

# Recent Advances in the Role of Edible Fungi in Sarcopenia: A Review

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## ABSTRACT

Sarcopenia, a degenerative skeletal muscle disease closely related to aging, has become a major threat to the health and quality of life of older adults. With the global trend of population aging, the social and economic problems caused by sarcopenia are becoming increasingly prominent. Currently, pharmacological treatments for sarcopenia are somewhat limited, whereas nutritional interventions have shown potential advantages in combating the condition. This review comprehensively discusses the bioactive components and functional properties of edible fungi and provides a thorough understanding of the severe health issues faced by sarcopenia patients, such as muscle degeneration and functional loss. Although animal experiments and early human studies support the positive effects of edible fungi, large-scale nutritional epidemiology studies in humans are still insufficient, which limits their application in the prevention and treatment of sarcopenia. Therefore, future research, such as randomized controlled trials, is needed to fully understand their effects on muscle health and to provide a solid scientific basis for the prevention and management of sarcopenia.

## KEYWORDS

Edible fungi; Sarcopenia; Antioxidation; Anti-inflammation Polysaccharides

## 1. INTRODUCTION

Sarcopenia, also known as muscle loss, muscle atrophy syndrome, or muscle failure, is a progressive and systemic skeletal muscle disease involving the accelerated loss of muscle mass and function. It is associated with an increased risk of various adverse outcomes, including falls and fractures, disability and partial disability, loss of independence, decreased quality of life, hospitalization, and mortality [1-5]. Sarcopenia is generally considered a part of the natural aging process in older adults but can also be associated with various disease states in middle-aged individuals [6]. Concurrently, the importance of non-pharmacological approaches has been increasingly recognized by the medical community [7].

Although the pathophysiological mechanisms of sarcopenia are not yet fully understood, current research indicates that the condition can be treated or improved through reversible pathways [8]. However, due to a lack of high-quality evidence and potential drug-related side effects, there are currently no specific pharmacological treatment strategies approved for the prevention or treatment of sarcopenia [6]. Concurrently, the importance of non-pharmacological approaches has been increasingly recognized by the medical community [9, 10] Previous research has shown that diet is a potentially modifiable factor that can have a positive impact on delaying the progression of sarcopenia [11].

Edible fungi are a type of high-value macrofungi, rich in nutritional components such as high-quality protein, carbohydrates, various vitamins, and mineral elements [12]. They are characterized by being high in protein, low in sugar, low in fat, and low in cholesterol [12]. Furthermore, edible fungi contain a variety of bioactive substances, such as polysaccharides, dietary fiber, steroids, and polyphenols [12-15]. Studies have found that extracts from edible fungi have ben However, to date, the effects of edible fungi on sarcopenia remain unclear. This review synthesizes the literature on the bioactive components and functional properties of edible fungi and provides a deep understanding of the serious health problems faced by patients with sarcopenia, such as muscle degeneration and functional loss. The aim is to explore whether edible fungi could be a potential nutritional intervention strategy for sarcopenia.

## 2. SARCOPENIA OVERVIEW

### Definition and Diagnosis

The term "sarcopenia" originates from the Greek phrase "poverty of flesh" and was first described in the 1980s as an age-related decline in lean body mass, which can affect an individual's mobility, nutritional status, and independence [17]. Subsequently, the definition has continued to evolve, marked by two significant milestones. First, since 2010, the concept of muscle function has been incorporated into six consensus definitions [1, 7, 18, 19]. Research indicates that muscle function is a more effective predictor of clinical-related outcomes than muscle mass alone [20, 21]. The second milestone occurred in 2016 when sarcopenia was coded as an independent disease in the International Classification of Diseases (ICD-10: M62 [22 23]). However, due to differences among various populations and disease states, the definition of sarcopenia continues to be a subject of ongoing evolution and discussion. Currently, the most widely cited definition was proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) [7], supported by the Asian Working Group for Sarcopenia (AWGS) [1], and updated to EWGSOP2 in January 2019 [24]. Its specific diagnostic criteria are as follows: (1) Low muscle strength: handgrip strength <27 kg for men, <16 kg for women. (2) Low muscle mass: appendicular skeletal muscle mass (ASM) <20 kg for men, <15 kg for women; or appendicular skeletal muscle mass index (ASMI) ( $ASMI = ASM/height^2$ ) <7.0 kg/m<sup>2</sup> for men, <5.5 kg/m<sup>2</sup> for women. (3) Low physical performance: gait speed  $\leq 0.8$  m/s. Possible sarcopenia is suspected in the presence of criterion (1); a diagnosis of sarcopenia is established upon the presentation of both criteria (1) and (2); and severe sarcopenia is diagnosed when criteria (1), (2), and (3) are all concurrently observed. In light of the cultural, background, and lifestyle differences between European and Asian populations, the AWGS modified its diagnostic algorithm and some criteria in 2019, while retaining the original definition of sarcopenia as "age-related loss of skeletal muscle mass, plus low muscle strength and/or low physical performance" [2]. The specific diagnostic criteria are: (1) Low muscle strength: handgrip strength <28 kg for men, <18 kg for women; (2) Low physical performance: 6-meter walk speed <1.0 m/s, or Short Physical Performance Battery (SPPB) score  $\leq 9$ , or 5-time chair stand test  $\geq 12$  seconds. (3) Low muscle mass: using dual-energy X-ray absorptiometry (DXA), ASMI <7.0 kg/m<sup>2</sup> for men, <5.4 kg/m<sup>2</sup> for women; using bioelectrical impedance analysis (BIA), ASMI <7.0 kg/m<sup>2</sup> for men, <5.7 kg/m<sup>2</sup> for women. When criterion (1) or the 5-time chair stand test  $\geq 12$  seconds from criterion (2) is met, it indicates possible sarcopenia. Based on this, if criterion (3) and/or criterion (2) are also met, sarcopenia can be diagnosed; when all three criteria (1), (2), and (3) are met simultaneously, it is diagnosed as severe sarcopenia.

### 3. EPIDEMIOLOGY OF SARCOPENIA

Although the prevalence of sarcopenia varies depending on the research and definitions used, it is a common condition among older adults and patients with various medical conditions. In a systematic review by Nascimento PR et al [25], the global prevalence of sarcopenia in older adults ranged from 5% (95% confidence interval [CI]: 1%–10%) according to EWGSOP2 criteria to 17% (95% CI: 11%–23%) according to the International Working Group on Sarcopenia (IWGS) [18]. However, in a study by Petermann-Rocha F et al. [26], the prevalence based on EWGSOP was as high as 22% (95% CI: 20%–25%), while the prevalence based on the Foundation for the National Institutes of Health (FNIH) criteria was the lowest at 11% (95% CI: 9%–14%). In the studies by Nascimento PR et al. [25] and Petermann-Rocha F et al. [26], the combined prevalence across all definitions was approximately 10% (95% CI: 7%–12%) and 16% (95% CI: 15%–17%), respectively. A recent meta-analysis indicated that the prevalence of sarcopenia in the global population aged 60 and over is between 10% and 27% [26]. In addition to being common in older adults, sarcopenia can also occur in middle age [6], and is prevalent in certain populations, such as patients with cancer [27], renal insufficiency [28], liver disease [29] and metabolic disorders [30]. Compared to the general population, the prevalence of sarcopenia is higher among these patients, ranging from 18% in diabetic patients [30] to 66% in patients with inoperable esophageal cancer [31]. Although evidence suggests that the incidence of sarcopenia increases with age, research on its incidence is relatively limited. One study reported an incidence of 1.6% in European men and women aged 40 to 79, according to the EWGSOP definition [32]. In a cohort of Chinese men and women with an average age of 72, the incidence of sarcopenia was 3.4% according to the AWGS definition [8].

Sarcopenia is one of the most common diseases among older adults today and is associated with multiple adverse health outcomes, including falls [33, 34], functional decline [35], frailty, reduced quality of life [36], increased healthcare costs, and mortality [37]. A systematic review and meta-analysis showed a consistent association between sarcopenia (defined by EWGSOP) and mortality, with a pooled odds ratio of 3.59 (95% CI: 2.96–4.27), and the effect was greater in men and women aged 79 and older [38]. Another systematic review confirmed that sarcopenia leads to a decline in overall quality of life, regardless of whether generic self-report tools or disease-specific questionnaires are used [36]. According to world population data, the number of people aged 65 and over is projected to double between 2019 and 2050, from 703 million to 1.5 billion, and the proportion of the older adult population will increase from 9% to 16% [7]. Sarcopenia is not only associated with a series of adverse health outcomes but also with increased medical expenditures [39]. Epidemiological surveys show that for hospitalized older adults, the direct and indirect costs for patients with sarcopenia are approximately five times higher than for those without the condition [40]. Furthermore, patients with sarcopenia have higher hospitalization rates and longer average hospital stays, with annual inpatient costs accounting for about 4% of the total national healthcare expenditure [41]. With the increasing proportion of the older adult population, the prevalence of sarcopenia will rise sharply in the coming years, leading to significant medical and economic burdens. Therefore, identifying modifiable risk factors for sarcopenia is of great public health importance.

### 4. PATHOPHYSIOLOGY

The homeostasis of skeletal muscle is determined by the balance between muscle hypertrophy, atrophy, and regeneration. With advancing age, this balance is disrupted, particularly manifesting as an imbalance between muscle protein synthesis and breakdown, which leads to a gradual loss of muscle mass and function, a state known as sarcopenia [6, 42]. Although the decline in muscle mass and function during aging is considered inevitable, the extent of this reduction varies significantly among individuals [43, 44]. The etiology of sarcopenia is multifactorial, involving genetic and environmental factors, but the specific mechanisms of these factors are not yet fully understood. Existing research has shown that factors such as oxidative stress [45, 46], chronic inflammation [47,

48], mitochondrial dysfunction [45], hormonal changes [49, 50], malnutrition [11, 51, 52] and reduced physical activity [53, 54] are closely related to the development of sarcopenia. In particular, oxidative stress and chronic inflammation play key roles in age-related muscle atrophy. They affect multiple intracellular signaling pathways, disrupt the balance between protein synthesis and breakdown, and promote apoptosis, thereby significantly reducing muscle mass [55]. Furthermore, previous studies have found that an increase in chronic low-grade inflammation induced by oxidative stress is detrimental to both human skeletal muscle and animal models [56].

Additionally, oxidative stress can directly damage macromolecules in skeletal muscle, such as lipids, nucleic acids, and proteins. Mitochondria are the primary source of reactive oxygen species (ROS), and excessive ROS production can lead to damage of mitochondrial DNA, affecting myocyte function and survival [57, 58]. Chronic low-grade inflammation can lead to a reduction in muscle protein synthesis and an increase in breakdown by activating the ubiquitin-proteasome system and altering mitochondrial dynamics, ultimately resulting in a loss of skeletal muscle mass and function [59]. Furthermore, chronic low-grade inflammation can also induce myocyte apoptosis and disrupt satellite cells, thereby limiting muscle repair and regeneration and promoting the onset of sarcopenia [9, 60]. Meanwhile, adequate nutritional status is crucial for maintaining skeletal muscle health, and a deficiency in essential amino acids and protein will reduce the rate of muscle synthesis, exacerbating the loss of muscle mass [61]. Conversely, nutritional interventions, such as supplementing with a mixture of leucine-rich essential amino acids and carbohydrates, have been shown to increase muscle protein synthesis, which is beneficial for preventing or treating sarcopenia [62, 63]. Moreover, research also indicates that combining resistance training with essential amino acid intake is an effective strategy for combating sarcopenia [64]. In summary, sarcopenia is a complex pathological condition driven by multiple factors.

## 5. OVERVIEW OF EDIBLE FUNGI

Fungi are a class of nutrient-rich and palatable macrofungi, including fleshy and gelatinous fruiting bodies or sclerotial tissues. Due to their nutritional composition and delicious taste, these fungi are widely used in food and traditional medicine around the world. According to the definition from the European International Life Sciences Institute, edible fungi are considered functional foods with potential therapeutic and disease-preventive properties due to their potential efficacy in improving, preventing, or treating certain diseases [65]. With the growing public awareness of healthy eating, the consumption of edible fungi has increased significantly, and it is projected to grow from approximately 12.74 million tons in 2018 to 20.84 million tons in 2026 [66].

Edible fungi are rich in protein, dietary fiber, essential amino acids, vitamins, and minerals, and are low in fat and calories, making them highly nutritious. Research indicates that bioactive components in edible fungi, such as polysaccharides [67], alkaloids [68], steroids [69], polyphenols [14] play important roles in natural antioxidation [70], anti-cancer [71], anti-aging [72], lipid-lowering [73], and immunomodulatory activities. In particular, polysaccharides from edible fungi have attracted considerable attention due to their excellent nutritional and therapeutic effects and are regarded as health compounds with broad application prospects. For instance, polysaccharides from *Lentinula edodes* (shiitake) exhibit significant antioxidant activity and can enhance the body's ability to kill tumor cells [74], while polysaccharides from *Auricularia auricula-judae* (black wood ear) can increase the activity of antioxidant enzymes in the heart and improve cardiac function [75]. Additionally, dietary fiber in edible fungi, as a key component, demonstrates multiple health benefits, such as enhancing immunity, anti-tumor activity, and lowering blood glucose, lipids, and cholesterol levels [76-80].

Recent studies have further revealed the relationship between edible fungi and chronic diseases, providing new insights for the field of public health. A prospective cohort study involving 19,830 Chinese adults showed a significant association between high consumption of edible fungi and a

lower risk of hyperuricemia [81], suggesting that edible fungi may help reduce the incidence of hyperuricemia. Similar conclusions were reached in a large-scale collaborative cross-sectional study in the United States and Japan, which also investigated the link between edible fungi and hyperuricemia. This study found that the consumption of edible fungi was associated with a lower risk of developing hyperuricemia in middle-aged Japanese men [82], further supporting the connection between edible fungi and health benefits. A meta-analysis emphasized that increased intake of mushrooms is associated with a reduced risk of cancer [83]. Furthermore, a prospective cohort study of 13,156 Chinese older adults aged 65 and above found that high-frequency intake of mushrooms and algae was negatively correlated with all-cause mortality, suggesting long-term health benefits of edible fungi. In addition, a clinical trial confirmed that long-term supplementation with *Hericium erinaceus* (12 weeks) can prevent memory decline and improve cognitive function [84]. These studies not only reveal the potential health benefits of edible fungi but also provide a scientific basis for their inclusion as part of a daily diet. However, one study, a large cohort study with over 2 million person-years of follow-up, found no significant association between mushroom consumption and biomarkers or risk of cardiovascular disease and type 2 diabetes in American adults [85], suggesting that mushroom intake may have a limited effect on these diseases.

## 6. THE ASSOCIATION BETWEEN EDIBLE FUNGI AND SARCOPENIA

Although the link between edible fungi and various chronic diseases has been extensively studied, research on their association with sarcopenia is relatively scarce. Recent studies have begun to fill this gap. For example, a cross-sectional study covering 32,308 Chinese adults found a positive correlation between the consumption of edible fungi and enhanced handgrip strength, suggesting that edible fungi may have the potential to improve muscle function [86]. Further support comes from a randomized controlled trial, which showed that Brazilian mushrooms (*Agaricus brasiliensis*) may have the potential to alleviate muscle fatigue [87]. Concurrently, animal studies have also shown that edible fungi can effectively inhibit the production of blood lactate and promote energy metabolism, thereby enhancing muscle endurance [88]. The experiments by Yusuke Komiya et al. further demonstrated that feeding mice edible fungi for eight consecutive weeks significantly increased their muscle endurance [89]. In *in vivo* and *in vitro* models of muscle atrophy, it was found that extracts from *Inonotus obliquus* (chaga mushroom) could promote muscle growth and regeneration, helping to prevent muscle atrophy [90]. Additionally, immunologically active substances isolated from black wood ear can promote the release of nitric oxide (NO). As an effective vasodilator, NO can increase muscle blood flow and mitochondrial respiration [91, 92], thereby reducing muscle fatigue, improving muscle contraction strength, and enhancing repair capabilities [93, 94]. Furthermore, research has also shown that edible fungi can enhance muscle endurance by promoting the expression of key metabolic regulatory factors, such as AMP-activated protein kinase and peroxisome proliferator-activated receptor delta (PPAR- $\delta$ ) [95]. This further reveals the potential molecular mechanisms of edible fungi in promoting muscle health.

Bioactive components in edible fungi, such as polysaccharides, polyphenols, and melanin [13-15], have received widespread attention for their significant antioxidant, anti-inflammatory, immunomodulatory, and anti-aging benefits [70, 72, 96]. Oxidative stress and molecular inflammation are key factors leading to muscle degeneration [97, 98], and the bioactive components in edible fungi seem to effectively intervene in this process. For example, studies have shown that black wood ear has significant *in vitro* antioxidant capacity, able to scavenge superoxide anions and hydroxyl radicals, with its efficacy being positively correlated with its molecular weight [99]. Crude polysaccharides from *Russula lepida* exhibit strong chelating and reducing abilities, as well as antioxidant activity, by scavenging hydroxyl and superoxide radicals [100]. Polysaccharides isolated from the mycelium of *Agrocybe aegerita* can enhance the activity of antioxidant enzymes, reduce the production of malondialdehyde (an indicator of oxidative stress), alleviate oxidative damage, and thus protect cells from ROS attack [101]. Further animal experiments have shown that polysaccharides

from *Lentinula edodes* can achieve an antioxidant state by reducing inflammatory factors and eliminating lipid peroxides, while also inhibiting the expression of aging-related markers, demonstrating significant anti-aging effects [102]. In another animal study, it was found that polysaccharides from edible fungi can also increase the secretion of interleukin-6 and inhibit the expression of lipofuscin and advanced glycation end products (an age-related indicator), significantly mitigating aging induced by oxidative stress [103]. Additionally, the polyphenolic compounds (including catechins and chlorogenic acid) and melanin in black wood ear can exert antioxidant effects by scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals and superoxide anions [15].

In summary, while the evidence for a potential association between edible fungi and enhanced muscle function and endurance is primarily derived from animal experiments and molecular mechanism studies, this research provides a preliminary scientific basis for the potential positive effects of edible fungi on human sarcopenia. In particular, these studies reveal that edible fungi may improve muscle health through mechanisms such as promoting the release of nitric oxide and enhancing antioxidant and anti-inflammatory responses. However, although a few cross-sectional studies have shown a positive correlation between edible fungi consumption and increased muscle function in humans, direct epidemiological evidence linking edible fungi to the risk of sarcopenia remains relatively scarce.

## 7. SUMMARY AND PROSPECTS

Muscle health plays a crucial role in promoting healthy aging. As an important and modifiable lifestyle factor, diet and nutrition are essential for maintaining muscle mass, enhancing muscle strength, and improving overall physical function. According to the existing research summarized here, edible fungi, due to their rich nutritional value, have shown potential benefits for muscle health in animal models. However, large-scale nutritional epidemiological studies on the effects of edible fungi on human muscle health are still relatively scarce, which limits their application in the prevention and treatment of sarcopenia. Although current research on the association between edible fungi and sarcopenia is still in its early stages, existing evidence has highlighted the importance of further exploring the potential role of edible fungi in the prevention and treatment of sarcopenia. Future research needs to employ large-scale, multi-center prospective cohort studies and randomized controlled trials to further investigate the effects of edible fungi on human muscle health, particularly their potential role in preventing and treating sarcopenia. This will not only lay a solid scientific foundation for the prevention and treatment of sarcopenia but may also open up new avenues and strategies for understanding and addressing other age-related health issues.

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