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Effects of green tea–derived natural products on resistance exercise training in sarcopenia: A retrospective narrative mini-review

Effects of green tea–derived natural products on resistance exercise training in sarcopenia: A retrospective narrative mini-review

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Abstract

Skeletal muscle function deficits result in metabolic disease development and physical dysfunction in older adults. Sarcopenia is characterized by a decrease in muscle mass and strength with advancing age, and it increases the risks of mobility impairments, disease development, and mortality. Lifestyle interventions involving a combination of diet and exercise to prevent and attenuate sarcopenia warrant substantial research attention. Resistance exercise training under supervision is a safe and the most effective approach to reducing age-related muscle loss and improving multiple aspects of overall health in the older population. The beneficial effects of resistance exercise training on skeletal muscle mass may be augmented by specific dietary supplements (i.e., green tea–derived natural products). The purpose of this mini review is to provide an up-to-date, evidence-based account of the effectiveness of green tea–derived natural products for supporting resistance training–induced adaptations to prevent or attenuate age-related muscle mass loss. Based on animal and clinical studies, we provide insights into supplementation with green tea–derived natural products, which may assist in the growth or maintenance of skeletal muscle and subsequently delay the onset of age-related metabolic diseases in older adults.

Keywords: Aging, Green tea extracts, Inflammation, Net muscle protein balance, Resistance training

1. Sarcopenia

Aging is associated with a progressive decline in lean body mass, particularly muscle mass. Sarcopenia, defined as the involuntary loss of skeletal muscle mass and strength, may result in the loss of independence, diminished quality of life, physical disability, increased risks of falls, mobility impairments, and high risks of mortality in older adults [1]. Skeletal muscle accounts for approximately 40% of the total body weight in young adults [2], and it decreases substantially after the age of 60 years [3]. Approximately 5%–13% of older adults aged more than 60 years are affected by low muscle mass and skeletal muscle function deficits, and the prevalence is as high as 50% in adults aged over 80 years [4,5]. Determining the mechanisms involved in the progression of age-related loss of skeletal muscle mass is essential for preventing and managing sarcopenia. How to incorporate the nutritional supplements and exercise training that may support the growth or maintenance of skeletal muscle and subsequently extend the healthy lifespan in older adults is also warranted (see Fig. 1).

2. Skeletal muscle and aging

Muscle mass is regulated by the dynamic balance between muscle protein synthesis and muscle protein breakdown. The insulin-like growth factor-1 (IGF-1)/AKT pathway plays a central role in the regulation of muscle protein synthesis and breakdown through the mammalian target of rapamycin (mTOR) and forkhead box O (FOXO) transcription factor, respectively [6,7]. As a crucial kinase downstream of the IGF-1/AKT signaling pathway, mTOR regulates the cap-dependent initiation of translation

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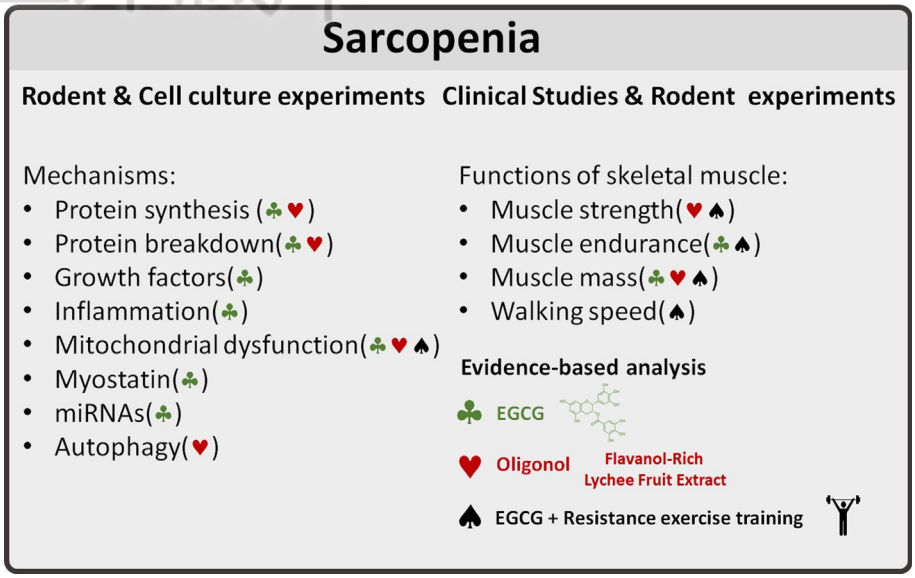

Fig. 1. Schematic summary depicting the possible effects of green tea–derived natural products and resistance exercise training on sarcopenia and its potential related mechanisms and clinical efficacy.

through the phosphorylation of substrates such as p70S6 kinase [8]. Age-related loss of skeletal muscle mass may occur through the reduction in the activity or sensitivity of anabolic signaling pathways such as the IGF-1/AKT pathway. Circulating levels of IGF-1 and IGF-1 binding proteins are decreased with advancing age, resulting in the reduction of mTOR activity in the skeletal muscle of older adults [9]. When the IGF-1/AKT pathway is intact, AKT phosphorylates FOXO transcription factors, thereby inhibiting the expression of atrophy-related genes such as muscle atrophy F-box (MAFbx) and Muscle RING finger 1 (MuRF-1) [10]. In age-related muscle loss, translocation of FOXO members to the nucleus is required for the upregulation of the muscle-specific ubiquitin ligases MAFbx and MuRF1, leading to ubiquitin-dependent protein degradation [10].

Low-grade inflammation has been suggested to be associated with the development of sarcopenia. Circulating tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) levels significantly increase with advancing age [11]. Proinflammatory cytokines, including IL-6 and TNF-α, stimulate inflammatory signaling pathways, impair the insulin signaling pathway and protein synthesis in skeletal muscle, and trigger protein degradation, thus leading to progressive muscle mass loss during aging. Nuclear factor-κB (NF-κB) plays a key role in the regulation of the inflammatory response. NF-κB upregulation stimulates the expression of various proinflammatory genes, including those encoding cytokines and chemokines [12]. NF-κB is highly expressed in older adults with muscle wasting [13], and its level is correlated with a decreased anabolic response [14]. In multiple preclinical models, NF-κB has been shown to limit myoblast differentiation and regeneration following injury [15]. Taken together, the evidence suggests that the inhibition of chronically activated NF-κB may alleviate aging-related muscle loss.

Prevention and management of sarcopenia are essential for the growing older population. In this review, we briefly summarize the current knowledge on the effects of resistance exercise and plant-derived natural products on skeletal muscle function through a review of laboratory preclinical research and the limited number of human studies.

3. Resistance exercise and muscle function

Lifestyle-based interventions have been demonstrated to be effective for improving physical function [16]. Long-term resistance exercise training has been shown to gradually increase muscle protein synthesis and induce muscle hypertrophy [17]. Thus, given its beneficial effects such as the increase in muscle mass and strength, resistance exercise is considered to be a promising intervention for sarcopenia prevention [18]. A review summarized that progressive resistance exercise training performed 2–3 times per week under a high load can improve physical function and strength [19]. The National Strength and Conditioning Association recommends the following frequency and duration for resistance exercise in older adults: 2–3 times per week on alternate days, with each workout lasting

30–60 min; 1–3 sets of 8–12 reps at 70%–80% of 1 repetition maximum (1RM), with monthly progressive adjustment [20]. A group of researchers compared high-load versus low-load resistance exercise training. These authors found that lifting low loads (30% 1RM) was equally effective in increasing muscle mass as was lifting high loads (80% 1RM) in young men [21]. For older adults at risk of injury or who prefer less challenging loads, lighter loads (<50% 1RM) may be suitable.

Resistance exercise training enhances muscle protein synthesis and increases lean muscle mass in healthy older adults [22], although muscle growth is not observed in all individuals [23]. The lack a response of the muscle of older patients to exercise is known as age-related anabolic resistance [24]. The decreased response of older adults in terms of muscle protein synthesis to anabolic stimuli may be linked to muscle and systemic insulin resistance [25]. Additionally, chronic low-grade inflammation stimulates the inflammatory signaling pathway and triggers protein degradation, which leads to progressive loss of muscle mass during aging [26]. Our previous study demonstrated that resistance training reduces the circulating levels of proinflammatory cytokines, monocyte chemoattractant protein-1, and TNF-α [27]. These results suggest that resistance exercise alone can aid in managing progressive muscle loss.

In addition to emphasizing the benefits of resistance exercise–induced muscle hypertrophy, the impact of muscle strength is greater than that of muscle mass on the health, mobility, functioning, and mortality of older adults [28]. A systematic review and meta-analysis confirmed a dose-response relationship between training intensity and muscle strength in healthy older adults, indicating that the largest gain in muscle strength was obtained under a training load of 70%–79% 1RM [29]. In our previous study, despite a similar increase in functional capacity, high-load resistance exercise training was found to be superior in enhancing muscle strength and muscle quality relative to the low-load resistance exercise training [30]. Overall, resistance exercise training under supervision is a safe and effective approach to enhancing muscle strength, mass, and quality, thereby ameliorating aging-related loss of skeletal muscle function.

4. Green tea catechins and muscle function

The substantial beneficial effects of popular nutraceuticals and functional foods such as curcumin, resveratrol [31], soy protein, and ginseng on sarcopenia have been reported [32]. In this report, we only summarize the effects of catechins and oligonol on skeletal muscle function based on the findings of previous studies.

Catechins are the major active ingredient (30% dry weight) in green tea [33] and contain numerous phenolic hydroxyl groups (-OH). Catechins are categorized into four monomers, namely (−)-epigallocatechin-3-gallate (EGCG), epicatechin, epigallocatechin, and epicatechin gallate. EGCG has shown promising effects on animals with sarcopenia. Significant increases in gastrocnemius muscle mass, the cross-sectional area of muscle fibers, and mRNA expression of IL-15 and IGF-1 in muscles were observed after 8 weeks of EGCG (200 mg/kg of body weight) intervention in 20-month-old Sprague Dawley rats compared with rats fed a control diet [34]. Muscle atrophy mediators, including 19S and 20S proteasomes, MuRF1, MAFbx, and myostatin, were inhibited in the aged Sprague Dawley rats administered EGCG compared with aged control rats [34]. In our previous study, EGCG reversed defects in the insulin signaling pathway through the suppression of protein kinase C activation and reduction of insulin receptor substrate 1 (IRS1) serine phosphorylation in skeletal muscle of senescence-accelerated mouse prone 8 (SAMP8) mice [35]. Our results further indicate that use of EGCG or its derived compounds attenuate age-related muscle loss through myostatin/microRNAs/ubiquitin-proteasome signaling in late passage mouse myoblast C2C12 cells and SAMP8 mice [36]. Collectively, the aforementioned evidence suggests that dietary EGCG supplementation preserves muscle in aged sarcopenic rodents by upregulating anabolic factors and attenuating protein degradation through the inhibition of the ubiquitin-proteasome pathway.

Reduction of circulating inflammatory cytokines, inhibition of the NF-κB pathway, and activation of the longevity factor sirtuin1 in the liver and kidney tissues were considered the mechanisms underlying the increases in the lifespan of Wistar rats following the lifelong administration of EGCG (25 mg/kg of body weight) [37]. In this regard, NF-κB mediated activation of inflammatory responses is considered the underlying mechanism of muscle protein degradation [38]. The evidence suggests that chronically inhibiting the NF-κB activity may limit aging-associated muscle loss. In summary, the green tea extract and its major bioactive compounds have several potential benefits for protecting against sarcopenia by improving insulin sensitivity and suppressing inflammation.

Clinical trials investigating green tea catechins and their effects on age-related decline in functional fitness and muscle mass are scant, and the existing rodent studies lack clinical evidence. Several clinical

studies have investigated the efficacy of green tea beverages enriched with catechins as a potential nutritional supplement for older adults. After 8-week epicatechin supplementation (1 mg/kg BW), the appendicular muscle mass index and the outcomes in the timed-up-and-go test were significantly enhanced in older men with sarcopenia [39]. The biologically active compounds in green tea extract, such as EGCG, may be involved in the control of systemic inflammation and may reduce the symptoms of muscle dysfunction.

5. Oligonol® and muscle function

Oligonol, a low-molecular-weight polyphenol, is a depolymerized flavanol derived from lychee fruit and green tea, and it consists of ≥80% flavanols and other phenolic compounds [40]. In our previous study, oligonol supplementation (200 mg/kg BW) for 8 weeks ameliorated the decline in skeletal muscle mass and grip strength in SAMP8 mice. Oligonol promoted protein turnover in the skeletal muscle of SAMP8 mice through the upregulation of AKT/mTOR-mediated protein synthesis and suppression of FOXO3a-MuRF1/MAFbx-mediated protein degradation [41]. In addition to the signaling pathways involved in protein synthesis and breakdown, we identified several novel mechanisms of action of oligonol and determined its potential use in sarcopenia treatment. First, oligonol was shown to restore mitochondrial DNA copy number as well as genes related to mitochondrial biogenesis, including nuclear respiratory factor 1 and mitochondrial transcription factor A. Additionally, the abundant accumulation of autophagosomes and lysosomes in the skeletal muscle of SAMP8 mice was limited by oligonol. Lastly, oligonol supplementation caused a reduction in the expression of the released cytochrome *c* and cleaved caspase-9 in the skeletal muscle of SAMP8 mice [41]. Oligonol exerted beneficial effects on a sarcopenia mouse model. However, little is known regarding its roles in the muscle function and muscle quality of older adults. A randomized controlled trial demonstrated that oligonol supplementation (200 mg per day) for 12 weeks significantly improved physical performance and muscle mass in older men [42]. These results from animal and human studies suggest that oligonol supplementation has beneficial effects on various components of sarcopenia.

6. Resistance exercise + tea catechins

Although definite evidence of the effectiveness of specific interventions for sarcopenia has yet to be established, nutritional supplementation combined with exercise seems to be effective for sarcopenia treatment. One study investigated the effects of endurance exercise combined with tea catechin ingestion (diet containing 0.35% tea catechins) in SAMP1 mice and found that tea catechins combined with the exercise intervention for 8 weeks was beneficial for suppressing the age-related decline in physical performance by increasing the mRNA levels of mitochondria-related molecules [43]. Nevertheless, few randomized controlled trials have examined the effects of exercise and supplementation with tea catechins on muscle function in older adults. A recent double-blinded controlled study demonstrated significant increases in leg press muscle strength and chest press muscle strength in men with sarcopenia after the 8-week resistance exercise training + epicatechin (1 mg/kg BW) supplementation compared with participants in the resistance exercise training, epicatechin, and placebo groups [39]. In another randomized controlled trial, women with sarcopenia were randomized into four groups: exercise + tea catechin (350 mL/day), exercise, tea catechin supplementation (350 mL/day), and health education for 3 months [44]. At postintervention, the exercise + catechin group exhibited significant improvements in leg muscle mass and usual walking speed compared with the health education group [44]. Collectively, the aforementioned findings indicate that exercise programs including both strength training and aerobic exercises combined with nutritional supplementation was the most promising approach to protecting against sarcopenia.

7. Conclusion and future directions

Sarcopenia is a physical dysfunction with high mortality and is one of the most important public health burdens in the growing older population worldwide. Studies have proposed numerous factors involved in the pathophysiology of sarcopenia, including age-related anabolic resistance, chronic inflammation, hormone imbalance, and suboptimal nutritional status. The significance of green tea-derived natural products in suppressing protein degradation and maintaining optimal muscle protein synthesis suggests that these natural products alone can provide significant benefits for muscle function. Future studies should verify if the mechanisms observed in rodent experiments (e.g., upregulation of AKT/mTOR-mediated protein synthesis and suppression of FOXO3a- MuRF1/MAFbx-mediated protein degradation from SAMP8 mice) are involved in the regulating the dynamic balance between

muscle protein synthesis and muscle protein breakdown in humans during long-term supplementation. The influence of resistance training on skeletal muscle in older adults can be augmented by incorporating rational evidence-based nutritional support strategies. Limited evidence suggests that specific dietary supplements (e.g., EGCG ~1 mg/kg BW and oligonol ~200 mg/day) support resistance exercise -induced adaptations. Resistance exercise combined with green tea–derived natural products seems to have a higher impact on the prevention of sarcopenia progression. However, key question remains to be answered to advance our understanding of natural products to support resistance exercise training on sarcopenia. Most importantly, future studies should aim to replicate the findings presented here, considering the small sample sizes and relatively short duration of supplementation in existing human studies. Additional well-designed clinical trials are needed to determine appropriate therapeutic interventions for sarcopenia through a thorough investigation of its underlying pathophysiology.

Disclosure of interest

The authors report no conflict of interest.

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