eccentric exercise, although no significant differences in the serum activity of CK or in the plasma levels of TNF-α were found. This rapid recovery of strength capacity and muscle regeneration during bodybuilding exercises results from the increased rate of MPS and increased strength gains induced by WP compared with other dietary proteins because WP proteins in WPH are rapidly digested and absorbed due to the hydrolysis process [Burd et al., 2012].

In contrast, Burnley et al. [2010] determined that WPI supplementation immediately after moderate eccentric exercise had no significant effect on muscle recovery in young men, most likely because the muscle injury was light and the supplementation dose was low. The authors concluded that a small quantity of protein supplementation might be insufficient to affect muscle injury recovery. The TNF-α and CK levels also remained unchanged in the study by Buckley et al. [2010], which may be explained by the short study period because serum CK activity can take up to 48 h to increase. Additionally, the absence of any effect on the plasma levels of TNF-α after maximal eccentric contractions may have resulted from the short duration of the exercise protocol used.

Strength generation capacity and accelerated recovery from muscle injury were observed 6 h after exercise when supplementation with WPH was performed 2 min after exercise, and the same improvements were also observed at 24 h after 2 additional administrations at 6 h and 22 h in experiments involving the induction of fatigue and injury in sedentary men [Buckley et al., 2010]. Isometric strength, as assessed by treadmill walking with a 25-kg load on the back, was recovered within 48 h when a WPI + WPH combination was administered. Protein supplementation favored the maintenance of an anabolic environment, which may have improved the repair of structural muscle proteins damaged during prolonged exercise with load, leading to the recovery of isometric muscle function [Blacker et al., 2010].

Therefore, for athletes, WPH has greater advantages than WPC or WPI [Biocatalysts, 2014] because WPH is digested and absorbed more rapidly [Burd et al., 2012] and shortens the recovery from muscle injury caused by strenuous physical exercise from days to hours [Biocatalysts, 2014]. It is likely that an increase in the supply of amino acids through WPH supplementation is responsible for accelerating repair of damaged skeletal muscle and its capacity to generate force [Brown et al., 2018].

**EFFECT OF SUPPLEMENTATION WITH WHEY PROTEIN CONCENTRATE, WHEY PROTEIN ISOLATE, OR WHEY PROTEIN HYDROLYSATE ON WEIGHT LOSS AND CHANGE IN BODY COMPOSITION**

Protein intake has been related to satiety and reduced energy intake compared with other macronutrients [Monteyne et al., 2018]. However, this satiety effect is dependent on the protein source [Chungchunlam et al., 2017]. WP supplements may be a good choice for a weight loss diet due to the presence of proteins BLG and ALA [Bendtsen et al., 2013]. ALA is considered to be easily and quickly ingested, having the highest content of tryptophan (6%) among all sources of food proteins [Markus et al., 2002], thus being considered a source of tryptophan, a precursor of serotonin, which is known to suppress food intake and satiety [Halford et al., 2011]. This makes the intake of ALA-enriched proteins, such as WP, a precursor of increased levels of tryptophan and serotonin in the brain [Markus et al., 2002].

Weight loss and increased satiety were observed upon consumption of an energetic breakfast with a high-protein content from WPC relative to other sources of protein (eggs, tuna and soy) [Jakubowicz et al., 2017]. The results also showed that the satiating effect of WPI was similar to that of BLG or ALA due to rapid protein digestion and absorption, high concentrations of amino acids in the bloodstream [Bendtsen et al., 2013] and the release of gastrointestinal hormones related to satiety, including cholecystokinin, glucagon-like peptide-1, and peptide tyrosine [Jakubowicz & Froy, 2013]. A rapid whey protein intake is more satiating than that of intact proteins, such as casein, slowly digested in the short term and quickly digested in the long term, which might be partially explained by the difference in blood amino acid rates and postprandial secretion of gastrointestinal hormones [Bendtsen et al., 2013].

In addition to the satiating effect and weight loss, WPH may help modulate weight and reduce body fat [Bendtsen et al., 2013]. Supplementation with WPH immediately before and after strength training and between meals on non-training days reduced body fat to a greater extent than supplementation with WPC (80%) or high-lactoferrin WPC (WPC-L) [Lockwood et al., 2017]. However, according to the authors, further research is required to elucidate in which form WPH affects adipose tissue physiology.

In addition to regular physical training, high-protein diets (Table 3) may have beneficial effects on anthropometry and body composition. Supplementation with WPC 30 minutes before lunch has beneficial effects on the appetite, caloric intake, anthropometry, and body composition of overweight and obese male workers [Tahavorgar et al., 2014]. Conversely, Chungchunlam et al. [2017] found no significant decrease in hunger, satiation, or energy intake in “ad libitum” meals.

The decrease in body fat mass is related to the intake of different protein varieties. For example, a study assessing the intake of a commercial WPI + WPC + WPH supplement 20 minutes before a high-intensity strength training session in trained men and women showed an increase in resting energy expenditure, which is an effective strategy to reduce body fat mass without decreasing muscle mass [Hackney et al., 2010]. Weight loss without affecting muscle mass occurred in young men with WPI intake 5 minutes after the strength training session when followed by a full meal 60 minutes after supplementation [Monteyne et al., 2018]. According to Devries & Phillips [2015], the increase in protein intake increases the gains in lean body mass during strength training and enhances high-quality weight loss.

Supplementation with WPC decreased total body and abdominal fat and increased muscle mass when administered to untrained men after strength training [Hulmi et al., 2015].
TABLE 3. Effects of supplementation with WPC, WPI, and WPH on weight loss and change in body composition.

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Groups</th>
<th>Type of study</th>
<th>Supplementation</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Hackney et al. [2010]</td>
<td>8 trained participants; men (n=5; 23.0 ± 3.8 years, 178 ± 6.4 cm, 85.6 ± 11.4 kg, 12.6% ± 7.5% BF) and women (n=3, 24.0 ± 1.5 years, 162 ± 6.4 cm, 65.1 ± 7.3 kg, 26.5% ± 6.7% BF)</td>
<td>Designer Whey® (WPI + WPC + WPH (n=8) and CHO (n=8))</td>
<td>double-blind, cross-sectional</td>
<td>18 g WPI + WPC + WPH, 2 g CHO and 1.5 LIP or CHO (1 g PTN, 19 g CHO and 1 g LIP); 20 min before the workout</td>
<td>without controlled diet</td>
<td>8 days</td>
<td>24-day TRP lower-limb and abdominal workouts</td>
<td>WPI + WPC + WPH increased REE 24 h after TRP, indicating increased BF oxidation at rest</td>
</tr>
<tr>
<td>Monteyne et al. [2018]</td>
<td>15 untrained but physically active men who included resistance exercise in their exercise routine (21 ± 1 years, 78.0 ± 11.9 kg, 1.78 ± 0.07 m)</td>
<td>2 groups: WPI and CHO</td>
<td>randomized, double-blind</td>
<td>0.3 g/kg weight (23.9 ± 3.6 g WPI or 26.5 ± 3.8 g CHO (dextrose) diluted in 400 mL water; 5 min after the workout; full meal (400 g pasta, 400 g bolognese sauce, and 32 mL olive oil = 12% PTN, 69% CHO, 19% LIP) 60 min after the workout</td>
<td>without controlled diet, only standard breakfast (15% VET=125 mL milk and 30 g cereal)</td>
<td>5 days</td>
<td>2 lower-limb strength workouts</td>
<td>WPI reduced energy intake without impairing muscle hypertrophy</td>
</tr>
<tr>
<td>Tahavorgar et al. [2014]</td>
<td>45 male workers of a company; WPC (39.4 ± 6.0 years, 171.1 ± 7.4 cm, 93.9 ± 11.5 kg, 32.1 ± 3.2 kg/m² BMD) and SPI (38.8 ± 8.8 years, 171.8 ± 8.5 cm, 95.2 ± 12.9 kg, 32.1 ± 2.7 kg/m² BMD)</td>
<td>2 groups: WPC (n=26) or SPI (n=19)</td>
<td>randomized double-blind</td>
<td>65 g WPC or 60 g SPI with strawberry flavoring (0.2 g for WPC and 0.1 g for SPI) and sucralose, dissolved in 500 mL water; 30 minutes before lunch</td>
<td>without controlled diet</td>
<td>12 weeks</td>
<td>usual physical activity</td>
<td>WPC showed a greater decrease in appetite, energy intake, anthropometry (weight, BMI, and WC) and body composition (BF loss and LM gain) than SPI</td>
</tr>
<tr>
<td>Chungchunlam et al. [2017]</td>
<td>20 normoweight, adult women (24.2 ± 0.8 years, 22.7 ± 0.4 kg/m² BMD)</td>
<td>3 groups: WPI (n=20), BLG (n=20) or ALA (n=20)</td>
<td>single-blind, controlled</td>
<td>60 g WPI, 54 g BLG, or 55 g ALA mixed with 190 g, 196 g, and 195 g marmalade, respectively, spread in 45 g bread with 100 mL water 2 h before eating the test meal; fried rice (white rice, chopped chicken, eggs, peas, corn, carrots, chicken broth, sugar, salt, and vegetable oil) “ad libitum” within 15 minutes</td>
<td>with controlled diet &quot;ad libitum&quot;</td>
<td>3 days, separated at least 3 days</td>
<td>without excessive physical exercise the night before the study day</td>
<td>WPI, BLG, and ALA failed to reduce the energy intake in the test meal “ad libitum” and failed to reduce the hunger, satiety, or food consumption</td>
</tr>
<tr>
<td>Hulmi et al. [2015]</td>
<td>78 untrained but physically active healthy men (34.4 ± 1.3 years, 1.80 ± 0.08 m, 83.6 ± 1.4 kg)</td>
<td>3 groups: WP (n=25), CHO (isocaloric (maltodextrin) (n=25) or WP + CHO (n=28)</td>
<td>randomized, controlled</td>
<td>37.5 g WPC (30 g PTN, 5 g lactose, &lt;1 g LIP), 34.5 g (maltodextrin) CHO, or 37.5 g WPC (30 g PTN) and 34.5 g maltodextrin; after exercise; with a full meal 1 to 2 h after the workout</td>
<td>without controlled diet</td>
<td>12 weeks</td>
<td>strength training</td>
<td>WPC reduced BF and abdominal fat and increased LBM</td>
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<tr>
<td>Study</td>
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<td>Gomes et al. [2017]</td>
<td>30 women who recovered at least 5% of the weight lost 24 months or longer after bariatric surgery (5 ± 11 years, 35.7 ± 5.2 kg/m² BMI, time elapsed since the surgery: 69 ± 23 months)</td>
<td>2 groups: WPC + hypocaloric diet (n=15) and hypocaloric diet (n=15)</td>
<td>randomized, double-blind, parallel</td>
<td>0.5 g/kg weight WPC + hypocaloric diet (1 g/kg weight day, 45% CHO, 20% LIP) or hypocaloric diet (1 g/kg weight day, 55% CHO, 20% LIP); WPC daily dose ingested in 3 portions: during breakfast and small meals (with fruit and milk, yogurt, or with water)</td>
<td>hypocaloric diet</td>
<td>16 weeks</td>
<td>usual physical activity</td>
<td>WPC showed increased weight and BF loss</td>
</tr>
<tr>
<td>Berryman et al. [2017]</td>
<td>63 men (25 ± 2.5 years, 178 ± 6, 83.8 ± 9.5 kg, 26.4 ± 2.1 kg/m² BMI)</td>
<td>3 groups: CON (n=21), MOD (n=24) or HIGH (n=18)</td>
<td>randomized, double-blind</td>
<td>CON (day: 64 g CHO, 1 g PTN; night: 113 g CHO, 6 g LIP, 5 g PTN, 0.9 g EAA, 0.4 g BCAA, 0.2 g leucine); MOD (day: 36 g CHO, 1 g LIP, 20 g WPI, 11.8 g EAA, 5.6 g BCAA, 3.1 g leucine; night: 64 g CHO, 3 g LIP, 44 g WPI, 18.9 g EAA, 8.7 g BCAA, 4.1 g leucine) and HIGH (day: 32 g CHO, 1 g LIP, 39 g WPI, 23.5 g EAA, 11.3 g BCAA, 6.2 g leucine; night: 56 g CHO, 9 g LIP, 55 g WPI, 23.6 g EAA, 10.9 g BCAA, 5.1 g leucine); in the form of a beverage; consumed immediately after exercise, between lunch and dinner, and before bed</td>
<td>without controlled diet</td>
<td>46 days</td>
<td>pre-supplementation and aerobic exercise and supplementation (unrestricted diet, aerobic training and supplementation)</td>
<td>no significant effects on weight, LBM, or % BF occurred in the CON, MOD, or HIGH groups</td>
</tr>
<tr>
<td>Jakubowicz et al. [2017]</td>
<td>56 participants (26 men and 30 women) (58.9 ± 4.5 years, 32.1 ± 0.9 kg/m² BMI)</td>
<td>3 groups: WBdiet (n=19), PBdiet (n=19) and CBDiet (n=18)</td>
<td>Parallel randomized clinical trial</td>
<td>High-energy and PTN breakfast (660 ± 25 kcal): WBdiet (25% LIP, 50% CHO and 25% PTN – 42 g, including 28 g WPC); PBdiet (25% LIP, 50% CHO and 25% PTN – 42 g, including 7 g eggs, 20 g tuna, 7 g soy; CBDiet (25% LIP, 64% CHO and 11% PTN, including 17 g soy).</td>
<td>With controlled diet: similar lunch (560 ± 20 kcal), and dinner (280 ± 15 kcal), but breakfast differed between groups</td>
<td>12 weeks</td>
<td>no data</td>
<td>WBdiet caused greater weight loss (7.6 ± 0.3 kg) and satiety than the PBdiet (6.1 ± 0.3 kg) and CBDiet (3.5 ± 0.3 kg)</td>
</tr>
</tbody>
</table>

CHO: carbohydrates; LIP: lipids; BF: body fat; PTN: proteins; TRP: high-intensity strength training; REE: rest energy expenditure; SPI: soy protein isolate; BMI: body mass index; WC: waist circumference; LBM: lean body mass; BLG: β-lactoglobulin; ALA: α-lactoalbumin; CON, MOD, and HIGH: names of the supplementation groups, wherein CON refers to the placebo and MOD and HIGH to moderate and high protein content. WBdiet: whey protein breakfast diet; PBdiet: protein breakfast diet; CBDiet: carbohydrate breakfast diet (from Jakubczyk et al. [2017]).
and promoted weight and body fat loss among women [Gomes et al., 2017]. These results can be attributed to the WP content, which correlates with decreased energy consumption because it increases satiety, thereby decreasing energy consumption [Bendtsen et al., 2013] and/or increasing resting energy expenditure [Hackney et al., 2010]. Furthermore, these proteins participate in beta-oxidation processes [Acheson et al., 2011] and lipolysis [Hector et al., 2015] and can be recommended for body fat loss after strength training [Hulmi et al., 2015]. Conversely, Berryman et al. [2017] found no changes in weight, lean body mass, or body fat measurements in young men supplemented with WPI 3 times per day immediately after aerobic physical exercise in the morning, between lunch and dinner, and before bed.

Nutritional monitoring and a training program in line with an individual’s goals are important for realizing beneficial effects from the consumption of different WP formulations because protein supplementation alone will most likely fail to cause the expected effects. As shown above, the RDA established by the DRI for the population is a key tool for nutritionists. Accordingly, the quantity of daily protein that should be ingested by a sedentary adult is 0.8 g/kg weight/day [IOM 2002/2005], whereas this need will vary with the individual’s physical training intensity and objectives. According to the Brazilian Society of Exercise and Sports Medicine [Sociedade Brasileira de Medicina do Exercício e do Esporte, 2009], an intake of 1.2 to 1.6 g/kg protein/day is recommended for endurance athletes, whereas strength athletes may benefit from an intake of 1.6 to 1.7 g/kg protein/day, although an intake higher than 3.0 g/kg protein/day may benefit body composition [Jäger et al., 2017]. To optimize protein supplementation, nutritionists must evaluate the individual’s diet, lifestyle, sports modality, goals, and training phase before choosing the supplement.

This study examined available evidence regarding the effects of consuming different varieties of WP on muscle hypertrophy, physical performance, response to muscle injury, weight loss, and body composition changes. However, this review had limitations due to difficulties in comparing studies that involve various methods and include small groups, heterogeneous samples, and differences in age, trained or untrained individuals, dosage, administration routes, supplement varieties, the degree of diet control, the study period length (ranging from hours to months), and the physical training modalities. These difficulties stress the need for further studies on WP supplementation with larger and more homogeneous samples and study periods longer than 12 weeks. Furthermore, more specific training protocols, which should focus on hypertrophy, physical performance, response to muscle injury, weight loss, and changes in body composition, are needed and should be adequately integrated with the supplementation protocol to consider dosage, administration route, and food intake to obtain more consistent results.

CONCLUSION

The papers analyzed in the present study showed that supplementation with either WPI or WPC was related to increased MPS and that WPH caused muscle hypertrophy and improved physical performance. Few studies showed results concerning muscle damage regarding the efficacy of WP varieties in reducing cell damage markers monitored by CK, LDH, and TNF-α. A higher reduction in weight, satiety, and improved body composition occurred with WPC supplementation, without compromising bodily lean mass loss.

WPH intake provided more advantages compared to WPC and WPI, and improved muscle torque and hypertrophy peak associated to strength exercise and reduced muscle damage, caused by reduced CK levels associated to aerobic exercises. With these findings, the present study contributes to assign the WP variety according to its use by athletes, sportspeople, and general population.

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CONFLICT OF INTERESTS

The authors declare they do not have any conflicts of interest.

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Effects of Whey Protein in Sports Nutrition


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Effects of Whey Protein in Sports Nutrition


