Current Nutrition Reports (2023) 12:281–298
https://doi.org/10.1007/s13668-023-00468-x

REVIEW

Nutritional Quality and Biological Application of Mushroom Protein as a Novel Protein Alternative

Francis Ayimbila[1,2] · **Suttipun Keawsompong**[1,2]

Accepted: 13 March 2023 / Published online: 10 April 2023

Abstract

Purpose of Review Global concerns about population growth, economic, and nutritional transitions and health have led to the search for a low-cost protein alternative to animal origins. This review provides an overview of the viability of exploring mushroom protein as a future protein alternative considering the nutritional value, quality, digestibility, and biological benefits.

Recent Findings Plant proteins are commonly used as alternatives to animal proteins, but the majority of them are low in quality due to a lack of one or more essential amino acids. Edible mushroom proteins usually have a complete essential amino acid profile, meet dietary requirements, and provide economic advantages over animal and plant sources. Mushroom proteins may provide health advantages by eliciting antioxidant, antitumor, angiotensin-converting enzyme (ACE), inhibitory and antimicrobial properties over animal proteins. Protein concentrates, hydrolysates, and peptides from mushrooms are being used to improve human health. Also, edible mushrooms can be used to fortify traditional food to increase protein value and functional qualities. These characteristics highlight mushroom proteins as inexpensive, high-quality proteins that can be used as a meat alternative, as pharmaceuticals, and as treatments to alleviate malnutrition.

Summary Edible mushroom proteins are high in quality, low in cost, widely available, and meet environmental and social requirements, making them suitable as sustainable alternative proteins.

Keywords Edible mushrooms · Alternative protein · Protein quality · Bioactive proteins

Introduction

Protein has long been regarded as an essential component of the health of man. In addition to being a source of energy, protein serves a variety of vital activities in biological tissues, hormones, or enzymes [1]. Human sources of proteins are mostly derived from animal products such as red and processed meat. Animal proteins are generally considered complete proteins because they contain all nine essential amino acids, but their production is incredibly expensive [2]. In addition, livestock occupies around one-third of all land on the earth. Meat production also contributes significant greenhouse gas emissions (about 14% of all human-caused greenhouse gas emissions), which has a significant environmental impact. Moreover, red and processed meat has been linked to a variety of human health problems, including heart disease and colon cancer [3]. In resolving these problems, plant-based proteins have gained popularity as an alternative to animal proteins in recent decades. This is due to the low cost of production, abundant supply, and presence of bioactive and phytochemical compounds in plant-based proteins [4•]. However, plant proteins are deficient in one or more essential amino acids; thus, plant-based proteins cannot be considered complete proteins [4•]. For instance, cereals contain low values of lysine, and legumes are deficient in sulfur amino acids (e.g., methionine and cysteine) [4•].

Recently, edible mushrooms are being recognized as safe sources of high-quality proteins owing to low fat, high fiber, and functional ingredients such as phenolics (Fig. 1). Mushrooms contain a high amount of protein content with an

✉ Suttipun Keawsompong
fagisuk@ku.ac.th

1 Specialized Research Units: Prebiotics and Probiotics for Health, Department of Biotechnology, Faculty of Agro-Industry, Kasetsart University, Bangkok 10900, Thailand

2 Center for Advanced Studies for Agriculture and Food, KU Institute of Advanced Studies, Kasetsart University (CASAF, NRU-KU), Bangkok 10900, Thailand

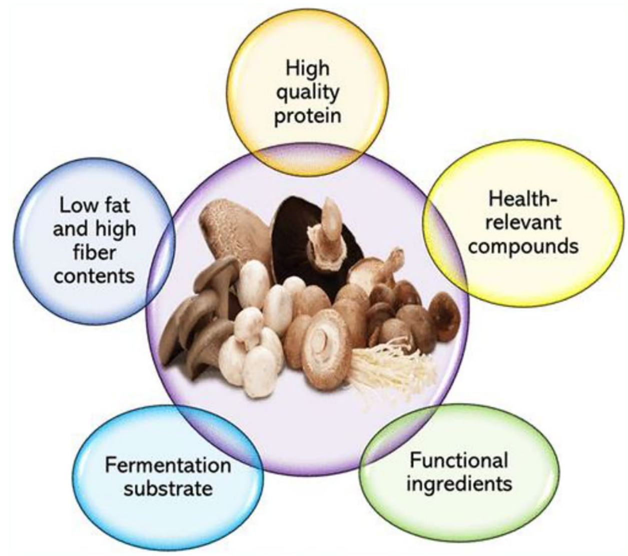

Fig. 1 Mushrooms as safe sources of quality proteins and functional ingredients [108]

average value of 23.80 g/100 g dry weight (DW). Mushroom proteins have lately gained acceptance in the food industry in view of their high nutritional value and complete essential amino acids [5–7]. When compared to animal and plant sources, mushroom proteins normally have a complete essential amino acid profile, meeting dietary requirements while having certain economic advantages. Several mushrooms can also grow in agro-industrial waste and produce high yields in a short time. Furthermore, mushroom proteins have a high branched-chain amino acid (BCAA) content, which is mostly found only in animal-based protein sources [8••]. Again, mushroom proteins have high thermal and pH stability and their digestibility of ranges from 60 to 70% [9]. However, the phenolics, phytates, and tannins found in mushrooms have been shown to inhibit digestive enzymes; amylase, pepsin, and pancreatin, while the high fiber content of mushrooms may cause some reducing sugars to be released during digestion, resulting in a Maillard reaction and a decrease in assimilable lysine, methionine, and tryptophan. The lipids that remain may also oxidize, leading to rancidity [10]. Fortunately, protein digestibility can be improved by removing the above-mentioned food components through processing [9]. It is worth noting that mushroom fruiting bodies are commonly consumed as a source of protein, which may provide a substantial portion of amino acids for body functioning as well as fermentable substrates to stimulate the microbiota for host health benefits [11], indicating the ability of both processed and unprocessed mushroom proteins to positively influence human health. Current studies have discovered that mushroom protein concentrates, hydrolysates, and peptides have potent angiotensin-converting enzyme (ACE) inhibitory, antioxidant, antimicrobial, anticancer, antiviral, and gut microbiota modulation properties [8••, 11]. Moreover, there are other bioactive proteins found in mushrooms include lectins, fungal immunomodulatory proteins (FIP), ribosome-inactivating proteins (RIP), antimicrobial/antifungal proteins, ribonucleases, and laccases [12]. Notably, these point to mushrooms as a viable source of bioactive proteins alternative to animal sources. However, because there are thousands of different kinds of mushrooms, the best mushroom species in terms of high protein quantity and quality are sought after by food industries for effective utilization.

Increased production of high-quantity and quality protein is required to meet the growing demand resulting from global population growth, economic and nutritional transitions, and health concerns [13]. It has been predicted that by 2050, the global population will be surpassed 9 billion, implying a rise in food consumption. According to the Food and Agriculture Organization (FAO), agricultural production will have to expand by 70% to fulfill demand [14]. Subsequently, global protein demand will rise, and in the absence of alternative sources, environmental resources will be under intense pressure. As a result, an alternative protein source, such as edible mushrooms, that can provide high-quality protein at a low cost, faster, and with little to no negative environmental impact, would be much preferred. This review aims to reveal the feasibility of using mushroom protein as an alternative protein to conventional protein sources, taking into account important factors such as protein quality, digestibility, and biological benefits. Because there is little available literature on the use of mushroom protein for future protein sources, this review may be especially useful in uncovering the importance of using this underutilized source of protein to combat malnutrition, as a meat substitute, and as a pharmaceutical compound.

Methods

To find relevant articles, we searched Google Scholar, PubMed, and Scopus using the terms “edible mushroom” OR “edible mushroom protein” with the filters “protein quality,” “protein digestibility,” and “biological functions” alone or in any combination. Several articles that were pertinent to the main subject were used, with the majority of them being those that were released in English between 2020 and 2022. Only very relevant earlier articles were added. Research on inedible mushrooms was not included.

Nutritional Value of Edible Mushroom Proteins

Mushrooms must be available as a high-protein sources before they can be considered an acceptable alternative protein source. In 2018 alone, about 9 million tons of cultivated mushrooms were produced worldwide according to data from the United Nations' Food and Agriculture Organization [15]. The most common farmed species are *Agaricus bisporus* (white button mushroom), *Lentinula edodes* (shiitake), *Pleurotus ostreatus* (oyster mushroom), and *Flammulina Velutipes* (golden needle mushroom). *Agaricus bisporus* is the most extensively consumed fungus in the world, followed by *Pleurotus spp*. and *Lentinus edodes* [9]. Several other edible mushrooms with high protein values are also cultivated worldwide. The human body requires a significant amount of protein for growth and maintenance as regards physiological functions, such as the vital performance of hormones and enzymes [8••]. Though the protein value of mushrooms varies depending on species and strains, maturation stage, the substrate used for cultivation, and other environmental factors, mushrooms provide significant protein at a lower cost than plant and animal sources [16].

Protein value is requisite since protein accounts for around 17% of total calorie consumption [13]. Many reports unveiled that crude protein is particularly found in high levels in mushrooms. Protein content in edible mushrooms ranged from 6.60 to 36.87 g/100 with an average value of 23.80 g/100 g dry weight [17] as shown in Table 1. *Tricholoma* exhibited the highest value of protein, while *Laetiporus sulphureus* and *Polyporus dictyopus* showed the lowest content [5]. Popular edible mushroom species such as *Lentinus edodes*, *Agaricus* spp., and *Pleurotus* spp. contained 14.87 to 27.13% [18], 26.60 to 39.84% [6], and 18 to 19.15 g/100 of protein [19], respectively. Crude protein ranged from 6.60 to 30.69 g/100 g among mushrooms obtained from the Kilum-Ijim forest in Cameroon [7]. *Lentinus squarrosulus* powder presented an excellent protein value of 30.12 g/100 g [11]. Even though the whole fruiting body of a mushroom is commonly consumed, it is interesting to note that different parts of the mushroom present different protein values. Nutritional analysis of growing mushrooms in South Africa revealed protein values ranging between 18% (*L. deliciosus*) to 37.0% (*B. edulis*), with the pileus having richer protein [20]. *Lentinus crinitus* comprised a protein value of 14.4% (pileus) and 9.5% (stipe) [21]. The data show that edible mushrooms have high protein levels, but this varies by species and morphology (pileus or stipe). Despite these influences, some edible mushrooms are noted to have a higher protein value than vegetables, fruits, and grains [5].

Table 1 Nutritional values of some edible mushrooms

Mushroom	Protein, g/100 g	Reference
Tricholoma	36.87	[5]
Copyinds comatus (MUII. Fr) Gray	30.90	
Volvariella volvacea (Bull.: Fr.) Sing.	28.10	
Russula vinosa Lindblad	27.26	
Agaricus blazei Murrill	26.60	
Morchella esculenta	25.85	
Cordyceps militaris	25.56	
Agrocybe aegerita	24.79	
Boletus	23.99	
Lentinus edodes (Berk.) Sing	23.26	
Pleurotus eryngii	19.15	
Dictyophora indusiate (Vent.ex Pers)	18.25	
Polyporus tenuiculus	10.89	[7]
Termitomyces striatus	21.76	
Termitomyces macrocarpus	30.69	
Auricularia polytricha	17.44	
Laetiporus sulphureus	8.62	
Termitomyces sp.1	28.24	
Termitomyces sp.2	21.26	
Polyporus dictyopus	6.60	
Boletus edulis	Pileus (37.0%), stipe (21.3%)	[20]
Boletus mirabilis	Pileus (33.0%), stipe (27.4%)	
Lactarius deliciosus	Pileus (20.8%), stipe (18.0%)	
P. ostreatus	18.08%	[19]
A. bisporus	29.64 to 39.84%	[6]
L. edodes	14.80 to 27.13%	[18]
L. squarrosulus	30.12 g/100 g	[11]

The nutritional value of mushroom protein is determined not only by its quantity but also by its ability to meet dietary requirements; recommended dietary allowance (RDA) and protein efficiency ratio (PER). Based on the data presented in Table 1 (reports within 2020–2022), species of *Tricholoma*, *Copyinds*, *Volvariella*, *Termitomyces*, *Lentinus*, and *Agaricus* exhibited high protein value (25–40%). Notably, 100 g of mushrooms can provide between 29.41 and 66.0% of the RDA for men and between 35.80 and 80.35% of the RDA for women, whereas beef jerky and whole milk can provide between 47.0 and 59.28% for men and between 57.22 and 67.75% for women [8••]. According to USDA data [22] and a review report [8••], *P. ostreatus* (black oyster) showed the highest protein efficiency ratio (PER) of any mushroom, surpassing beef jerky. *A. bisporus* (Portobello) and *A. brasilensis* also outperformed jerky in terms of PER. *A. bisporus* (Champignon) had a PER comparable to lentils, *Pleurotus djamor*, *Pleurotus eryngii*, and *Pleurotus ostreatus* (white oyster) displayed PER similar to black beans, and *Flammulina velutipes* and *L. edodes* had the lowest PER of the mushrooms, equivalent to whole milk. It is important to point out that a lack of information in the literature limits the realization of RDA and PER of other high-protein mushrooms. Meanwhile, the information presented indicates that mushroom species such as *Agaricus* and *Pleurotus* appear to have good protein value and PER.

The protein value of animal sources (on a dry basis) is 27% for milk, 53% for eggs, 37–83% for meat, and 58–90% for fish and crustaceans. Proteins are found in legumes at 22–40%, cereals at 8–18%, nuts at 4–20%, other seeds at 18–32%, and tubers at less than 10% [13]. Some edible mushrooms can provide protein values that are higher than or comparable to animal sources such as milk, egg, meat, and fish, as well as the highest plant-based protein sources. Thus, edible mushrooms are an excellent source of high-quality protein that can be produced more easily, more cheaply, and with less impact on the environment [8••]. Edible mushrooms as a protein source offer an appealing alternative to animal and other plant protein sources.

Quality of Mushroom Protein

Mushroom proteins have attracted more attention in recent times beside the lower production costs and environmental issues over animal and other plant proteins and pose some unique qualities that make them suitable alternative protein sources in the future. The ability to provide essential amino acids for growth and bodily functions is the essence of mushroom quality [23]. Several protein-containing food scoring systems have been developed to effectively compare the quality of protein foods.

Extensive review reports on strategies for scoring protein-containing foods have lately been published [8••, 13]; hence, this section will focus on some commonly used methods. The Essential Amino Acid Score (EAAS), also known as the chemical score, compares the proportion of each essential amino acid in a test protein to a reference standard that contains all of the essential amino acids in the appropriate quantities to meet the demands, according to the WHO/FAO/UNU reference [8••, 24]. On the report of González et al., *A. bisporus*, *P. djamor*, *P. ostreatus*, and *Lentinus edodes* recorded EAA scores > 1.0, which met EAA requirements, whereas *Agaricus brasilensis*, *Pleurotus eryngii*, *Pleurotus ostreatus*, and *Flammulina velutipes* had EAA scores less than 1.0 due to limiting in some individual amino acids such as isoleucine and valine, leucine, leucine, and leucine, respectively. Even though these values vary greatly among mushrooms, they indicate that mushrooms can provide a high amount of quality protein, particularly *Agaricus* spp., *Pleurotus* spp. and *Letinus edodes*. Moreover, *Pleurotus citrinopileatus*, *Pleurotus geesteranus*, *Pleurotus eryngii*, *Oudemansiella raphanipes*, *Pholiota adiposa*, and *Hericium erinaceus* were shown to have a complete range of amino acids and Amino Acid Scores comparable to the WHO standard [25]. *Lentinula edodes* strains, particularly the strain named Shenxiang 18, exhibited good amino acid profile and protein quality [26]. The quality of the amino acid profile is determined by the combination of free and bound amino acids (AA). *Hericium erinaceus*, *P. cystidiosus*, *P. eryngi*, and *P. sajor-caju* had the highest levels of essential free and bound AAs and chemical scores for isoleucine, tryptophan, and phenylalanine. The free proportion of used mushrooms had isoleucine (Ile) levels equivalent to or more than the best five plant sources, whereas tryptophan (Trp) levels were nearly double [27]. Leucine, valine, and glutamic acid were the three most prevalent essential amino acids (EAA) in *P. colossus*. Other EAA included lysine, phenylalanine, histidine, tryptophan, and methionine [28]. In another study, six amino acids, aspartic acid, glycine, alanine, proline, histidine, and arginine, were found in *Cordyceps militaris* fruiting bodies [29].

The levels of amino acids, for example, varied among *Agaricus bisporus* from the same source, indicating the influence of production conditions. Cooking also resulted in 50% losses of glutamic acid, arginine, glycine, serine, threonine, proline, and alanine. During canning, however, glutamic acid, serine, valine, proline, arginine, glycine, and aspartic acid losses were higher (70%) [30]. A study investigated free amino acid profile changes in raw, sautéed, and roasted portobello and shiitake, and certain volatiles from mushroom culinary preparation. Cooking methods caused a significant free amino acid loss, while mushroom variety significantly impacted most amino acid contents [31]. *L. edodes* grown on logs had lower levels of amino acids than sawdust [32]. *L. edodes* fruiting body extracts revealed the presence of 36 essential primary metabolites, including amino acids, organic acids, and sugars. A study looked into the effects of different packaging on the umami taste and aroma of dried *Suillus granulatus*. The content of l-Aspartic acid was significantly lower than that of l-Glutamic acid. During storage, the changes in l-Glutamic acid and total Monosodium glutamate (MSG)-like amino acids were consistent. After 2, 4, and 6 months of storage, the total content of MSG-like amino acids in light-proof packaging (LPP) was higher than that in light-transparent packaging (LTP), but lower than that in LTP at 8 and 10 months [33]. Indicating that a variety of factors interact to determine the amino acid concentration during storage. Free amino acids play a very important role in the presentation of the taste and deliciousness of edible mushrooms. A recent study found that the value of EAA/ (EAA + NEAA) among the five types of edible fungus studied ranged from 32.20 to 41.87%, and the value of EAA/NEAA was 47.48 to 72.03%. EAA/ (EAA + NEAA) and EAA/NEAA values were lowest in *Lentinus edodes* but *Pleurotus citrinopileatus* best fulfilled the optimal protein standard [18]. In all, the above data point to the fact that mushroom proteins have a complete essential amino acid profile, though the amount varied by variety of factors such as species, production, and processing conditions, but cannot be generalized. This rather determine whether a particular mushroom can offer high-quality protein as best substitute protein.

Protein digestibility is useful for estimating protein nutritional quality. The amount of protein accessible for absorption after digestion is determined by how easily peptide linkages are hydrolyzed. Protein Digestibility Corrected Amino Acid Score (PDCAAS) is one of the earliest methods the Food and Agriculture Organization and the World Health Organization devised to evaluate protein quality. Protein digestibility-correlate amino acid score (PDCAAS) assesses protein quality by taking into account both human amino acid needs and digestive capabilities. PDCAAS values for several edible mushroom species and other plant and animal-origin foods have been reported. PDCAAS values for mushrooms ranged from 0.35 to 0.70 based on in vitro and in vivo digestibility studies. Scores for *Agaricus brasiliensis*, *Lentinus edodes*, *Pleurotus ostreatus*, *Agaricus macrosporus*, and *Tricholoma terreum* were 0.36, 0.38, 0.44, 0.40, and 0.70, respectively. Compared to other protein sources some mushrooms outperformed oilseeds; 0.48, fruits; 0.64 and cereals; 0.58 and comparable to tubers; 0.73 and vegetables; 0.74, but lower than meat and dairy with a score of 0.94. It should also be highlighted that using mushrooms two times the weight of meat and dairy could result in a score equivalent to or higher than these animal proteins.

Moreover, the Biological Value (BV) of protein is the percentage of amino acids ingested by the intestines that the body retains. The amount of nitrogen consumed and excreted is used for the calculation. First, the required nitrogen losses in the urine and feces must be estimated, which necessitates giving nitrogen-free diets [8••]. The BV score of mushrooms (80) is at par with milk (100) and meat (80–85), and higher than cereal (40–45) and legume (50–55) [34]. The excellent digestion justifies the use of mushroom protein as an alternative protein in the future.

Mushroom protein digestion has been studied both in vitro and in vivo. The digestibility of mushroom protein can be altered by a variety of factors, including antinutritional factors (phenolics, phytates and tannins, trypsin inhibitors and hemagglutinins). This content, however, is below the WHO toxicity level and poses no risk to humans [8••]. Few works have reported the digestibility of processed and unprocessed mushroom proteins, particularly in the last 3 years. Protein concentrate was produced from *Pleurotus ostreatus* [9]. When Pleurotus mushrooms with 18.3% protein were digested in vitro with trypsin, the digestibility was 68.2% [35]. INFOGEST in vitro digestion (which simulates oral, gastric, and intestinal conditions) revealed that the concentrate digested greatly than mushroom flour. After gastric digestion, the hydrolysis degree (HD) of the mushroom flour and the protein concentrate were 16.5% and 20.3%, respectively. The HD of the protein concentrate increased the most when it transitioned from the gastric to the intestinal phase, rising to an HD of 76.2 ± 1.3%, whereas mushroom flour only reached an HD of 23.5 ± 4.6%. Several proteolytic enzymes are secreted during intestinal digestion, and it is most likely that these enzymes in the pancreatin completely digest the proteins from the concentrate into smaller peptides. It was also found that [36], cooking and canning reduced the number of amino acids present, but in vitro, gastric and intestinal digestion increased the overall amino acid concentration and allowed the detection of two new amino acids (arginine and methionine). The majority of the amino acids were released during the intestinal phase of in vitro digestion. Mushrooms provide enough amino acids per gram of protein that meet the majority of FAO amino acid patterns for adults after in vitro digestion. Overall, mushroom protein digestibility is excellent, supporting PDAAS and BV ratings. This makes edible mushrooms an important part of human nutrition.

The Biological Role of Mushroom Proteins in Human Diet

Conventionally, mushrooms have been consumed as a source of protein as part of a meal and as an ingredient in food preparations. In both ways, the digestibility of the mushroom protein fraction is vital in terms of impacting host physiology and health. High digestion of protein is paramount in releasing amino acids to support host physiology. Concurrently, unhydrolyzed protein may improve health by stimulating the gut microbiota as revealed in previous studies. Ayimbila et al. found that simulated gastro-intestinal digestion of *L. squarrosulus* powder resulted in 58.59% of its protein hydrolyzed in gastric condition and only reached 59.59% after hydrolysis in intestinal condition [11]. Protein profile and digestibility of *G. lingzhi* (GZ) and *G. lucidum* (GL)-Madrid mushroom proteins in simulated gastric fluid differ significantly. GL and GZ contain some proteins that are totally or partially resistant to simulated gastric fluid [37]. Partially hydrolyzed protein components in the mushroom are fermentable by gut microbes to release branch-chain fatty acids to enhance host health [11]. Dietary fiber in the aforementioned mushrooms may have reduced protein digestibility by obstructing enzymatic diffusion and limiting protein hydrolysis. This renders mushrooms suitable for consumption as part of a regular diet in typical food matrixes [38]. Edible mushrooms have recently been used for food fortification or enrichment. According to the Codex General Principles for the Addition of Essential Nutrients to Foods, "fortification" is defined as the addition of one or more essential nutrients to a food product, whether or not that nutrient is typically present in the food. Fortification helps to prevent, reduce, and control micronutrient deficiencies [8••]. Incorporating mushrooms into food products boosts nutritional value, particularly protein, as evidenced by the following studies. The addition of *L. edodes* (5–15%) and *A. auricula* (15%) increased the protein content of sorghum biscuits. However, the protein content of *T. fuciformis* inclusion was comparable to that of control biscuits. Proteins in biscuits had major bands with molecular weights ranging from 18 to 28 kDa before hydrolysis. After in vitro digestion, *L. edodes* and *T. fuciformis* enrichment increased the soluble protein content (small peptide) of sorghum biscuits. The protein profile of 15% *T. fuciformis* contained a small band at 12 kDa, indicating an increase in the small Mw protein fractions after in vitro digestion [39]. By adding 5% *A. bisporus* flour to beef patties, the protein content increased significantly, along with an increase in dietary fiber and a decrease in fat and sodium [40]. Also, cakes fortified with 10% to 15% *Agaricus bisporus* powder increased protein and were found to be the most satisfying [41]. According to a study, adding 15% shiitake powder increased the protein content of noodles. Noodles (15.64 ± 0.12%) with shiitake cap powder had a higher protein content than noodles (14.44 ± 0.02%) with stem powder and noodles (15.23 ± 0.06%) with whole shiitake powder compared to the control (13.35 ± 0.06%) [42]. Kolawole et al. indicated that with the addition of 30% sclerotium flour to Orange Fleshed Sweet Potato (OFSP) and sclerotium of *Pleurotus tubberegium* blended cookies (OFSP) flour, the protein and fiber contents of the cookies increased by approximately 95% while ash content increased by 62% [43]. *Pleurotus ostreatus* mushroom enriched noodles (MFN) had greater protein, fiber, iron, calcium, and potassium content. Mushroom powder supplements of 5%, 8%, and 10% increased the protein content (g/100 g) to 14.40, 14.72, and 16.58, respectively, as opposed to the 12.75 in noodles made solely of wheat flour [44]. Indeed, the inclusion of mushrooms in food products increase the protein value as well as the dietary fiber required to improve health.

Furthermore, food that is nutritious, delicious, and high in protein from plants and mushrooms is becoming more popular. These meat substitutes satisfy dietary requirements and enhance personal well-being. In addition to providing dietary protein, lipids and fatty acids, vitamins, fiber, and flavor, mushrooms can enhance the organoleptic or sensory qualities of processed foods, such as meat substitutes. Mushrooms are fibrous, which makes the meat analogues that are made from them more chewable. *Fusarium gramineara* was the first edible filamentous fungus to be used in sausages and burger patties. The sweetness and umami flavor of fungi gives food a taste that is similar to meat and improves palatability [45]. Mushrooms in meat analogues-based products provide nutrients and promote the appearance, texture, and flavor of the product. To create an extruded mushroom-based meat substitute with a 35% water content, 15% each of *Lentinus edodes* (LE), *Pleurotus ostreatus* (PO), and *Coprinus comatus* (CC) and soybean protein isolate were used. The textural profiles of the CC derived meat were strikingly similar to those of real beef [46]. The products from the LE and CC mushrooms, however, had hardness values that were most similar to those of beef. Regardless of this, springiness of meat analogues and various mushroom species was comparable. Thus, the addition of various mushroom species has a significant impact on the texture of the meat analogues. Also, the textural qualities and antioxidant activity of the full fat soy (FFS)-based meat analog were improved by the addition of oyster mushrooms [47]. The addition of soy proteins creates a fibrous-structured of meat analog in which the oyster mushroom content reduced the expansion ratio and enhanced water absorption indices [48]. Therefore, mushrooms are an important ingredient in muscle foods because of the fibrous structure, which resembles that of meat and imparts a distinct umami flavor.

Therapeutic Properties of Edible Mushroom Proteins

Mushroom bioactive components are also appealing to consumers and food scientists because they can improve health and reduce the risk disease. Specifically, after the SARS-CoV-2 (COVID-19) pandemic era, people are becoming more interested in using food to improve health (41). In terms of human health, red and processed meats have been linked to cardiovascular disease and colon cancer. This is because some animal-derived foods contain high levels of cholesterol and saturated fat, both of which are harmful to the heart. Concerning colon cancer, it is thought to be caused by protein fermentation in the distal colon, releasing toxic metabolites such as ammonia, amines, phenols, and sulfides [8••]. Long-term high protein diets increase the risk of type 2 diabetes (T2DM), obesity, central nervous system (CNS) diseases, and cardiovascular disease (CVD) by increasing the production of amines, H2S, and ammonia in the colon [27]. Contrary, mushroom proteins have been linked with medicinal properties, and specific protein preparations or isolates such as concentrates, hydrolysates, peptides, ageritins, lectins, fungal immunomodulatory proteins (FIP), ribosome-inactivating proteins (RIP), antimicrobial/antifungal proteins, ribonucleases, and laccases [12] have been studied. They exert a variety of health benefits such as improved digestion, absorption of exogenic nutritional constituents, immune function modification to help the host defend against pathogen invasions, and suppression of specific enzyme activity [49].

This occurs as a result of the ability to induce angiotensin-converting enzyme (ACE) inhibitory, antioxidant, antimicrobial, and anticancer properties (Fig. 2). In Table 2, the biological function of these protein fractions from edible mushrooms is shown. The production of protein concentrates from mushrooms may result in enhanced digestibility since many of the components that impede digestion may have been eliminated. Few studies have been reported on the health effects of mushroom protein concentrates recently. A *Boletus edulis* anti-tumor protein (BEAP) with a MW of 16.7 KD displayed strong anti-cancer activity on A549 (human non-small-cell lung cancer) cells both in vitro and in vivo. BEAP cytotoxicity was aided by the activation of apoptosis and the arrest of A549 cells in the G1 phase of the cell cycle [50]. Likewise, the protein extract, PS60 from *P. tuber-regium sclerotium* was the most effective protein extract against the breast cancer cell line MDA-MB-23. In MDA-MB-231 cells, PS60 elicited cytotoxic effects that resulted in apoptosis and cell cycle arrest at the G1/G0 and S phases [51]. Yet, *Pholiota nameko* protein (PNAP) displayed anti-proliferative and apoptosis-inducing effects in a human breast cancer cell line (MCF-7). The malignant proliferation of MCF-7 solid tumors can be successfully stopped by PNAP, according to in vivo tests. This is because PNAP can effectively activate the mitochondrial apoptosis and death receptor pathways of MCF-7 tumor cells in vivo, causing the cancer cells to wither [52]. Protein extracts from *Auricularia auricula-judae* were effective as ciprofloxacin and fluconazole in inhibiting *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, yeast (*Candida albicans*), and dermatophytic

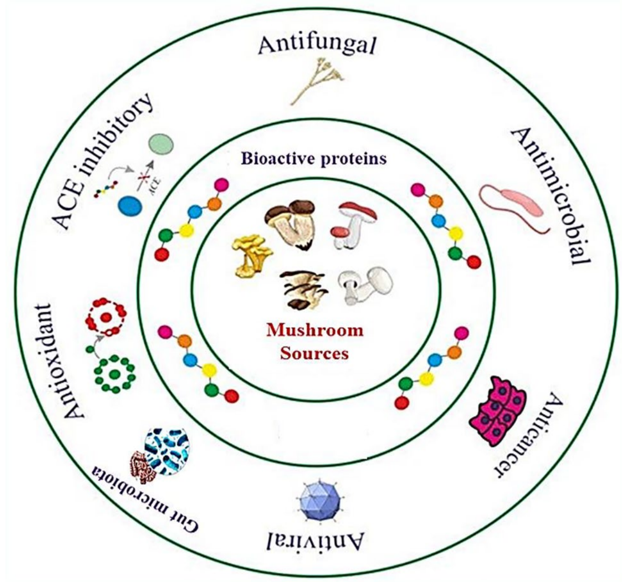

Fig. 2 Importance of mushroom proteins as bioactive compounds [78•]

pathogens [53]. Protein extracts from two different mushroom species (oyster and button) demonstrated significant antimicrobial activity against *P. aeruginosa* and *B. subtilis* [54]. Hence, it would be interesting to exploit mushroom protein concentrates to control various diseases and live a healthy life.

Protein hydrolysates contain a mixture of polypeptides, oligopeptides, and free amino acids that can be produced by chemical (using acids or alkalis) or enzymatic (using proteases) methods [55]. By simulating gastrointestinal digestion, protein hydrolysates with neuroprotection made from *Pleurotus geesteranus* proteins showed a good pre-protective impact in oxidatively damaged PC12 cells. The hydrolysate pre-protection may also change the expression of endogenous antioxidant enzymes [56]. Protein hydrolysates with varying degrees of hydrolysis were found to have an anti-oxidative, ACE inhibitory, and antiproliferative properties [57]. *P. geesteranus* protein hydrolysates show neuroprotective activity in H_2O_2-damaged pheochromocytoma (PC12) cells by reducing ROS production and increasing antioxidant enzymatic system activity [58]. Also, protein hydrolysates (MTT) derived from *Pleurotus ostreatus* exhibited profound antioxidative and ACE inhibitory activities. Besides, remarkable antiproliferative properties of MPHs against the human cervical carcinoma cell line (HeLa) were shown [57]. In other reports, *Pleurotus ostreatus* protein hydrolysate (POPEP-III) induced strengthened serum ALT and AST activities, and oxidative liver histological alteration in mice. It was reported *Pleurotus geesteranus* hydrolysates (PGPH) induced superior antioxidant and cytoprotective effects [59], while Lingzhi protein hydrolysates displayed good antioxidant activity and reduced lipid peroxidation [60].

Table 2 Health benefits of some mushroom proteins in human diet and as therapeutic agents

Protein isolates	Health benefits	Source	Features	Reference
Peptides	ACE inhibitory	*Lentinula edodes*	1265.43 Da N-terminal: KIGSRSRFDVT	[66]
		S. rugosoannulata	Peptide mixtures	[67]
		Agaricus bisporus	Peptide mixtures	[68]
		Ganoderma sinense	Peptide mixtures	[109]
		Grifola frondose (mycelia)	Peptide mixtures	[69]
	Antioxidant	*Schizophyllum commune*	MW < 0.65 kDa	[74]
		Hericium erinaceus	MW 0.65 kDa	[75]
		Agrocybe aegerita	Peptide mixtures	[76]
	Antioxidant and ACE inhibitory	Boletus mushroom	KBMPHF1 (> 10 kDa), KBMPHF2 (3–10 kDa), KBMPHF3 (1–3 kDa), and KBMPHF4 (1 kDa)	[80]
	Antioxidant	*Agaricus bisporus*	Peptides, 1–3 kDa fraction	[77]
	Antioxidant activity, ACE inhibitory activity, and anticancer activity	King Boletus mushroom	Peptide mixtures	[81]
		Morchella importuna	831 Da Ser-Leu-Ser-Leu-Ser-Val-Ala-Arg	[52]
	Hepatoprotective and gut microbiota modulation	*Pleurotus citrinopileatus*	Peptide mixtures	[84]
	Neuroprotection and gut microbiota modulation	Se-enriched *Cordyceps militaris*	VPRKL(Se)M (Se-P1) and RYNA(Se)MNDYT (Se-P2)	[85]
	Antiviral (coronaviruses)	*Pseudoplectania nigrella, Russula paludosa, and Clitocybe sinopica*	Peptide mixtures	[82]
	Anti-inflammation	*Tricholoma matsutake*	Peptide mixtures N-terminal: SDLKHFPF and SDIKHFPF	[86]
Ribonuclease	Anti-HIV viral	*Lepista personata*	Ribonuclease 27.8 kDa	[90]
Ribotoxin-like proteins		*C. aegerita*	ribotoxin-like proteins (enzymes) 15 kDa	[110]
Ostreatin	Novel tool for biotechnological applications	*Pleurotus ostreatus*	ribotoxin-like proteins: 131 amino acid and 14,263.51 Da	
Extract	Antitumor	*Pleurotus tuber-regium*	Protein extract	[51]
		Pholiota nameko	Protein extract	[52]
		Boletus edulis	Protein extract 16.7 KD	[50]
	Antimicrobial	*Auricularia auricula-judae*	Aqueous protein extracts	[53]
		Mushroom (Oyster and button)	Protein extracts	[54]
		Inonotus hispidus	Mixtures of peptides, proteins and other compounds	[111]
Protein hydrolysates	Neuroprotective effects	*Pleurotus geesteranus*	Hydrolysates	[58]
	Antioxidative, angiotensin rennin converting enzyme (ACE) inhibitory and antiproliferative activities	*Pleurotus ostreatus*	Hydrolysates	[57]
	Hepatoprotective effects	*Pleurotus ostreatus*	Hydrolysates	[112]
	Antioxidant properties and cytoprotective effects	*Pleurotus geesteranus*	Hydrolysates	[59]
	Antioxidants and reduction of lipid peroxidation	*Ganoderma lucidum*	Hydrolysates	[60]

Protein hydrolysates with hydrolysis degree ≥ 10% are usually intended for the development of specialized food products. Athletes make extensive use of food products containing protein hydrolysates [8••]. Protein hydrolysates are known to be more easily and quickly absorbed than native proteins, and when combined with carbohydrates, they produce an insulinotropic effect, proving useful for increasing muscle glycogen and muscle mass. This aids digestion and is useful in the production of products for patients with impaired gastrointestinal function [61]. Also, protein hydrolysates are suitable for the development of hypoallergenic foods due to a reduced or eliminated antigenic potential. Although the bitter taste that is produced when some hydrophobic peptides are released during hydrolysis limits the use of protein hydrolysates in the food industry, the bitterness can be masked with other flavors, removed through enzymatic and chromatographic methods, or processed using activated charcoal [62]. As a result, edible mushrooms are a safe source of bioactive protein hydrolysates.

Therapeutic Role of Bioactive Proteins from Edible Mushrooms

Recent findings on the biological function of proteins are shown in Table 2. Bioactive peptides (BAPs) are small fragments of proteins that provide some physiological health benefits [63]. Edible mushrooms are interesting sources of bioactive peptides because they contain a considerable quantity of high-quality proteins. The biological function of most bioactive proteins has been attributed to the encoded BAPs that can be released without losing their bioactivities [64]. Current reports showed that mushroom peptides render antihypertensive, antioxidant, antimicrobial, and other functions [17].

Angiotensin-Converting Enzyme (ACE) Inhibitory Property

Hypertension is a chronic health problem that causes patients to have high blood pressure leading to heart disease, stroke, aneurysm, and renal failure. Fortunately, ACE inhibitors including peptides are available to treat hypertension [65]. ACE inhibitory peptides with different molecular weights (MW) and amino acids composition from mushrooms have been reported lately. A synthesized peptide from *Lentinula edodes*, named KIGSRSRFDVT with MW of 1265.43 Da, induced ACE inhibitory activity (IC_{50}) of 37.14 μM. KIGSRSRFDVT is a non-competitive inhibitor that binds at an inactive ACE site to inhibit ACE activity [66]. It was shown that *Stropharia rugosoannulata* peptides can bind to zinc ions, critical amino acids, or amino acid residues in the ACE active pocket, which inhibits the action of ACE [67]. Hydrolysis of *A. bisporus* scraps yielded three novel ACE inhibitory peptides; LVYP, VYPW, and YPWT which exhibited an average ACE inhibitory activity of 80.68%, and the IC_{50} value was 0.9 mg/mL. They also showed good tolerance to temperature, pH, and gastrointestinal digestive enzymes, indicating excellent properties for the development of drugs for lowering blood pressure [68]. Peptides from *Grifola frondosa* mycelia hydrolysate induced higher ACE inhibitory activity [69]. When compared to chemosynthetic medications, mushroom peptides may have fewer negative effects on humans and have the ability to decrease blood pressure. However, clinical studies are needed to endorse these claims.

Antioxidant Effects

In the process of normal cellular metabolism, free radicals and reactive species, such as reactive oxygen species (ROS), are created continuously in the human body. Endogenous enzymatic and nonenzymatic defense systems quickly remove free radicals and reactive species; however, under certain conditions, such as drug use, inflammation, air pollution, smoking, and irradiation, endogenous antioxidant systems can be overwhelmed, resulting in oxidative stress, which can cause aging, cancer, and atherosclerosis [70, 71]. Although numerous studies have revealed that hydrolyzed peptides and proteins reduce enzymatic and nonenzymatic oxidation by eliminating free radicals and chelating metal ions, the exact mechanism by which mushroom peptides exert antioxidant properties is still not entirely understood. Peptides may act as antioxidants to eliminate free radicals directly by supplying protons and/or electrons, or indirectly by suppressing endogenous oxidases (e.g., via activation of the Keap1-Nrf2 signaling pathway), and chelating metal ions implicated in a radical generation [17, 72, 73]. Antioxidant peptides contain 5–16 amino acids. Studies have confirmed excellent antioxidant peptides (0.65–3 kDa) from *Schizophyllum commune* [74], *Hericium erinaceus* [75], *Agrocybe aegerita* [76], and *A. bisporus* [77]. Peptide composition, structure, and hydrophobicity are primarily responsible for their antioxidant capabilities [78•].

Antitumor Property

Active ingredients with antitumor effects have been isolated from mushrooms. A new peptide (MIPP) from *Morchella importuna* lowered human cervical cancer HeLa cell line viability. MIPP inhibited cell proliferation via a mitochondrial-dependent mechanism, as evidenced by Bcl-2/Bax down-regulation, facilitation of cytochrome C transport from the mitochondria to the cytoplasm, and activation of caspase-9 and caspase-3 [79]. Four novel bioactive peptides > 10 kDa obtained from Boletus mushroom displayed antioxidant and ACE inhibitory activity greatly by KBMPHF4 fraction [80]. Again, King Boletus mushroom protein hydrolysate or bioactive peptide (eb-KBM) isolated by enzymatic method demonstrated high antioxidant activity, ACE inhibitory activity, and anticancer activity-relevant cytotoxicity in ChaGo-K1 (undifferentiated lung carcinoma) and HEP-G2 (hepatocarcinoma) cells. It was concluded that eb-KBM elicits a high biological activity due to the high content of hydrophobic and aromatic amino acids [81].

Other Bioactivities

Several studies have revealed that mushroom protein has the potential to be used control pathogenic microbes and other human diseases. Peptides derived from *Pseudoplectania nigrella*, *Russula paludosa*, and *Clitocybe sinopica* exhibited binding affinity and the ability to modulate the flexibility and stability of selected coronavirus proteins, including ACE-related carboxypeptidase, SARS-Coronavirus HR2 Domain, and COVID-19 main protease [82]. Nowadays, the hepatoprotective effects of polysaccharide-peptides from mushrooms have been evaluated against nonalcoholic fatty liver disease (NAFLD). It is known that nutrient digestion and absorption are mediated by the hepatointestinal system. Dysbiosis in the gut and modifications to its metabolic processes are linked to NAFLD [83]. *Pleurotus citrinopileatus* polysaccharide-peptides (PSI and PSII) were shown by Huang et al. [84] to exhibit hepatoprotective effects in injured HepG2 cells by increasing the survival rates of injured cells, decreasing the accumulation of intracellular TGs, increasing the intracellular activity of SOD, reducing extracellular transaminase release, and maintaining cell integrity. PSI and PSII boosted both the richness and diversity of the human gut microbiota. *Escherichia*-*Shigella* genera were less prevalent due to PSI and PSII, while SCFAs were improved, which impacted liver functioning. Therefore, PSI and PSII may induce effects via the liver-gut axis system. Similarly, two novel selenium peptides (Se-Ps), VPRKL(Se)M (Se-P1) and RYNA(Se)MNDYT (Se-P2), isolated from Se-enriched *Cordyceps militaris* induced pre-protection against LPS-induced inflammatory and oxidative stress in the colon and brain by inhibiting the production of proinflammatory mediators. Se-Ps improved intestinal mucosa and positively affected gut microbiota dysbacteriosis [85]. Also, *Tricholoma matsutake*-derived peptides (SDLKHFPF and SDIKHFPF) attenuated ethanol-induced inflammatory responses and apoptosis by suppressing NF-κB signaling activation [86]. The peptides SDIKHFPF and SDLKHFPF produced from the *Tricholoma matsutake* improved barrier function by controlling TJ protein expression and the release of pro-inflammatory cytokines [87] as shown in Fig. 3.

Ageritin is a particular ribonuclease that is isolated from the edible fungus *Cyclocybe aegerita* (also known as *Agrocybe aegerita*). It cleaves a single phosphodiester bond present within the universally conserved alpha-sarcin loop (SRL) of 23-28S rRNAs. Apoptosis, which is the process by which cells die, occurs after this cleavage inhibits protein production. Ageritin exhibits ribonucleolytic activity on ribosomes, ribonuclease activity on Tobacco Mosaic Virus (TMV) RNA, endonuclease activity on a plasmid and genomic DNAs, and antiproliferative and defense activities, which have been fully reviewed in recent review paper [88]. Ageritin has considerable beneficial impacts on the viability of cancer SVT2 cells, but only slightly on healthy BALB/c 3T3 cells, according to a study on the selective toxicity of the toxin against malignant cells [89]. In addition, ageritin induces antifungal, entomotoxic, and nematotoxic, antibacterial activities [88]. Additionally, the *Lepista personata* ribonuclease suppressed HIV-1 reverse transcriptase [90]. Discovering new medications to stop the worldwide pandemic infection using natural bioactive molecules could be a promising avenue.

Ways to Exploit Mushroom Protein in the Future

Edible mushrooms and their proteins have the potential to be extensively involved in a variety of areas with diverse applications in the future. Feeding the growing world population, mitigating and adapting to climate change, reducing pollution, waste and biodiversity loss, and preserving human health are just a few of the many issues that the modern food and agriculture sector must address quickly. Food should also be tasty, affordable, convenient, and safe [91]. By 2050, 9.2 billion people are expected to live on earth and consume twice as many resources as today. FAO estimates that agricultural production will need to increase by 70% to feed the entire population [92]. Based on nutritional value, quality, and digestibility, as well as the associated health benefits and economic advantages, mushrooms can be used as source of protein in a variety of ways (Fig. 4).

Mushrooms Provide Future Alternative Protein to Fight Food Insecurity and Malnutrition

Asia and Africa are coping with serious challenges with hunger and malnutrition, based on the Global Hunger Index report in 2020. Also, due to the COVID-19 epidemic, the ensuing economic collapse, and a significant desert locust outbreak in the Horn of Africa, millions of people are experiencing food and nutrition insecurity [93]. The increase in COVID-19 also had an indirect effect on human health.

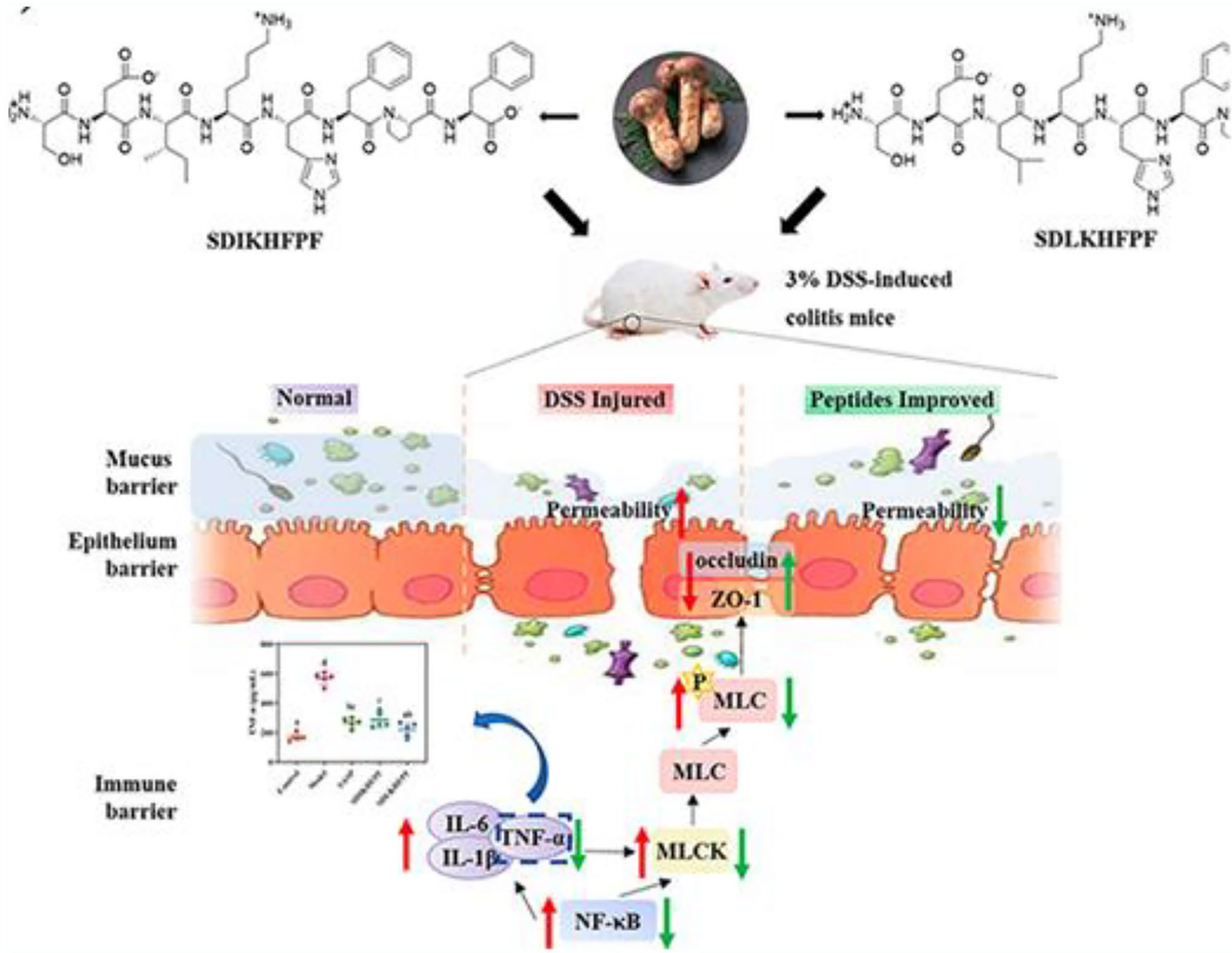

Fig. 3 Molecular mechanism through which *Tricholoma matsutake*-derived peptides SDIKHFPF (left) and SDLKHFPF (right) suppress the NF-κB/MLCK/p-MLC signaling pathway in DSS-induced colitis mice [113]

Moreover, because of the significant increase in poverty and food insecurity recently, people are compelled to switch to less healthy and low-quality diets. As a result, the risks of undernutrition, especially protein deficits, have increased, affecting both high- and low-income countries [91, 93]. By 2030, governments around the world must achieve food security, reduce hunger, and improve nutrition, especially for the underprivileged and most vulnerable populations, including infants. Nearly 690 million people or 8.9% of the world's population are estimated to be undernourished, mostly in Asia (381 million), Africa (250 million), Latin America, and the Caribbean (48 million) (WHO 2020).

The ever-increasing human requirement for protein-rich food and the inefficiency of conventional technologies have necessitated the need to carefully investigate options for creating affordable and novel protein-rich foods, with related health benefits. Using mushrooms in a form of eating the whole fruiting body (fresh or powder), protein concentrates, and hydrolysates offers nutrition and medicinal advantages [23]. In addition, the immunomodulatory agents released during digestion could stimulate intestinal immunity to fight diseases. Undigested mushroom carbohydrates and proteins constitute the major substrates at the disposal of the microbiota, which have been shown to stimulate the microbiota by promoting the growth of beneficial microbes and SCFA production [11, 94]. Mushrooms clearly provide bioactive substances that can aid in disease control and improvement in malnourished populations.

Additionally, mushroom protein, agentin have useful applications in agriculture. Given the increasing worldwide food demand caused by population growth, novel management measures for crop protection against pathogens or pests must be tested, while minimizing the use of ecologically damaging phytochemicals [88]. Given that the ageritin protein product has insecticidal activity, transfecting the ageritin gene into plant cells could be a potential strategy for controlling diseases or pests. This is feasible in light of recent developments in in vitro cultures and genetic plant engineering.

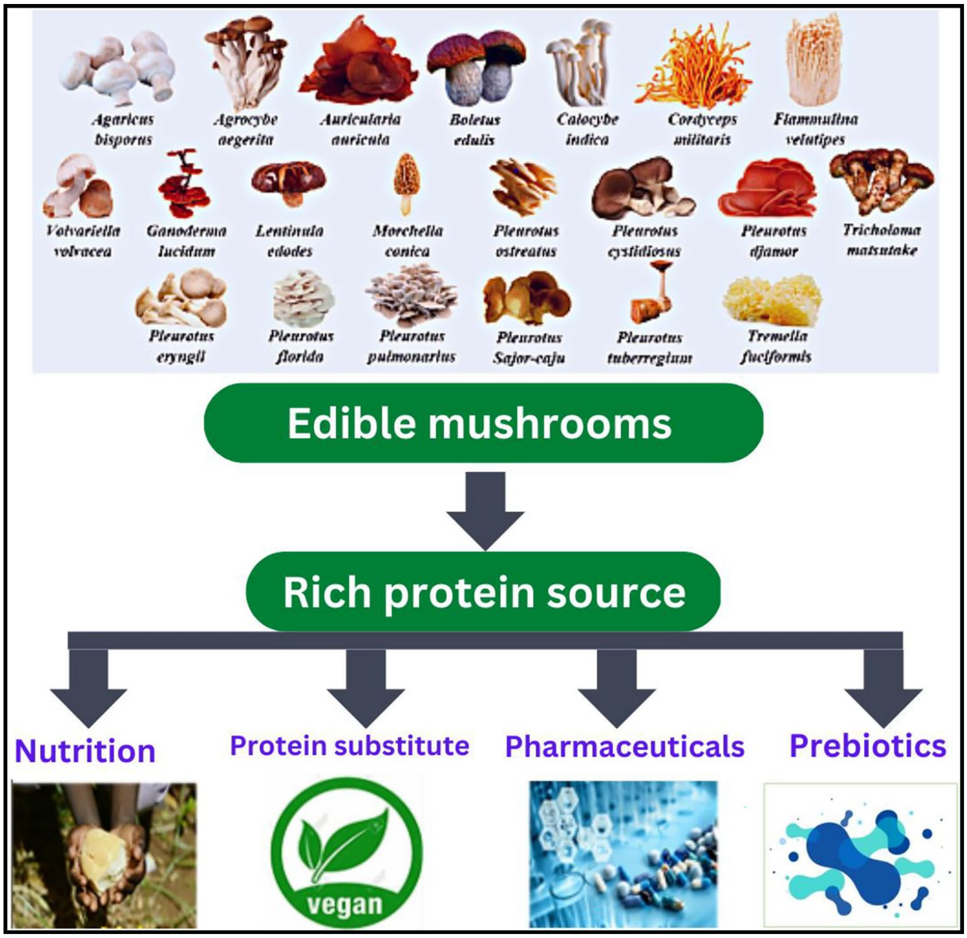

Fig. 4 Different ways to exploit mushroom proteins [114]

Given Ageritin's antifungal action, a similar experimental strategy is helpful for preventing fungal illnesses. Because 'Ageritin' toxin is present in Pioppino edible mushroom, which is commonly consumed, the use of Ageritin for plant protection against diseases can be easily accepted by the public [89]. Overall, the broad framework supports additional research on Ageritin and homologous members of the RL-Ps group for controlling pathogens in crops in order to increase food production.

Mushroom Protein is an Excellent Substitute for People Who Do Not Consume Animal Protein

The nutritional demands of individuals who do not eat animal products are met by meat substitutes [95]. Religious convictions and animal compassion are the main motivations for consuming such non-animal products, beside nutritional and health benefits and environmental considerations [8••]. A vegetarian or vegan diet is gaining popularity. According to research and market alternatives, there are two generations of products based on traditional proteins such as soy or gluten, as well as newer generation proteins such as peas or faba beans [96]. Edible mushrooms offer a cheap and less resource-intensive source of protein to partially replace meat or meat products [97]. Mushrooms may play a key role in meat analogs by delivering nutrients and stimulating the development of sensory qualities such as the appearance, texture, and flavor [46]. Edible mushrooms have been utilized in meat product as meat replacements or fillers to increase the physicochemical and sensory attributes and nutritional quality. Mycoprotein is a high-protein, low-fat dietary ingredient that is created by manufacturers by fermenting fungal spores with glucose and other ingredients [98, 99]. According to Singh et al., although *Fusarium venenatum* is grown to produce mycoprotein and make meat substitutes, it is rarely employed to generate meat analogues due to its limited digestibility [100]. Mycoproteins have a biological value comparable to typical meats and are high in quality proteins, dietary fiber (-glucans and chitin), and other nutrients. Mycoproteins are also highly digestible (0.99), equivalent to animal protein sources such as milk, and important amino acids [101]. Consuming mycoprotein is linked to lower glycaemic indicators and energy density consumption [102]. Many Asian countries use *Monascus purpureus*, which is treated with yeast to produce red rice, and *Aspergillus oryzae*, which is fermented with soy to make hamanato, miso, and shoyu. The British-developed meat alternative QuornTM is now offered in the European market. The use of *P. albidus* mycoprotein flour can aggregate nutritional and biological value in chocolate cookies [98]. Therefore, future years will undoubtedly witness an increase in the need for non-animal protein as we search for alternative protein sources to satisfy the demands of the growing population. Mushrooms offer some optimism because of their nutrient hub and simplicity of modification. Notably, products made from mushroom mycoproteins are a promising new generation of functional alternative proteins since they have a meaty flavor, excellent nutrition, and biological properties.

Mushroom Proteins are Important Pharmaceutical Agents

Another important feature of bioactive proteins is the ability to be used as pharmaceutical agents. Mushroom proteins and peptides have antihypertensive, immunomodulatory, antifungal, antibiotic, and antibacterial activities, and anticancer, antiviral, antioxidant, and ACE inhibitory effects [50, 52, 78•, 86]. Considering the different biological activities in Table 1 (searched articles within 2020–2022) it emerged that about 25% of bioactive proteins possessed ACE inhibitory activity, mainly peptides (single and mixture) and only one protein hydrolysate. Whereas about 30% mostly being peptides and protein hydrolysates exhibited antioxidant activity, while about 25% composed of peptides, hydrolysates, and extracts showed hepatoprotective, antiviral, and anticancer activities, and the others displayed neuroprotection, antimicrobial, gut modulation anti-inflammation properties. These bioactive proteins were obtained from popular mushrooms including *A. bisporus*, *Lentinula edodes*, *Pleurotus* spp, and *Ganoderma* spp. Others include *Schizophyllum commune*, *Auricularia auricula-judae*, *Inonotus hispidus*, Boletus mushroom, and *Tricholoma matsutake*, with *Pleurotus* species emerged as the primary source of bioactive proteins and peptides making up majority of the proteins. Nevertheless, compared to the enormous number of peptides isolated from plants and animals, only a small number of peptides derived from mushrooms are currently recognized. Also, less than 0.5% of the thousands of documented mushroom species are utilized for food and medicine, which include *Lentinula edodes*, *Pleurotus* spp., *Agaricus* spp., and *Ganoderma* spp. Other edible mushrooms, however, have significant or even high protein content that can be exploited.

Lectins are also of therapeutic or pharmaceutical interest. Lectins are non-catalytic proteins that reversibly bind to sugars. Individual lectins typically bind their ligands with a high degree of stereochemical selectivity. The applications of lectins from mushrooms in terms of their antiproliferative activity, immune-stimulating, antimicrobial, and antioxidant effects have been highlighted [103]. *A. bisporus* lectin (ABL) and *A. bisporus* mannose-binding protein (Abmb) exhibited anti-proliferative effects on cancer cells as well as an immune system-stimulating property [104]. Yousra et al. review report indicated that mushroom lectins have potent inhibitory activity against a variety of human pathogenic viruses including HIV, herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), hepatitis C virus (HCV), and influenza virus. The lectins work by preventing viral entry and inhibiting replication through enzyme inactivation [105]. Despite that, lectins differ in structure, molecular weight, and carbohydrate specificity, which influences their pharmaceutical applications. Lectins have been discovered in mushroom species such as *Hygrophorus*, *Agaricus*, Boletus, *Russula*, *Pleurotus*, *Agrocybe*, *Lentinus*, *Grifola*, and *Ganoderma*. Lectins include fungal immunomodulatory proteins, ubiquitin-like proteins, enzymes, and unclassified proteins that are carbohydrate-free or possess less than 1–2% carbohydrate. The low-carbohydrate proteins and peptides (LCP) exert anticancer activities via specific pathways including DNase activity, endoplasmic reticulum stress, PI3K/Akt/mTOR-signaling pathway, and ubiquitin-mediated pathway, which are different from the common extrinsic or intrinsic apoptosis pathways [106].

Lately, interest in prebiotic property of mushroom fruity bodies (fresh or powder) and extracted compounds such as polysaccharide-peptides is growing. Prebiotics are food compounds that affect the gut microbiota's composition or metabolism positively, including bifidogenic bacteria (*Bifidobacterium* sp.) and lactic acid bacteria (*Lactobacillus* sp.). Prebiotics are involved in pathogenic suppression, gastrointestinal tolerance, and probiotic growth stimulation. Polysaccharides in edible mushrooms, such as hemicellulose, chitin–and–glucans, mannans, xylans, and galactans slow digestion [17, 107]. The hydrolysates can serve as substrates to promote the growth of beneficial gut microbes and their metabolite production leading to health benefits. Short-chain fatty acids (SCFA), primarily acetic, butyric, and propionic acids, are the primary end products of bacterial fermentation of unhydrolyzed carbohydrates and proteins in the gut [11].

Concerns over the effects of gut dysbiosis on diseases like inflammatory bowel disease (IBD), diabetes, cancer, obesity, and liver disease have lately grown. The digestion and absorption of nutrients have an impact on health. Humans have long used mushrooms as food and medicine, and potential applications for mushroom components such as protein are currently being explored. Recent work revealed that polysaccharide-peptides (PSI and PSII) from *P. citrinopileatus* excite protective effects on hepatoprotective and gut microbiota [84]. The adiponectin pathway was stimulated by PSI and PSII, which also resulted in less lipid buildup in liver cells, modulated gut microbiota, and increased butyric and acetic acids production, suggesting that the liver-gut axis system is a mechanism through which PSI and PSII elicit these beneficial effects. In another report, the simulated digestion of protein extracted from selenium-enriched *Cordyceps militaris* yielded two selenium peptides, VPRKL(Se)M (Se-P1) and RYNA(Se)MNDYT (Se-P2). Se-Ps promoted biological activities such as lessening inflammation and oxidative stress (OS) in the brain, reducing LPS-Induced inflammation and OS in the colon, and potentially modulating the relative abundance of gut microbiota of LPS-Injured mice. Se-P2 increased the abundance of *Lactobacillus* and *Alistipes* but decreased the abundance of *Akkermansia and Bacteroides*. Thus, Se-Ps collectively affected the gut and gut microbiota, which may offer a crucial strategy to lessen neuroinflammation and associated Alzheimer's disease via the microbiota-gut-brain axis [85]. Thus, the use of mushrooms as a future alternative protein source may provide bioactive compounds that can stimulate the gut microbiota to control or prevent a variety of human diseases. However, more research into how mushroom proteins affect human gut microbiota and the health implications is required to gain a deeper understanding.

Conclusion and Prospects

Edible mushrooms are a valuable source of protein for both food and medicine. Mushrooms contain more protein than vegetables, fruits, and grains. Mushroom proteins are safer than meat proteins, with little to no risk of diseases. As a result, they meet dietary requirements: recommended dietary allowance (RDA) and protein efficiency ratio (PER). In addition, mushroom protein is of high protein quality in terms of complete essential amino acids and excellent digestibility. Consequently, mushrooms are utilized in food product fortification to increase nutritional value, particularly protein. Also, mushroom peptides, concentrate, and hydrolysates have been associated with an angiotensin-converting enzyme (ACE) inhibitory, antioxidant, antimicrobial, anticancer, and gut microbiota modulation properties. In contrast, significant progress has been made in the study of mushroom proteins from the species of *Agaricus*, *Lentinus*, and *Pleurotus*. However, several high-protein mushrooms, such as *Tricholoma*, *Copyinds comatus*, and *Volvariella volvacea* are yet to be fully utilized. Furthermore, it is widely acknowledged that the chemical structure of protein isolates such as peptides is directly related to their activities and mechanisms of action (42). However, some of the current research, particularly those on ACE-inhibitory, antioxidant, and antimicrobial activities have only been done on protein mixtures, without detailed physiochemical composition or purification and identification of active components, let alone studying the mechanisms of action.

Finally, edible mushrooms provide suitable alternative protein sources for increasing protein production to meet the growing demand due to global population growth. Mushroom-based proteins can be used to combat food insecurity and malnutrition, as a meat substitute, as pharmaceutical agents, and as substrates to stimulate the gut microbiota to enhance human health. Notably, mushroom proteins are future high-quality protein substitutes that are easily accessible to both wealthy and underprivileged populations.

Acknowledgements This work was financially supported by the Office of the Ministry of Higher Education, Science, Research and Innovation, and the Thailand Science Research and Innovation through the Kasetsart University Reinventing University Program 2022.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Adhikari S, Schop M, de Boer IJ, Huppertz TJN. Protein quality in perspective: a review of protein quality metrics and their applications. Nutrients. 2022;14(5):947.
2. Singh BP, Bangar SP, Albaloosh M, Ajayi FF, Mudgil P, Maqsood S. Plant-derived proteins as a sustainable source of bioactive peptides: recent research updates on emerging production methods, bioactivities, and potential application. Crit Rev Food Sci Nutr. 2022;1–22.
3. Leroy F, Beal T, Gregorini P, McAuliffe GA, Van Vliet S, Hills J. Nutritionism in a food policy context: the case of 'animal protein.' Anim Prod Sci. 2022;62(8):712–20.
4.• Sá AGA, Moreno YMF, Carciofi BAM. Plant proteins as high-quality nutritional source for human diet. Trends Food Sci Technol. 2020;97:170–84. **This critical review discusses the primary sources of plant proteins as well as their nutritional composition in terms of protein quantity and amino acid profile. It also aims to inspire and clarify the possibility of using plants as protein sources, emphasizing the nutritional benefits for humans and technological implications for industrial processing.**
5. Yu Q, Guo M, Zhang B, Wu H, Zhang Y, Zhang L. Analysis of nutritional composition in 23 kinds of edible fungi. J Food Qual. 2020;2020:8821315.
6. Krishnamoorthi R, Srinivash M, Mahalingam PU, Malaikozhundan B. Dietary nutrients in edible mushroom, Agaricus bisporus and their radical scavenging, antibacterial, and antifungal effects. Process Biochem. 2022;121:10–7.
7. Ache NT, Manju EB, Lawrence MN, Tonjock RK. Nutrient and mineral components of wild edible mushrooms from the Kilum-Ijim forest, Cameroon. Afr J Food Sci. 2021;15(4):152–61.

8.•• González A, Cruz M, Losoya C, Nobre C, Loredo A, Rodríguez R, et al. Edible mushrooms as a novel protein source for functional foods. Food Funct. 2020;11(9):7400–14. **This review discusses the use of mushrooms as sustainable functional food.**
9. González A, Nobre C, Simões LS, Cruz M, Loredo A, Rodríguez-Jasso RM, et al. Evaluation of functional and nutritional potential of a protein concentrate from Pleurotus ostreatus mushroom. Food Chem. 2021;346:128884.
10. Yadav D, Negi PS. Bioactive components of mushrooms: processing effects and health benefits. Food Res Int. 2021;148:110599.
11. Ayimbila F, Siriwong S, Nakphaichit M, Keawsompong S. *In vitro* gastrointestinal digestion of Lentinus squarrosulus powder and impact on human fecal microbiota. Sci Rep. 2022;12(1):1–17.
12. Fung S-Y, Razif MF. Bioprospecting macrofungi for biotechnological and biomedical applications. In: Advances in macrofungi. CRC Press; 2021. p. 53–69.
13. Floret C, Monnet A-F, Micard V, Walrand S, Michon C. Replacement of animal proteins in food: how to take advantage of nutritional and gelling properties of alternative protein sources. Crit Rev Food Sci. 2021;63:920–46.
14. Scialabba NE-H. Livestock and future food supply scenarios. In: Managing health livestock production and consumption. Elsevier; 2022. p. 107–21.
15. Singh M, Kamal S, Sharma VP. Status and trends in world mushroom production-III-world production of different mushroom species in 21st century. Solan: Mushroom Society of India; 2021.
16. Kaur J, Singh J, Bhadariya V, Gogna S, Jarial S, Rasane P, et al. Edible mushrooms: a source of quality protein. In: Wild mushrooms. CRC Press; 2022. p. 169–92.
17. Zhou J, Chen M, Wu S, Liao X, Wang J, Wu Q, et al. A review on mushroom-derived bioactive peptides: preparation and biological activities. Food Res Int. 2020;134:109230.
18. Li J, Ma J, Fan S, Mi S, Zhang Y. Comparison of the nutritional and taste characteristics of 5 edible fungus powders based on the composition of hydrolyzed amino acids and free amino acids. J Food Qual. 2022;2022:3618002.
19. Dilfy SH, Hanawi MJ, Al-bideri AW, Jalil AT. Determination of chemical composition of cultivated mushrooms in Iraq with spectrophotometrically and high performance liquid chromatographic. J Green Eng. 2020;10(12 (1)):6200.
20. Rasalanavho M, Moodley R, Jonnalagadda SB. Elemental bioaccumulation and nutritional value of five species of wild growing mushrooms from South Africa. Food Chem. 2020;319:126596.
21. Murillo W, Suárez HJH. Evaluation of nutritional values of wild mushrooms and spent substrate of Lentinus crinitus (L.) Fr. Heliyon. 2020;6(3):e03502.
22. McKillop K, Harnly J, Pehrsson P, Fukagawa N, Finley J. FoodData Central, USDA's Updated approach to food composition data systems. Curr Dev Nutr. 2021;5(Supplement_2):596.
23. González A, Cruz M, Losoya C, Nobre C, Loredo A, Rodríguez R, et al. Edible mushrooms as a novel protein source for functional foods. Food Funct. 2020;11(9):7400–14.
24. WHO. Protein and amino acid requirements in human nutrition, vol. 935. 2007.
25. Huang Q, Wang L, Zhang L, Wang Q, Liang L, Chen J, Lin J. Evaluation of amino acid characteristics and nutrient composition of six edible fungi cultivated by cinnamon[J]. Chin J Trop Crops. 2021;42(12):3529–36.
26. Li Q, Liu J, Shang X, Li Y, Zhang L, Li Z, et al. Characterizing diversity based on the chemical and nutritional composition of shiitake culinary-medicinal mushroom Lentinula edodes (Agaricomycetes) commonly cultivated in China. Int J Med Mushrooms. 2021;23(8):51–64.
27. Cai J, Chen Z, Wei Wu, Lin Q, Liang Y. High animal protein diet and gut microbiota in human health. Crit Rev Food Sci Nutr. 2022;62(22):6225–37.
28. Liaotrakoon W, Liaotrakoon V. Amino acid profile, phytochemical composition and antimicrobial activities of edible tropical bolete mushroom (Phlebopus colossus (R. Heim) Singer). J Food Meas Charact. 2022;16(3):1967–73.
29. Ha SY, Jung JY, Park HM, Yang J-K. Comparison of the metabolic profile of the mycelia and fruiting bodies of artificially cultured Cordyceps militaris. J Mushroom. 2022;20(1):13–21.
30. Reis GC, Guidi LR, Fernandes C, Godoy HT, Gloria MBA. UPLC-UV method for the quantification of free amino acids, bioactive amines, and ammonia in fresh, cooked, and canned mushrooms. Food Anal Methods. 2020;13(8):1613–26.
31. Sissons J, Davila M, Du X. Sautéing and roasting effect on free amino acid profiles in portobello and shiitake mushrooms, and the effect of mushroom-and cooking-related volatile aroma compounds on meaty flavor enhancement. Int J Gastron Food Sci. 2022;28:100550.
32. Nam M, Choi JY, Kim M-S. Metabolic profiles, bioactive compounds, and antioxidant capacity in Lentinula edodes cultivated on log versus sawdust substrates. Biomolecules. 2021;11(11):1654.
33. Feng Y, Xin G, Wei Y, Xu H, Sun L, Hou Z, et al. Comparison of the umami taste and aroma of dried Suillus granulatus packed using four different packaging methods. Food Chem. 2022;366:130570.
34. Thakur M. Advances in mushroom production: key to food, nutritional and employment security: Aareview. Indian Phytopathol. 2020;73(3):377–95.
35. Schimbator M, Culețu A, Susman I, Duță DE. Digestibility of proteins from different sources. Ann Univ Dunarea Jos Galati Fascicle VI Food Technol. 2020;44(2):43–50.
36. Reis GC, Dala-Paula BM, Tavano OL, Guidi LR, Godoy HT, Gloria MBA. In vitro digestion of spermidine and amino acids in fresh and processed Agaricus bisporus mushroom. Food Res Int. 2020;137:109616.
37. Fraile-Fabero R, Ozcariz-Fermoselle MV, Oria-de-Rueda-Salgueiro JA, Garcia-Recio V, Cordoba-Diaz D, del P. Jiménez-López M, et al. Differences in antioxidants, polyphenols, protein digestibility and nutritional profile between Ganoderma lingzhi from industrial crops in Asia and Ganoderma lucidum from cultivation and Iberian origin. Foods. 2021;10(8):1750.
38. Venturella G, Ferraro V, Cirlincione F, Gargano ML. Medicinal mushrooms: bioactive compounds, use, and clinical trials. Int J Mol Sci. 2021;22(2):634.
39. Tu J, Brennan MA, Wu G, Bai W, Cheng P, Tian B, et al. Delivery of phenolic compounds, peptides and β-glucan to the gastrointestinal tract by incorporating dietary fibre-rich mushrooms into sorghum biscuits. Foods. 2021;10(8):1812.
40. Cerón-Guevara MI, Rangel-Vargas E, Lorenzo JM, Bermúdez R, Pateiro M, Rodriguez JA, et al. Effect of the addition of edible mushroom flours (Agaricus bisporus and Pleurotus ostreatus) on physicochemical and sensory properties of cold-stored beef patties. J Food Process Preserv. 2020;44(3):e14351.
41. Al-zamani Z, Kumar A, Al-dalali S, Aleryani H, Abdo A. Development of protein-enriched cake incorporated with mushroom powder (*Agaricus bisporus*). Int J Food Sci Nutr. 2022;7(2):23–28.
42. Wang L, Zhao H, Brennan M, Guan W, Liu J, Wang M, et al. In vitro gastric digestion antioxidant and cellular radical scavenging activities of wheat-shiitake noodles. Food Chem. 2020;330:127214.
43. Kolawole FL, Akinwande BA, Ade-Omowaye BI. Physicochemical properties of novel cookies produced from orange-fleshed sweet potato cookies enriched with sclerotium of edible mushroom (Pleurotus tuberregium). J Saudi Soc Agric Sci. 2020;19(2):174–8.
44. Parvin R, Farzana T, Mohajan S, Rahman H, Rahman SS. Quality improvement of noodles with mushroom fortified and its comparison with local branded noodles. NFS J. 2020;20:37–42.
45. Oosone S, Kashiwaba A, Yanagihara N, Yoshikawa J, Kashiwagi Y, Maehashi K, et al. The role of amylolytic and proteolytic

enzyme activities of vegetables, fruits, and edible fungi in flavor enhancement during cooking. Int J Gastron. 2020;22:100264.
46. Yuan X, Jiang W, Zhang D, Liu H, Sun B. Textural, sensory and volatile compounds analyses in formulations of sausages analogue elaborated with edible mushrooms and soy protein isolate as meat substitute. Foods. 2021;11(1):52.
47. Cho SY, Ryu GH. Effects of oyster mushroom addition on physicochemical properties of full fat soy-based meat analog by extrusion process. Ind Food Eng. 2021;25(2):85–94.
48. Mohamad Mazlan M, Talib RA, Chin NL, Shukri R, Taip FS, Mohd Nor MZ, et al. Physical and microstructure properties of oyster mushroom-soy protein meat analog via single-screw extrusion. Foods. 2020;9(8):1023.
49. Altaf U, Hashmi S, Sharma YP. Therapeutic potential of mushroom bioactive nutraceuticals. In: Biology, cultivation and applications of mushrooms. Singapore: Springer; 2022. p. 357–86.
50. Zhang Y, Zhou R, Liu F, Ng TB. Purification and characterization of a novel protein with activity against non-small-cell lung cancer in vitro and in vivo from the edible mushroom Boletus edulis. Int J Biol Macromol. 2021;174:77–88.
51. Abdullah E, Abidin NZ, Aminudin N, Abdullah N. Characterization of cytotoxic proteins from king tuber oyster medicinal mushroom, Pleurotus tuber-regium (Agaricomycetes), sclerotium for human breast MDA-MB-231 cancer cells. Int J Med Mushrooms. 2022;24(5):27–40.
52. Zhang Y, Zhang Y, Gao W, Zhou R, Liu F, Ng TB. A novel antitumor protein from the mushroom Pholiota nameko induces apoptosis of human breast adenocarcinoma MCF-7 cells in vivo and modulates cytokine secretion in mice bearing MCF-7 xenografts. Int J Biol Macromol. 2020;164:3171–8.
53. Oli AN, Edeh PA, Al-Mosawi RM, Mbachu NA, Al-Dahmoshi HO, Al-Khafaji NS, et al. Evaluation of the phytoconstituents of Auricularia auricula-judae mushroom and antimicrobial activity of its protein extract. Eur J Integr Med. 2020;38:101176.
54. Bansal V, Tyagi S, Ghosh K, Gupta A. Extraction of protein from mushroom and determining its antioxidant and anti-inflammatory potential. Res J Pharm Technol. 2020;13(12):6017–21.
55. Hou Y, Wu Z, Dai Z, Wang G, Wu G. Protein hydrolysates in animal nutrition. In: Bioactive peptides from food. CRC Press; 2022. p. 209–32.
56. Wu S, Chen M, Liao X, Huang R, Wang J, Xie Y, et al. Protein hydrolysates from Pleurotus geesteranus obtained by simulated gastrointestinal digestion exhibit neuroprotective effects in H2O2-injured PC12 cells. J Food Biochem. 2022;46(4):e13879.
57. Goswami B, Majumdar S, Das A, Barui A, Bhowal J. Evaluation of bioactive properties of Pleurotus ostreatus mushroom protein hydrolysate of different degree of hydrolysis. LWT. 2021;149:111768.
58. Wu S, Chen M, Liao X, Huang R, Wang J, Xie Y, et al. Protein hydrolysates from Pleurotus geesteranus obtained by simulated gastrointestinal digestion exhibit neuroprotective effects in H2O2-injured PC12 cells. J Food Biochem. 2022;46(4):e13879.
59. Liao X, Zhu Z, Wu S, Chen M, Huang R, Wang J, et al. Preparation of antioxidant protein hydrolysates from Pleurotus geesteranus and their protective effects on H2O2 oxidative damaged PC12 cells. Molecules. 2020;25(22):5408.
60. Krobthong S, Choowongkomon K, Suphakun P, Kuaprasert B, Samutrtai P, Yingchutrakul Y. The anti-oxidative effect of Lingzhi protein hydrolysates on lipopolysaccharide-stimulated A549 cells. Food Biosci. 2021;41:101093.
61. López-Martínez MI, Miguel M, Garcés-Rimón M. Protein and sport: alternative sources and strategies for bioactive and sustainable sports nutrition. Front Nutr. 2022;9:926043.
62. Hu X, Zhang Q, Zhang Q, Ding J, Liu Y, Qin W, et al. An updated review of functional properties, debittering methods, and applications of soybean functional peptides. Crit Rev Food Sci. 2022;1–16.
63. Bhandari D, Rafiq S, Gat Y, Gat P, Waghmare R, Kumar V. A review on bioactive peptides: physiological functions, bioavailability and safety. Int J Pept Res Ther. 2020;26(1):139–50.
64. Montesano D, Gallo M, Blasi F, Cossignani L. Biopeptides from vegetable proteins: new scientific evidences. Curr Opin Food Sci. 2020;31:31–7.
65. Sonklin C, Alashi MA, Laohakunjit N, Kerdchoechuen O, Aluko RE. Identification of antihypertensive peptides from mung bean protein hydrolysate and their effects in spontaneously hypertensive rats. J Funct Foods. 2020;64:103635.
66. Paisansak S, Sangtanoo P, Srimongkol P, Saisavoey T, Reamtong O, Choowongkomon K, et al. Angiotensin-I converting enzyme inhibitory peptide derived from the shiitake mushroom (Lentinula edodes). J Food Sci Technol. 2021;58(1):85–97.
67. Li W, Chen W, Ma H, Wu D, Zhang Z, Yang Y. Structural characterization and angiotensin-converting enzyme (ACE) inhibitory mechanism of Stropharia rugosoannulata mushroom peptides prepared by ultrasound. Ultrason Sonochem. 2022;88:106074.
68. Wang R, Yun J, Wu S, Bi Y, Zhao FJF. Optimisation and characterisation of novel angiotensin-converting enzyme inhibitory peptides prepared by double enzymatic hydrolysis from Agaricus bisporus Scraps. Foods. 2022;11(3):394.
69. Kheng YS, Jeng YL, Nor MM, Jia GB. The analysis of Angiotensin-I Converting Enzyme (ACE) by maitake (Grifrola frondosa) mycelia. J Trop Resour Sustain Sci. 2020;8(2):69–72.
70. Kurek M, Benaida-Debbache N, Elez Garofulić I, Galić K, Avallone S, Voilley A, et al. Antioxidants and bioactive compounds in food: critical review of issues and prospects. Antioxidants. 2022;11(4):742.
71. Qu H, Sun Q, Pang J, Ding D, Bai J. Molecular structure design of polyhydroxyl antioxidants and mechanism of hydroxyl radical scavenging reaction. Sch J Agric Vet Sci. 2022;4:54–9.
72. Arias A, Feijoo G, Moreira MT. Exploring the potential of antioxidants from fruits and vegetables and strategies for their recovery. Innov Food Sci Emerg Technol. 2022;77:102974.
73. Yang X, Sun Z, Wang W, Zhou Q, Shi G, Wei F, et al. Developmental toxicity of synthetic phenolic antioxidants to the early life stage of zebrafish. Sci Total Environ. 2018;643:559–68.
74. Wongaem A, Reamtong O, Srimongkol P, Sangtanoo P, Saisavoey T, Karnchanatat A, et al. Antioxidant properties of peptides obtained from the split gill mushroom (Schizophyllum commune). J Food Sci Technol. 2021;58(2):680–91.
75. Sangtitanu T, Sangtanoo P, Srimongkol P, Saisavoey T, Reamtong O, Karnchanatat AJF, et al. Peptides obtained from edible mushrooms: Hericium erinaceus offers the ability to scavenge free radicals and induce apoptosis in lung cancer cells in humans. Food Funct. 2020;11(6):4927–39.
76. Song R, Liang T, Shen Q, Liu J, Lu Y, Tang C, et al. The optimization of production and characterization of antioxidant peptides from protein hydrolysates of Agrocybe aegerita. LWT. 2020;134:109987.
77. Kimatu BM, Fang D, Zhao L, Hu Q. Agaricus bisporus peptide fractions confer cytoprotective ability against hydrogen peroxide-induced oxidative stress in HepG2 and Caco-2 cells. J Food Meas Charact. 2020;14(5):2503–19.
78.• Landi N, Clemente A, Pedone PV, Ragucci S, Di Maro A. An updated review of bioactive peptides from mushrooms in a well-defined molecular weight range. Toxins. 2022;14(2):84. **This review reported on the present state of bioactive peptides isolated and described from mushrooms over the last 20 years, with 'peptide' defined as a succession of 2 to 100 amino acid residues.**
79. Xiong C, Li P, Luo Q, Phan CW, Li Q, Jin X, et al. Induction of apoptosis in HeLa cells by a novel peptide from fruiting bodies of Morchella importuna via the mitochondrial apoptotic pathway. Evid Based Complementary Altern Med. 2021;2021:5563367.

80. Kaprasob R, Khongdetch J, Laohakunjit N, Selamassakul O, Kaisangsri N. Isolation and characterization, antioxidant, and antihypertensive activity of novel bioactive peptides derived from hydrolysis of King Boletus mushroom. LWT. 2022;160:113287.
81. Khongdetch J, Laohakunjit N, Kaprasob R. King Boletus mushroom-derived bioactive protein hydrolysate: characterisation, antioxidant, ACE inhibitory and cytotoxic activities. Int J Food Sci Technol. 2022;57(3):1399–410.
82. Oso BJ, Ogidi CO. Repositioning of fungal-based peptides as modulators of angiotensin-converting enzyme-related carboxypeptidase, SARS-coronavirus HR2 domain, and coronavirus disease 2019 main protease. J Transl Intern Med. 2021;9(3):190–9.
83. Rodríguez-Pastén A, Pérez-Hernández N, Añorve-Morga J, Jiménez-Alvarado R, Cariño-Cortés R, Sosa-Lozada T, et al. The activity of prebiotics and probiotics in hepatogastrointestinal disorders and diseases associated with metabolic syndrome. Int J Mol Sci. 2022;23(13):7229.
84. Huang Y, Gao Y, Pi X, Zhao S, Liu W. In vitro hepatoprotective and human gut microbiota modulation of polysaccharide-peptides in Pleurotus citrinopileatus. Front Cell Infect Microbiol. 2022;12:892049.
85. Wu S, Wu Q, Wang J, Li Y, Chen B, Zhu Z, et al. Novel selenium peptides obtained from selenium-enriched Cordyceps militaris alleviate neuroinflammation and gut microbiota dysbacteriosis in LPS-injured mice. J Agric Food Chem. 2022;70(10):3194–206.
86. Li M, Lv R, Xu X, Ge Q, Lin S. Tricholoma matsutake-derived peptides show gastroprotective effects against ethanol-induced acute gastric injury. J Agric Food Chem. 2021;69(49):14985–94.
87. Li X, Zhang ZH, Zabed HM, Yun J, Zhang G, Qi X. An insight into the roles of dietary tryptophan and its metabolites in intestinal inflammation and inflammatory bowel disease. Mol Nutr Food Res. 2021;65(5):2000461.
88. Ragucci S, Landi N, Russo R, Valletta M, Pedone PV, Chambery A, et al. Ageritin from pioppino mushroom: the prototype of ribotoxin-like proteins, a novel family of specific ribonucleases in edible mushrooms. Toxins. 2021;13(4):263.
89. Lampitella E, Landi N, Oliva R, Gaglione R, Bosso A, De Lise F, et al. Toxicity and membrane perturbation properties of the ribotoxin-like protein Ageritin. J Biochem. 2021;170(4):473–82.
90. Xu L, Geng X, Chang M, Meng J, Wang H, Ng TB. A novel ribonuclease with HIV-1 reverse transcriptase inhibitory activity purified from the field Blewit Mushroom Lepista personata (Agaricomycetes). Int J Med Mushrooms. 2020;22(10):991–1000.
91. Aborode AT, Ogunsola SO, Adeyemo AO. A crisis within a crisis: Covid-19 and hunger in African children. Am J Trop Med Hyg. 2021;104(1):30.
92. Grimblatt V. The challenge of agriculture: increase the productivity in a sustainable way. In: 2021 Forum on specification & Design Languages (FDL). IEEE; 2021.
93. Padhani ZA, Das JK, Akhtar S, Ismail T, Bhutta ZA. Tackling protein-calorie malnutrition during world crises. Ann Nutr Metab. 2022;78(1):6–16.
94. Li M, Yu L, Zhao J, Zhang H, Chen W, Zhai Q, et al. Role of dietary edible mushrooms in the modulation of gut microbiota. J Funct Foods. 2021;83:104538.
95. Santo RE, Kim BF, Goldman SE, Dutkiewicz J, Biehl E, Bloem MW, et al. Considering plant-based meat substitutes and cell-based meats: a public health and food systems perspective. Front Sustain Food Syst. 2020;4:134.
96. Kurek MA, Onopiuk A, Pogorzelska-Nowicka E, Szpicer A, Zalewska M, Półtorak A. Novel protein sources for applications in meat-alternative products–insight and challenges. Foods. 2022;11(7):957.
97. Lee HJ, Yong HI, Kim M, Choi Y-S, Jo C. Status of meat alternatives and their potential role in the future meat market–a review. Asian Australas J Anim Sci. 2020;33(10):1533.
98. Stoffel F, de Oliveira SW, Fontana RC, Camassola M. Use of Pleurotus albidus mycoprotein flour to produce cookies: evaluation of nutritional enrichment and biological activity. Innov Food Sci Emerg Technol. 2021;68:102642.
99. Hashempour-Baltork F, Hosseini SM, Assarehzadegan MA, Khosravi-Darani K, Hosseini H. Safety assays and nutritional values of mycoprotein produced by Fusarium venenatum IR372C from date waste as substrate. J Sci Food. 2020;100(12):4433–41.
100. Singh M, Trivedi N, Enamala MK, Kuppam C, Parikh P, Nikolova MP, et al. Plant-based meat analogue (PBMA) as a sustainable food: a concise review. Eur Food Res Technol. 2021;247(10):2499–526.
101. Coelho MO, Monteyne AJ, Dunlop MV, Harris HC, Morrison DJ, Stephens FB, et al. Mycoprotein as a possible alternative source of dietary protein to support muscle and metabolic health. Nutr Rev. 2020;78(6):486–97.
102. Cherta-Murillo A, Frost GS. The association of mycoprotein-based food consumption with diet quality, energy intake and non-communicable diseases' risk in the UK adult population using the National Diet and Nutrition Survey (NDNS) years 2008/2009–2016/2017: a cross-sectional study. Br J Nutr. 2022;127(11):1685–94.
103. Singh RS, Walia AK, Kennedy JF. Mushroom lectins in biomedical research and development. Int J Biol Macromol. 2020;151:1340–50.
104. Tirta Ismaya W, Tjandrawinata RR, Rachmawati H. Lectins from the edible mushroom Agaricus bisporus and their therapeutic potentials. Molecules. 2020;25(10):2368.
105. El-Maradny YA, El-Fakharany EM, Abu-Serie MM, Hashish MH, Selim HS. Lectins purified from medicinal and edible mushrooms: insights into their antiviral activity against pathogenic viruses. Int J Biol Macromol. 2021;179:239–58.
106. Rezvani V, Pourianfar HR, Mohammadnejad S, Madjid Ansari A, Farahmand L. Anticancer potentiality and mode of action of low-carbohydrate proteins and peptides from mushrooms. Appl Microbiol Biotechnol. 2020;104(16):6855–71.
107. Balakrishnan K, Dhanasekaran D, Krishnaraj V, Anbukumaran A, Ramasamy T, Manickam M. Edible mushrooms: a promising bioresource for prebiotics. In: Advances in probiotics. Elsevier; 2021. p. 81–97.
108. You SW, Hoskin RT, Komarnytsky S, Moncada M. Mushrooms as functional and nutritious food ingredients for multiple applications. ACS Food Sci Technol. 2022;2(8):1184–95.
109. Zheng S, Zhu N, Shi C, Zheng HJP. Genomic data mining approaches for the discovery of anticancer peptides from Ganoderma sinense. Phytochemistry. 2020;179:112466.
110. Ragucci S, Landi N, Russo R, Valletta M, Citores L, Iglesias R, et al. Effect of an additional N-terminal methionyl residue on enzymatic and antifungal activities of Ageritin purified from Agrocybe aegerita fruiting bodies. Int J Biol Macromol. 2020;155:1226–35.
111. Jaloot AS, Owaid MN, Naeem GA, Muslim RF. Mycosynthesizing and characterizing silver nanoparticles from the mushroom Inonotus hispidus (Hymenochaetaceae), and their antibacterial and antifungal activities. Environ Nanotechnol Monit Manag. 2020;14:100313.
112. Zhang L, Lu Y, Feng X, Liu Q, Li Y, Hao J, et al. Hepatoprotective effects of Pleurotus ostreatus protein hydrolysates yielded by pepsin hydrolysis. Catalysts. 2020;10(6):595.
113. Li M, Ge Q, Du H, Jiang P, Bao Z, Chen D, et al. Potential mechanisms mediating the protective effects of Tricholoma matsutake-derived peptides in mitigating DSS-induced colitis. J Agric Food Chem. 2021;69(19):5536–46.

114. Kumar H, Bhardwaj K, Sharma R, Nepovimova E, Cruz-Martins N, Dhanjal DS, et al. Potential usage of edible mushrooms and their residues to retrieve valuable supplies for industrial applications. J Fungi. 2021;7(6):427.