

# Protein

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Protein is a critical macronutrient for maintenance of normal bodily functions. Required daily protein intake varies by age, sex, and degree of daily activity, but is critical to maintain muscle mass and strength throughout an individual's lifespan.

Keywords: dietary protein ; pea ; older adult population ; muscle protein synthesis

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## 1. Introduction

Muscle mass and muscle strength are positively correlated, independent of age and gender <sup>[1]</sup>. Generally, greater lean mass is associated with better overall health <sup>[2]</sup> and prevention of functional declines associated with aging <sup>[3]</sup>. However, after the age of 30 year, muscle mass declines at a rate of 0.3 to 0.8% per year <sup>[4]</sup>. The reduction in lean mass is attributed to the reduction in number, and to some extent area size, of myofibers <sup>[5]</sup>. Factors affecting muscle mass include age-related muscle atrophy, decreased mitochondrial function, increased oxidative stress, impaired satellite cell function, and inflammation <sup>[6]</sup>. In addition, muscle strength is a major predictor of disability and all-cause mortality in older adults <sup>[7][8]</sup> with some research suggests muscle strength is a more meaningful predictor of health outcomes compared to muscle mass <sup>[8]</sup>. Concomitant with muscle atrophy, muscle strength also declines with age, especially after 50–60 year <sup>[9]</sup> <sup>[10]</sup> at a rate of 2 to 4% <sup>[11]</sup> or greater in the lower limbs every year <sup>[12]</sup>. Therefore, it is imperative to prevent age-associated losses in muscle mass and strength to enhance overall performance throughout the lifespan.

Sarcopenia, or age-related musculoskeletal decline, is characterized by: (1) low muscle strength (tested via grip strength and chair stand test); (2) low muscle quantity or quality (confirmed via dual-energy x-ray absorptiometry (DXA), computed tomography (CT), or magnetic resonance imaging (MRI), etc.); and (3) low physical performance (assessed via gait speed, 400 m walk test, etc.) <sup>[13]</sup>. The potential etiology of sarcopenia is a combination of declines in physical function, loss of muscle mass, increased inflammation, altered hormone balance, inadequate nutrition intake, and anabolic resistance <sup>[14]</sup>. Sarcopenia currently affects 6–19% of individuals worldwide over the age of 60 year <sup>[15]</sup>. Individuals with sarcopenia are at an increased risk of falls, fractures, decreased quality of life, cardiovascular disease, respiratory disease and cognitive impairment <sup>[13]</sup>. Risk of sarcopenia is dependent upon age, ethnicity, living conditions, and pre-existing medical conditions <sup>[13]</sup>. The condition was estimated to cost \$18.5 billion of direct health care costs in the year 2000 <sup>[16]</sup> and individuals with sarcopenia will endure double the cost of hospitalization compared to those without sarcopenia <sup>[17]</sup>. Due to the increasing number of older adults living longer it is imperative to identify solutions to prevent and treat this debilitating disease.

Currently, there are no approved medications for the treatment of sarcopenia. The standard of care for hospitalized or institutionalized older adults with frailty or sarcopenia includes participation in resistance-training and weight-bearing exercises <sup>[18][19][20]</sup>. However, the transition from a hospital bed to rehabilitation is challenging, as many patients are unable to engage in physical activity due to lack of exercise equipment, social support, and self-motivation to exercise <sup>[21]</sup>. Diet is a modifiable lifestyle factor that may serve a strong role in preventing and treating sarcopenia <sup>[20]</sup>. For example, greater protein intake is linked to improvements in muscle mass and strength <sup>[22][23]</sup>. However, the current recommended daily allowance (RDA) from the World Health Organization (WHO) <sup>[24]</sup> and National Academies of Sciences <sup>[25]</sup> of 0.8 g/kgbodyweight/day for adults may not be sufficient to combat sarcopenia in older adults. Recent evidence suggests that protein intake closer to 1.2–1.5 g/kgbodyweight/day, in combination with adequate exercise, is more beneficial in preventing age-related declines in muscle mass and strength, improving health status, and reducing the risk of early mortality <sup>[2][26][27][28]</sup>. Despite growing evidence that a higher RDA for dietary protein is beneficial to older adults, there are numerous barriers to reaching this dietary goal. Older adults face an increased risk of protein-energy malnutrition due to social isolation <sup>[29]</sup>, lack of appetite, and potential issues with mastication <sup>[30]</sup>. In addition, protein increases satiety, and therefore, older adults are less likely to meet their protein requirements due to feelings of fullness and meal skipping. Therefore, it is critical to provide sustainable, nutrient-dense protein sources that will maximally enhance muscle mass and strength to reduce the risk of developing sarcopenia in this at-risk group.

A consensus on whether protein sources differentially affect the progression of sarcopenia has yet to be determined. Animal and plant protein-containing foods differ in their amino acid content [31], absorption kinetics, and nutrient to food matrix interaction [32]. Protein quality and digestibility are distinguishing features between animal and plant proteins. Traditionally, whey protein, has been commonly used for dietary protein supplementation because of its high digestibility and complete amino acid profile [33]. Meanwhile, there is growing clinical and consumer market interest in vegetarian and vegan diets due to their potential health benefits, environmental sustainability, and ethical issues surrounding raising animals for the sole purpose of consumption [34]. Historically, soy protein has been the go-to plant-based protein due to its near complete essential amino acid (albeit low methionine) profile; however, pea protein is gaining popularity among consumers due to recent advances in industry produced meat alternative products. Despite their growing consumer popularity, there is little scientific research on whether plant protein alternatives are effective in preventing age-associated muscle losses compared to animal protein counterparts.

## **2. Protein Quality and Digestibility Differs by Protein Source**

Skeletal muscle mass is regulated by the balance between the rate of muscle protein synthesis (MPS) and the rate of muscle protein breakdown (MPB), which are both regulated by a variety of factors. During muscle accrual, the rate of MPS is greater than MPB. It is generally accepted that dietary protein and physical activity stimulate MPS either independently [35][36][37][38] or interdependently [39][40]. Muscle protein synthesis is a process dependent on postprandial availability of essential amino acids (EAAs) [31]. The amount and diversity of EAAs to meet human nutritional needs is defined as protein quality [41]. The most widely adopted indexes of protein quality are the Protein Digestibility Corrected Amino Acid Score (PDCAAS) and the Digestible Indispensable Amino Acid Score (DIAAS). Protein food sources vary widely in their PDCAAS and DIAAS scores. For example, milk, whey, egg, casein, and soy protein isolate scored 1.00 (highest possible score) on the PDCAAS. In comparison, cooked yellow pea or *Pisum sativum*, pea protein concentrate (NUTRALYS®), and pea protein isolate (NUTRALYS®, manufactured by Roquette, Lesterm, France ) have a PDCAAS of 0.67 [42][43], 0.893 [44] and 0.93 [45], respectively. When compared using DIAAS, whey protein isolate, whey protein concentrate, soy protein isolate, and pea protein concentrate have a DIAAS of 100, 107, 84, and 62, respectively [46]. Therefore, animal and soy-based protein foods, generally have a higher protein digestibility score compared to pea-sourced protein, regardless of the scoring method used.

In addition, protein digestibility and absorption kinetics will dictate the amount of immediate EAA available to stimulate MPS response [47]. Faster protein digestion and absorption typically lead to a more acute MPS response and a higher peak compared to slower absorbing proteins [48]. Depending on the processing method and the presence of “antinutritional factors”, it is generally shown that plant-based proteins have lower digestibility compared to animal-based proteins [43]. Antinutritional factors are food components or compounds such as tannins, phytate, oxalate, saponins, lectins, alkaloids, protease inhibitors, cyanogenic glycosides [49] inside the food matrix that interfere with the absorption of certain nutrients. An example of an antinutritional factor that interferes with protein absorption is Bowman-Birk trypsin inhibitor, which can be found in foods such as soybean grits, soymilk, soy isolate, and soy protein concentrate [50], which inhibits the enzymatic action of pepsin and trypsin in the gut [51]. Certain antinutritional factors can be inactivated through cooking to improve protein digestibility [52]. Also, it is important to note that ingested plant protein (e.g., soy protein) increases protein oxidation [53], which suggests amino acids from plant protein is used for the production of urea and therefore, less amino acids are available to stimulate MPS [43][54][55]. Due to the differences in digestibility and quality among protein sources, it is important to take these factors into consideration when developing nutrition interventions to prevent age-associated muscle losses.

### **2.2. Muscle Response to Animal Versus Plant Protein Sources May Not Differ at Higher Protein Intakes**

Research comparing the anabolic properties of the various plant- and animal-based protein sources is important to determine whether specific nutrition regimens can be formulated to maximize the muscle health of older adults. Differences between milk protein, particularly whey, versus soy protein have been well studied in adults and young adults. It has been shown that soy protein ingestion results in a lower MPS compared to whey [53][56] during both rested and post-exercise conditions. Volek, et al. [57] conducted an experiment on 63 randomized healthy adults that performed whole body resistance training program and consume isocaloric supplements containing carbohydrate, whey (24 g), or soy protein (24 g) for 9 months. The authors show that whey supplementation significantly increased fasting plasma leucine concentration and lean body mass gains compared to carbohydrate and soy protein supplementation regimens. However, other studies suggest when higher protein supplementation doses are consumed (>30 g) in combination with an exercise regimen, muscle outcomes are similar across protein subtypes. For example, a study where omnivorous participants followed an 8-week progressive, non-linear resistance training protocol in addition to supplementation with 48 g of either

rice or whey protein isolate showed that there was no difference in body composition and exercise performance [58]. Similarly, other studies with isonitrogenous supplementation of 33 g soy or whey protein resulted in similar increases in muscle mass after exercise training in omnivorous participants [59][60]. A meta-analysis conducted by Messina, et al. [61] concluded that soy protein supplementation did not yield any differences in lean body mass and strength in response to resistance exercise training in healthy omnivorous adults between the age of 18 to 70 years compared to whey protein. However, the authors noted that the independent influence of age or sex could not be identified, and, thus, they recommend more research, specifically among older individuals. In a diet study of whole foods without an exercise intervention, Campbell, et al. [62] show that older women who consumed an omnivorous diet ( $1.0 \pm 0.08$  g/kgbodyweight/day of protein) gained more lean body mass over 12-weeks compared to those consuming a lacto-ovo-vegetarian diet ( $0.78 \pm 0.1$  g/kgbodyweight/day of protein). In subsequent research [63], they found that the observed difference was attenuated by increasing the amount of protein consumed by the lacto-ovo-vegetarian diet to 1.15 g/kgbodyweight/day. Although these findings do not directly compare animal versus strictly plant protein diets, the results suggest that ingestion of higher amounts of total dietary protein may overcome the different properties of animal versus plant proteins and their influence on muscle outcomes.

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