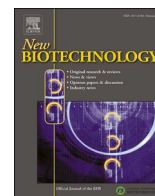


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## New BIOTECHNOLOGY

journal homepage: [www.elsevier.com/locate/nbt](http://www.elsevier.com/locate/nbt)

## Food and human health applications of edible mushroom by-products

Pablo Navarro-Simarro <sup>a</sup>, Lourdes Gómez-Gómez <sup>a,b</sup>, Oussama Ahrazem <sup>a,c,\*</sup>, Ángela Rubio-Moraga <sup>a,c,\*</sup><sup>a</sup> Instituto Botánico. Universidad de Castilla-La Mancha, Campus Universitario s/n, Albacete 02071, Spain<sup>b</sup> Facultad de Farmacia. Departamento de Ciencia y Tecnología Agroforestal y Genética. Universidad de Castilla-La Mancha, Campus Universitario s/n, Albacete 02071, Spain<sup>c</sup> Escuela Técnica Superior de Ingeniería Agronómica y de Montes y Biotecnología. Departamento de Ciencia y Tecnología Agroforestal y Genética. Universidad de Castilla-La Mancha, Spain

## ARTICLE INFO

## Keywords:

Mushroom  
Byproducts  
Food  
Health  
Antioxidants  
Prebiotics

## ABSTRACT

Mushroom waste can account for up to 50% of the total mushroom mass. Spent mushroom substrate, misshapen mushrooms, and mushroom stems are examples of mushroom byproducts. In ancient cultures, fungi were prized for their medicinal properties. Aqueous extracts containing high levels of  $\beta$ -glucans as functional components capable of providing prebiotic polysaccharides and improved texture to foods have been widely used and new methods have been tested to improve extraction yields. Similarly, the addition of insoluble polysaccharides controls the glycemic index, counteracting the effects of increasingly high-calorie diets. Numerous studies support these benefits *in vitro*, but evidence *in vivo* is scarce. Nonetheless, many authors have created a variety of functional foods, ranging from yogurt to noodles. In this review, we focus on the pharmacological properties of edible mushroom by-products, and the possible risks derived from its consumption. By incorporating these by-products into human or animal feed formulations, mushroom producers will be able to fully optimize crop use and pave the way for the industry to move toward a zero-waste paradigm.

## 1. Introduction

Global mushroom production reached 12.74 million tons in 2018 and is projected to reach 20.84 million tons by 2026 [1]. The increase in demand for these products has created an urgent need for innovation in the use of edible mushroom by-products, given the waste generated in their production. These by-products are divided into spent mushroom substrate, misshapen mushrooms and mushroom stems. Mushroom waste can account for up to 50% of the mass of the whole mushroom. In oyster mushroom production, between 165 and 502 g of mushroom stalk waste is discarded for every kg of oyster mushroom commercialized [2]. These by-products are characterized by a higher fiber content than the fruiting body (*Lentinus sajor-caju*: cap - 16.32 g/100 g; stem - 26.34 g/100 g [3]). Fungal polysaccharides are beneficial in maintaining a healthy microbiota because of their prebiotic potential [4–6]. In addition, misshapen mushrooms contain a large number of phenolic compounds and other molecules with high antioxidant properties [7,8]. The presence of interesting active compounds in fungal by-products provides an opportunity for their exploitation in different industries and the

development of new products of cosmetic, pharmaceutical and food interest (Fig. 1). The inclusion of these bioactive compounds derived from fungi in cosmetic formulations has great potential for improving skincare and beauty products. The natural anti-inflammatory, antimicrobial, and antioxidant qualities of these substances can be used to boost the effectiveness of cosmetic formulations [9]. In addition, the compounds' varied pharmacological activities, such as their antiviral, anticancer, and immunomodulatory effects [10,11], offer promising opportunities for the development of pharmaceutical interventions that address unmet medical needs and diseases. Furthermore, the food industry has a great deal of potential to create functional foods with improved nutritional and health-promoting qualities by incorporating fungal by-products. These fungal derivatives contain bioactive substances such as polyphenols, peptides, and polysaccharides that can enhance flavor and help create functional food products with potential health benefits. This helps to keep up with the current trend of health-conscious consumer preferences.

The consumption of mushrooms dates back to the dawn of civilization and has played a transcendental role in both culinary and medicinal

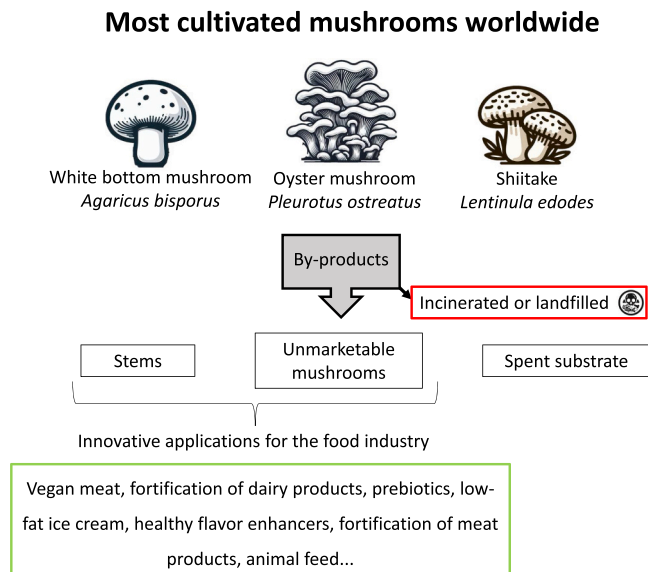
\* Corresponding authors at: Instituto Botánico. Universidad de Castilla-La Mancha, Campus Universitario s/n, Albacete 02071, Spain  
E-mail addresses: [Oussama.ahrazem@uclm.es](mailto:Oussama.ahrazem@uclm.es) (O. Ahrazem), [Angela.Rubio@uclm.es](mailto:Angela.Rubio@uclm.es) (Á. Rubio-Moraga).

<https://doi.org/10.1016/j.nbt.2024.03.003>

Received 11 January 2024; Received in revised form 11 March 2024; Accepted 20 March 2024

Available online 22 March 2024

1871-6784/© 2024 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Most cultivated mushrooms worldwide and the potential of their by-products (stems and unmarketable mushrooms) for the food industry.

contexts. Prominent species such as *Agaricus bisporus*, *Amanita caesarea*, *Lentinula edodes*, *Lactarius deliciosus* and *Pleurotus eryngii* have been revered for their gustatory qualities for thousands of years. However, in addition to their gastronomic delights, these enigmatic fungi have been prized for their medicinal properties in various ancient cultures. *A. bisporus* was valued for its antioxidant and immunomodulatory properties [12]. *A. caesarea*, also known as oronja, was very popular in the Roman world and was noted for its antimicrobial and anti-inflammatory effects [13]. *L. edodes*, known as shiitake, has been revered in traditional Asian medicine for its immunomodulatory, antiviral, and antioxidant capacity, cholesterol regulation and blood pressure control [14]. These iconic examples highlight the historical and current importance of mushrooms as a source of nutrition, and their potential therapeutic benefits in medicine.

There is a growing interest and commitment from companies, governments, and researchers to maximize the use of the abundant organic waste from edible fungi. This review covers a wide range of applications in food, as well as its implications for human health. Aside from the obvious environmental benefits, the use of these by-products from waste materials not only demonstrates its potential but also opens new prospects and opportunities across a variety of productive sectors.

## 2. Chemical composition of mushroom by-products

Edible mushrooms present active compounds of great value in the food industry. Among them, we find polysaccharides such as  $\beta$ -glucans, phenolic compounds, alkaloids, sterols, and microelements such as Selenium, of which special mention will be made because of its great importance. Knowing the chemical composition of edible mushrooms and their by-products is vital for guaranteeing a beneficial and safe product for the consumer.

### 2.1. Nutrient profile

Edible mushrooms are a tasty and healthy food that is consumed worldwide. They mainly contain carbohydrates (50–65% dry weight (dw)), proteins (19–35% dw) and fats (2–6% dw) [15]. In addition, they are a great source of microelements and vitamins such as vitamins B, C and D. Vitamin B is present in different variants (B1, B2, B3, B5, B6, B12), the latter being very important to prevent its deficiency in vegan diets [16]. The nutritional composition varies slightly between the

mushroom cap and stem, with the most significant difference being that the stem contains more fiber [17]. Due to its fibrous texture, the edible mushroom stem has been distanced from the general palate. However, as will be seen in the following sections, its use as a functional ingredient is widespread.

### 2.2. Polysaccharides

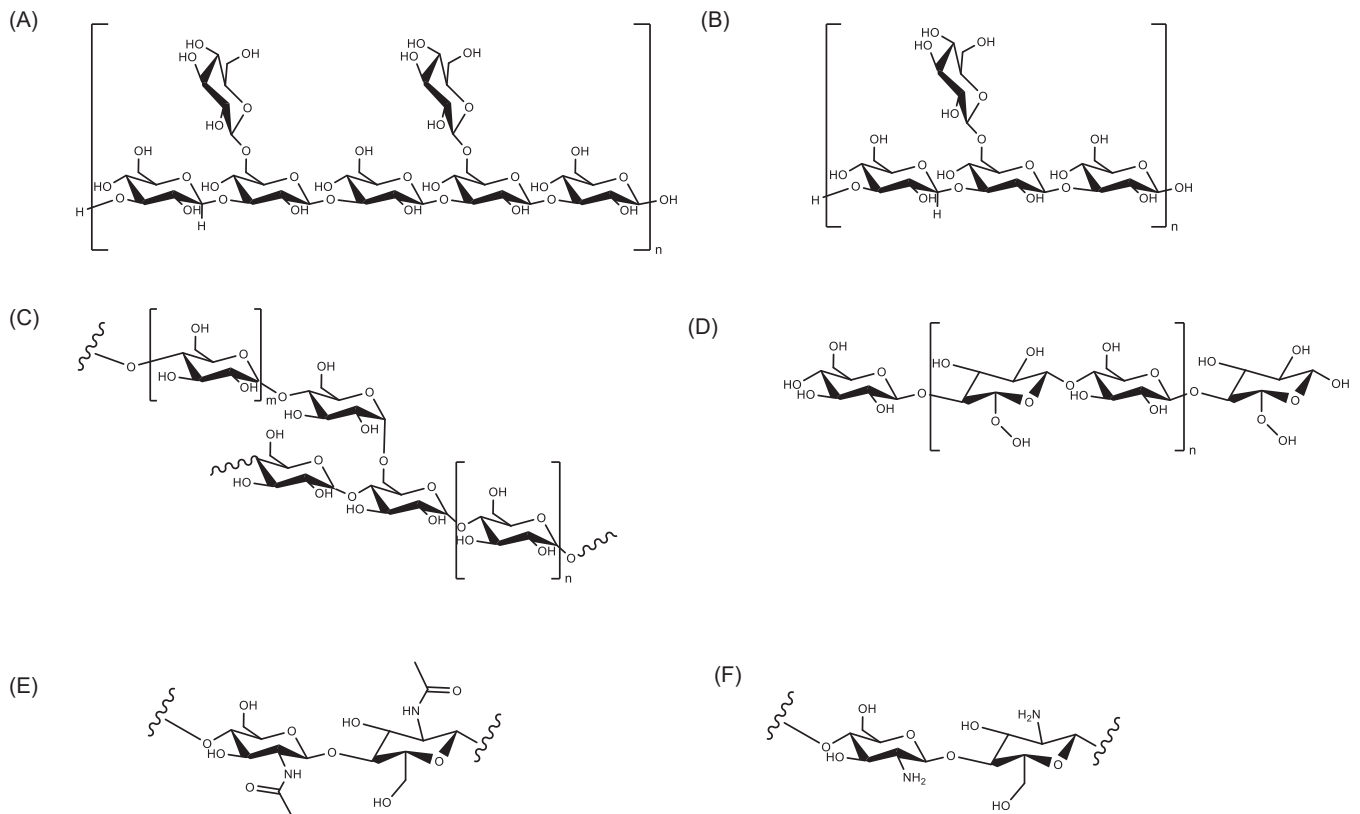
Fungal polysaccharides constitute a part of the cell wall of both the mycelium and the fruiting body. The most abundant among them are D-glucans, which occur as  $\alpha$ -D-glucans,  $\beta$ -D-glucans and  $\alpha,\beta$ -D-glucan mixtures [11,18]. The main peculiarity of these molecules is that, in addition to (1→3) linkages, they also have (1→6) linkages that confer numerous ramifications. In fungi, glucans are part of the cell wall, and their function is mainly structural (Fig. 2). Regarding human health, numerous studies have demonstrated the immunomodulatory, anti-tumour and anti-inflammatory effects of some glucans found in edible mushrooms [19,20]. Among all the edible mushroom polysaccharides, the best known is lentinan, which is found in the shiitake mushroom (*L. edodes*). This polysaccharide is composed of a main chain of (1→3)  $\beta$ -D-glucopyranose with the ramifications of (1→6)  $\beta$ -D-glucopyranose at a frequency of two branches every five units of the main chain. It exhibits antitumour, antiviral and immunomodulatory activities [11]. Ahn *et al.* (2017) reported, the effect of lentinan on inflammasome activation in myeloid cells [10]. Bone marrow-derived mouse macrophages were treated with lentinan, with or without inflammasome activators, and the results showed that lentinan selectively inhibited inflammasome activation, which is absent in melanoma 2 (AIM2). They also evaluated the effect of lentinan in mice treated with *Listeria monocytogenes* or lipopolysaccharide as an AIM2 or non-canonical inflammasome-mediated model. Lentinan attenuated IL-1 $\beta$  secretion resulting from *Listeria*-mediated AIM2 inflammasome activation and reduced endotoxin lethality.

Chitin is another polysaccharide found in the cell walls of fungi and the exoskeletons of arthropods. This polymer is composed of N-acetylglucosamine units with  $\beta$ -(1→4) linkages. In recent years, chitin has attracted considerable interest because its deacetylation leads to the production of chitosan. Wu *et al.* (2004) analysed the accumulation of chitin by *A. bisporus* and showed that its degree of acetylation (75.8–87.6%) is similar to that of crustaceans, which is exploited at an industrial scale [21]. The researchers used by-products of mushroom production, particularly stalks, and obtained yields of 0.65%–1.15% chitin in fresh weight. Given the large amount of this by-product that is discarded, mushroom stems could be a source of 1000 tons of crude fungal chitin per year.

The extraction methods to obtain mushroom polysaccharides at the industrial level is a major consideration in the choice of a cost-effective, environmentally friendly process to produce a safe product for human consumption. A cheap way to extract polysaccharides is hot water extraction for soluble polysaccharides and acid or alkaline extraction for soluble and insoluble polysaccharides. New methods have been developed to increase the extraction yield, such as ultrasound treatment [22], gamma-irradiation [23], microwave-assisted extraction [24] or subcritical liquid extraction [25]. The main advantage of these new methods are the lower use of extraction solvent and the higher yield of obtaining polysaccharides, although the investment in equipment is more expensive.

### 2.3. Phenolic compounds

Phenolic and polyphenolic compounds are hydroxylated aromatic compounds that possess one or more aromatic rings with one or more hydroxyl groups and are commonly found in plants and in fungi (Table 1) [8,26–28]. These compounds exhibit various biological effects due to their free radical scavenging and antioxidant activity. Palacios *et al.* (2011) analysed the phenolic content of eight species of edible



**Fig. 2.** Structure of polysaccharides present in fungi, plants and arthropods. (A) Lentinan (*L. edodes*). Main chain:  $\beta$ -1 $\rightarrow$ 3 branched by chains of  $\beta$ -1 $\rightarrow$ 6. (B) Pleuran (*P. ostreatus*). Main chain:  $\beta$ -1 $\rightarrow$ 3 branched by chains of  $\beta$ -1 $\rightarrow$ 6. (C) Amylopectin (plants). Main chain:  $\alpha$ -1 $\rightarrow$ 4 branched by chains of  $\beta$ -1 $\rightarrow$ 6 (Roughly one branching every 25 residues). (D) Cellulose (plants): Main chain:  $\beta$ -1 $\rightarrow$ 4. (E) Chitin (Fungi and arthropods). Main chain:  $\beta$ -1 $\rightarrow$ 4. (F) Chitosan (Chitin deacetylation). Main chain:  $\beta$ -1 $\rightarrow$ 4.

mushrooms, including *A. bisporus*, *Boletus edulis* and *Pleurotus ostreatus* [26]. Using the Folin-Ciocalteu method, clear differences were observed between the different species, with *B. edulis* ( $\approx 5$  mg/g) and *A. bisporus* ( $\approx 3$  mg/g) having the highest phenolic content, in contrast to *P. ostreatus* ( $\approx 1.5$  mg/g). The different phenolic compounds were then quantified by HPLC-MS, including gallic acid, caffeic acid, homogentisic acid, protocatechuic acid, chlorogenic acid, ferulic acid, gentisic acid, myricetin, p-coumaric acid and pyrogallol. These phenolic compounds are found in both the fruit body and stems. Banerjee *et al.* (2020), examined the total phenolics of an extract of Enoki mushroom (*Flammulina filiformis*) stems revealing a value of 6.26 mg/g dw [29].

#### 2.4. Alkaloids and eritadenine

Edible mushrooms contain other non-phenolic active compounds that affect human health, such as alkaloids and eritadenine. Alkaloids are widely known to be responsible for the psychotropic effects in some wild mushrooms, such as those of the genus *Psilocybe* [44]. The majority of cultivated edible mushrooms, such as *A. bisporus*, contain alkaloids but in low concentrations ( $0.034 \pm 0.01$  g/100 g of aqueous extract) [45]. Regarding shiitake mushroom, new studies are trying to identify new secondary metabolites with a potential use in the pharmaceutical industry. In the study by Zhao *et al.* (2023), nine pyrrole alkaloid derivatives were found, of which four were previously unknown [46].

One of the most studied edible mushroom alkaloid is eritadenine (Fig. 3), an adenosine analogue present in *L. edodes* that has traditionally been attributed to an anticholesterolemic effect [47]. In addition, a recent study conducted by Gutiérrez-Rodelo *et al.* (2023) highlighted the potential of eritadenine as a promising option for the treatment of anxiety disorders [48]. Behavioral test results indicate a marked anxiolytic and sedative-hypnotic effect in mice, suggesting that eritadenine,

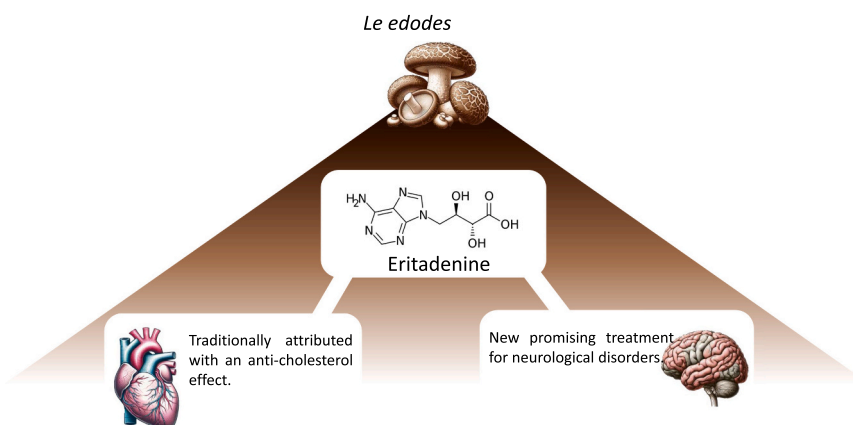
as an adenosine analogue modulates locomotor functions via adenosine 2 A receptors. The presence of eritadenine in shiitake is between 5.6 and 16.6 mg/100 g dw, considering that some heat treatments can alter its concentration [49].

#### 2.5. Sterols

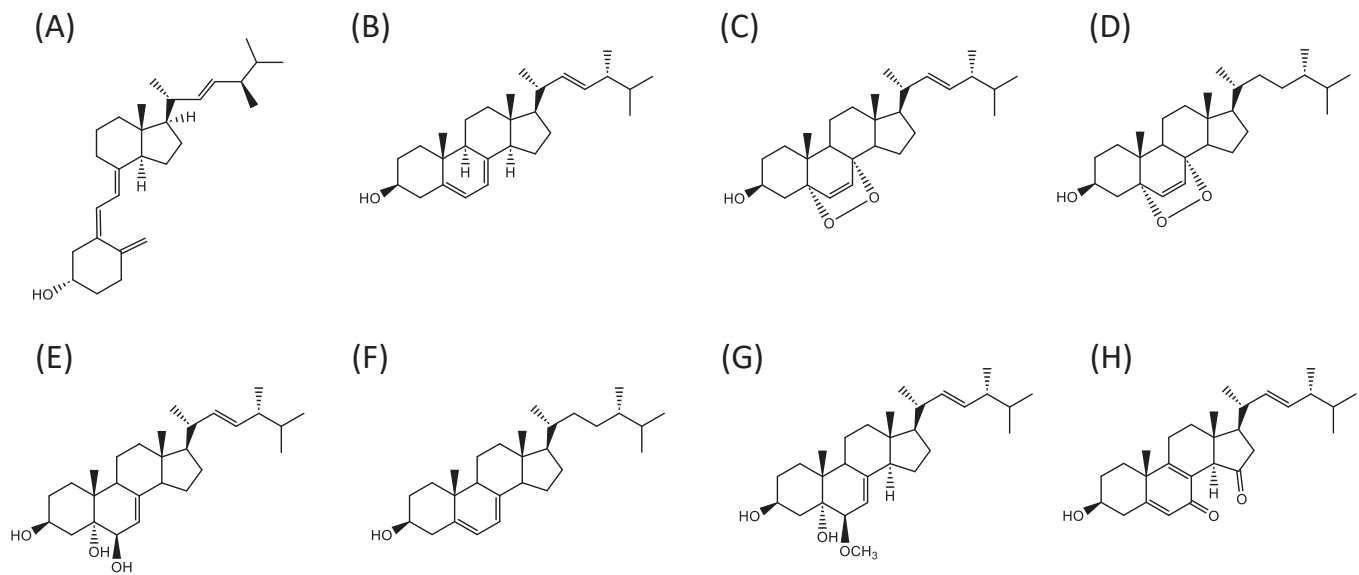
Other interesting compound found in edible mushrooms is free (22*E*)-ergosta-5,7,22-trien-3 $\beta$ -ol (ergosterol) due to its antioxidant and anti-inflammatory activity [50,51], for modulating adipogenesis and glucose uptake [52] and even thought for its aromatase inhibiting activity [53]. On the other hand, other ergosterol derivatives (Fig. 4) described in edible mushrooms have demonstrated biological activity at different levels (Table 2). Free ergosterol is naturally present in the cell membranes of mushrooms and is of nutritional interest because it is converted to ergocalciferol, a form of vitamin D, when exposed to UV light. Free ergosterol has been quantified in several edible mushrooms, including *A. bisporus*, *L. edodes*, *A. caesarea*, *Fistulina hepatica*, *Macrolepiota procera*, *M. esculenta* [50,54], *Flammulina velutipes* [54,56], *C. cibarius* [51,54], *L. deliciosus* [54,57]. Guan *et al.* (2016) investigated the effects of UV-C light treatment and refrigerated storage on ergosterol and vitamin D content of white button mushroom and brown button mushroom [58]. Ultraviolet light treatment (2.0 kJ/m<sup>2</sup>) increased the amount of vitamin D<sub>2</sub> (mg/100 g dw) from 0.79 to 1.34 in caps and from 0.66 to 1.17 in white mushroom stems, as well as from 0.43 to 0.95 in caps and from 0.56 to 1.05 in brown mushroom stems. It was also observed that while mushroom caps lost vitamin D during the first 7 days of refrigeration, the vitamin D content in brown button mushroom stems increased during the entire period (14 days). These results are of great interest for the development of post-harvest methods.

**Table 1**  
The main phenolic compounds identified in mushrooms.

Phenolic compound	Mushrooms	Most reviewed effect
Gallic acid	<i>Russula aurora</i> , <i>Ganoderma lucidum</i> , <i>A. bisporus</i> , <i>B. edulis</i> , <i>Cantharellus cibarius</i> , <i>Craterellus cornucopioides</i> , <i>Calocybe gambosa</i> , <i>Hygrophorus marzuolus</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> .	Antioxidant, anti-inflammatory and anti-cancer[30].
Caffeic acid	<i>Amanita vaginata</i> , <i>Coprinus atramentarius</i> , <i>Laetiporus sulphureus</i> , <i>Morchella elata</i> , <i>Amanita flavoconia</i> , <i>Strobilomyces floccopus</i> , <i>Amanita pantherina</i> , <i>B. edulis</i> , <i>Agaricus arvensis</i> , <i>Boletus frostii</i> , <i>Ramaria flava</i> , <i>G. lucidum</i> , <i>Boletus luridus</i> , <i>A. bisporus</i> , <i>C. cibarius</i> , <i>C. gambosa</i> , <i>H. marzuolus</i> , <i>L. deliciosus</i> , <i>Fomes fomentarius</i> , <i>Gymnopilus penetrans</i> , <i>Hyphodontia paradoxa</i> , <i>Lenzites betulinus</i> .	Antioxidant and antimicrobial[27].
Protocatechuic acid	<i>A. flavoconia</i> , <i>S. floccopus</i> , <i>A. pantherina</i> , <i>A. arvensis</i> , <i>B. frostii</i> , <i>R. flava</i> , <i>Lycoperdon perlatum</i> , <i>Sarcodon imbricatus</i> , <i>Hypomyces lactifluorum</i> , <i>A. bisporus</i> , <i>B. edulis</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>H. marzuolus</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> , <i>Amanita citrina</i> , <i>Amanita porphyria</i> , <i>Bjerkandera adusta</i> , <i>Cortinarius armillatus</i> , <i>F. formentarius</i> , <i>Fomitopsis pinicola</i> , <i>G. penetrans</i> , <i>Hygrophoropsis aurantiaca</i> , <i>H. paradoxa</i> , <i>Lactarius helvus</i> , <i>L. betulinus</i> , <i>Pseudoclitocybe cyanthiformis</i> , <i>Psilocybe fascicularis</i> , <i>Rhodocollybia maculata</i> , <i>Russula fragilis</i> , <i>Scleroderma citrinum</i> , <i>Thelephora terrestris</i> , <i>Trametes hirsuta</i> , <i>Trichaptum fuscoviolaceum</i> .	Anti-inflammatory, antioxidant and antimicrobial[27].
Chlorogenic acid	<i>Lactarius indigo</i> , <i>A. pantherina</i> , <i>B. frostii</i> , <i>S. imbricatus</i> , <i>B. luridus</i> , <i>A. bisporus</i> , <i>B. edulis</i> , <i>C. gambosa</i> , <i>L. deliciosus</i> .	Antioxidant, antibacterial, hepatoprotective, cardioprotective, anti-inflammatory, antipyretic, neuroprotective, antiviral and antimicrobial[31].
Ferulic acid	<i>Russula delicata</i> , <i>A. flavoconia</i> , <i>Russula emetica</i> , <i>A. arvensis</i> , <i>B. frostii</i> , <i>A. bisporus</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> , <i>D. confragosa</i> , <i>H. paradoxa</i> , <i>L. aurantiacus</i> , <i>L. betulinus</i> , <i>T. fuscoviolaceum</i> .	Antioxidant used as food preservative[27].
Catechins	<i>A. vaginata</i> , <i>R. emetica</i> , <i>B. frostii</i> , <i>R. flava</i> , <i>G. lucidum</i> , <i>Cortinarius alboviolaceus</i> , <i>B. luridus</i> , <i>H. lactifluorum</i> , <i>A. bisporus</i> , <i>C. cibarius</i> .	Lowers blood glucose levels and prevents type-2 diabetes[13].
Coumarins	<i>Chroogomphus rutilus</i> , <i>A. bisporus</i> .	Anticancer[32].
Ellagic acid	<i>Clitocybe odora</i> .	Antiinflammatory, antiapoptotic, antioxidant and hepatoprotective[33].
p-Hydroxybenzoic acid	<i>Lepista nuda</i> , <i>L. indigo</i> , <i>A. flavoconia</i> , <i>S. floccopus</i> , <i>B. edulis</i> , <i>A. arvensis</i> , <i>A. bisporus</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>H. marzuolus</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> , <i>A. citrina</i> , <i>A. porphyria</i> , <i>B. adusta</i> , <i>Clavicornia pyxidata</i> , <i>Cortinarius sanguineus</i> , <i>D. confragosa</i> , <i>F. formentarius</i> , <i>F. pinicola</i> , <i>G. penetrans</i> , <i>Heterobasidion annosum</i> , <i>H. aurantiaca</i> , <i>H. paradoxa</i> , <i>Lactarius aurianticus</i> , <i>L. helvus</i> , <i>P. fascicularis</i> , <i>P. cyanthiformis</i> , <i>Psilocybe lateritia</i> , <i>S. citrinum</i> , <i>Stereum hirsutum</i> , <i>T. terrestris</i> , <i>T. hirsuta</i> , <i>T. fuscoviolaceum</i> .	Antimicrobial and antifungal[34].
Rosmarinic acid	<i>Tapinella panuoides</i> .	Antimicrobial, antioxidant[35].
Cinnamic acid	<i>A. bisporus</i> , <i>A. flavoconia</i> , <i>S. floccopus</i> , <i>B. edulis</i> .	Prevention of post-harvest browning of mushrooms[36].
Kaempferol	<i>L. indigo</i> , <i>G. lucidum</i> .	Antioxidant and anticancer[37].
Isorhamnethin	<i>B. frostii</i> , <i>R. flava</i> , <i>L. perlatum</i> .	Anti-obesity[38].
Sinapic acid	<i>S. floccopus</i> , <i>B. edulis</i> , <i>A. arvensis</i> , <i>Amanita virosa</i> , <i>B. frostii</i> , <i>R. flava</i> , <i>L. perlatum</i> .	Antioxidant[39].
Gentisic acid	<i>B. edulis</i> , <i>C. cibarius</i> , <i>C. gambosa</i> , <i>H. marzuolus</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> .	Antioxidant[40].
Homogentisic acid	<i>A. bisporus</i> , <i>B. edulis</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>H. marzuolus</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> .	Liver protection after ethanol consumption[41].
Pyrogallol	<i>A. bisporus</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>L. deliciosus</i> .	Synergism with antibiotics[42].
Myricetin	<i>L. indigo</i> , <i>A. flavoconia</i> , <i>R. emetica</i> , <i>A. virosa</i> , <i>B. frostii</i> , <i>C. alboviolaceus</i> , <i>S. imbricatus</i> , <i>A. bisporus</i> , <i>B. edulis</i> , <i>C. cibarius</i> , <i>C. cornucopioides</i> , <i>C. gambosa</i> , <i>L. deliciosus</i> , <i>P. ostreatus</i> .	Antioxidant, antitumor, anti-inflammatory, cardio-cerebrovascular protection, anti-neurogenerative, immunomodulatory and antimicrobial[43].
Vanillic acid	<i>Coprinus atramentarius</i> , <i>R. flava</i> , <i>B. adusta</i> , <i>D. confragosa</i> , <i>H. paradoxa</i> , <i>L. betulinus</i> , <i>T. fuscoviolaceum</i> .	Antimicrobial, anticancer and antioxidant[27].
p-Coumaric acid	<i>Morchella esculenta</i> , <i>A. bisporus</i> , <i>B. edulis</i> , <i>H. marzuolus</i> , <i>P. ostreatus</i> , <i>C. armillatus</i> , <i>C. sanguineus</i> , <i>D. confragosa</i> , <i>F. formentarius</i> , <i>F. pinicola</i> , <i>G. penetrans</i> , <i>H. aurantiaca</i> , <i>H. paradoxa</i> , <i>L. aurantiacus</i> , <i>L. helvus</i> , <i>P. cyanthiformis</i> , <i>P. fascicularis</i> , <i>S. hirsutum</i> , <i>T. terrestris</i> , <i>T. hirsuta</i> , <i>T. fuscoviolaceum</i> .	Antioxidant, anti-inflammatory, antimutagenic and anti-ulcer[27].



**Fig. 3.** Eritadenine is an adenosine analogue found in *L. edodes* that shows potential pharmacological applications.



**Fig. 4.** Ergocalciferol, ergosterol and derivatives present in mushrooms. (A) Ergocalciferol; (B) (22E,24 R)-ergosta-5,7,22-trien-3 $\beta$ -ol or ergosterol; (C) 5 $\alpha$ ,8 $\alpha$ -epidioxy-(22E,24 R)-ergosta-6,22-dien-3 $\beta$ -ol or ergosterol peroxide; (D) 5 $\alpha$ ,8 $\alpha$ -epidioxy-(24 S)-ergosta-6-en-3 $\beta$ -ol; (E) 5 $\alpha$ -ergosta-7,22-diene-3 $\beta$ ,5,6 $\beta$ -triol or cerevisterol; (F) (22E)-ergosta-5,7,22-trien-3 $\beta$ -ol or 22,23-dihydroergosterol; (G) (22E)- 6 $\beta$ -methoxyergosta-7,22-diene-3 $\beta$ ,5 $\alpha$ -diol; (H) 3 $\beta$ -Hydroxyl-(22E,24 R)-ergosta-5,8,22-trien-7,15-dione.

**Table 2**

Ergosterol derivatives described in edible mushrooms that have demonstrated biological activity.

Steroid	Mushrooms	Most reviewed effect
5 $\alpha$ ,8 $\alpha$ -epidioxy-(22E,24 R)-ergosta-6,22-dien-3 $\beta$ -ol or ergosterol peroxide	<i>C. cibarius</i> [51], <i>Lactarius hatsudake</i> [59], <i>L. edodes</i> [60], <i>M. esculenta</i> [55,61], <i>P. ostreatus</i> [62,63].	Antimicrobial, cytotoxic and immunosuppressive[64], Amoebicidal Effect against <i>Entamoeba histolytica</i> [62], Trypanocidal Activity[63], Phospholipase A2 inhibitors [59], and NF- $\kappa$ B inhibitory activity[51].
5 $\alpha$ ,8 $\alpha$ -epidioxy-(24 S)-ergosta-6-en-3 $\beta$ -ol	<i>L. hatsudake</i> [59]	Phospholipase A2 inhibitors [59].
5 $\alpha$ -ergosta-7,22-diene-3 $\beta$ ,5,6 $\beta$ -triol or cerevisterol	<i>C. cibarius</i> [51], <i>L. hatsudake</i> [59], <i>M. esculenta</i> [55].	NF- $\kappa$ B inhibitory activity [55][51].
22,23-dihydroergosterol or (22E)-ergosta-5,7,22-trien-3 $\beta$ -ol	<i>F. velutipes</i> [56].	Cytotoxicity assay of FVS against U251 cells and HeLa cells[56].
(22E)- 6 $\beta$ -methoxyergosta-7,22-diene-3 $\beta$ ,5 $\alpha$ -diol	<i>P. eryngii</i> [53].	Inhibitory Effects on Aromatase as anticancer treatment[53].
(3 $\beta$ -Hydroxyl-(22E,24 R)-ergosta-5,8,22-trien-7,15-dione	<i>P. eryngii</i> [65].	Inhibitor of macrophage activation through inhibitory effects on nitric oxide[65].

### 2.6. Selenium

Selenium is an essential micronutrient present in fungi in the form of various compounds such as sodium selenite (Na<sub>2</sub>SeO<sub>3</sub>), hydrogen selenide (H<sub>2</sub>Se), Se-polysaccharides and Se-proteins. In humans, selenium is required for the synthesis of several selenoproteins, such as glutathione peroxidase [66]. Although selenium can be toxic in high concentrations, its deficiency can lead to diseases such as Kashin-Beck disease. Therefore, a daily intake of 60  $\mu$ g of selenium is recommended for men and 53  $\mu$ g for women [67].

Selenium is found in higher concentrations in wild mushrooms than in cultivated mushrooms (Table 3). Falandysz (2008) compared the concentration of this element in 190 species of mushrooms, most of which are edible [7]. The wild species with the highest selenium concentrations were *Albatrellus pes-caprae* (200  $\mu$ g Se/g dw), *B. edulis* (20  $\mu$ g

**Table 3**

Comparison of the concentrations of some essential metals among wild/cultivated fungi and cap/stipe of *P. ostreatus*.

Essential elements	Microelement concentration (mg/100 g dw)			
	Polish wild mushrooms [71]	<i>P. ostreatus</i> cap[72]	<i>P. ostreatus</i> stipe[72]	Polish <i>A. bisporus</i> mineral concentration 1977-2008-2020 [73]
Se	0.01-1.83			0.05-0.20-0.17
Mg		140-240	88-240	128-106-148
Fe	4.82-28.78	2.2-11	1.2-12	8.04-4.30-4.79
Cu	2.04-2.45	0.30-1.8	0.18-1.2	5.27-1.04-5.95
Mn	0.24-3.3	0.28-1.1	0.039-0.48	0.81-0.57-0.68
Zn	0.36-12.81	14-92	1.1-8.3	6.58-2.99-6.14
Na		4.6-92	6.2-80	121-24-49.1

Se/g dw) and *Amanita strobiliformis* (20  $\mu$ g Se/g dw). Noted that the values presented are averages and it is important to consider that within the same species, there can be wide variability in selenium concentration. For example, a maximum concentration of 70  $\mu$ g Se/g dw was found in *B. edulis*, which is 3.5 times the average concentration. The reason for this, apart from the selenium uptake capacity of each species, is due to factors such as the chemical composition of the soil and climatic conditions.

Cultivated species such as *A. bisporus* (2.82 ( $\pm$  1.48)  $\mu$ g Se/g dw [68]) have rather low selenium levels, which presents a challenge for the production of dietary supplements and other compounds of interest, such as metal nanoparticles. However, to address this demand, bio-fortified cultures of *A. bisporus* have been developed that achieve higher selenium levels, ranging from 30 to 110  $\mu$ g Se/g dw [7]. These selenium-rich fungi and their by-products represent a potentially valuable source of raw materials for both nanotechnology and medicine, opening new opportunities and applications in these fields [69,70].

### 2.7. Other essential elements

In addition to being a rich source of selenium, edible mushrooms contain modest but significant amounts of major essential elements such as Ca, K, Mg, Na and P and essential trace elements including B, Cr, Cu,

Fe, Mn, Mo, Ni and Zn, which are necessary for the proper physiological functioning of organisms [73]. For edible mushrooms such as *A. bisporus*, the work by Koyyalamudi et al. (2013) conducted a mineral analysis of various harvests from several producers in Australia [74]. The results showed that the levels of B, Cu and Se present in the mushrooms were significant in the diet, whereas Na, K, Mg, Ca and Mn were nutritionally insignificant. In both cultivated and wild mushrooms, there is a great variability in micronutrient content within the same species and even within the same individual. These differences are attributed to the availability of micronutrients in the soil, the species, the level of maturity of the mycelium or the part of the mushroom. For example, the study by Golian et al. (2021) compared the concentration of some metallic elements in the cap and stem of 59 varieties of *P. ostreatus* (Table 3) [72]. Elements such as Cu, Fe, K, Mg, Mn and Zn mainly accumulated in the cap, while no significant differences were observed with respect to Al, Ca and Na.

The differences in microelement concentrations between wild and cultivated mushrooms are significant even if they come from the same area. In the case of Poland, the study by Sotek et al. (2023) studied the concentration of Se, Cu, Zn, Mn and Fe in specimens of *B. edulis*, *Imleria badia* and *Leccinum scabrum* grown in forests in the northwest of the country [71]. Of the three mushrooms, *B. edulis* was the highest bio-accumulator and was considered as a great source of the analyzed trace elements for the human diet. Despite this, its high selenium content makes its extensive consumption not recommended, as this micro-nutrient can be harmful at high doses. In the case of edible mushrooms also cultivated in Poland, the excessive concentration of microelements has not been a limitation. In the study of Siwulski et al. (2022), the concentration of microelements in polish *A. bisporus* from 1977 to 2020 was analyzed [73]. It could be observed that in this range of time mushrooms presented variations in the microelement profile due to changes in substrate processing and optimization of cultivation methods, being always within acceptable values. In conclusion, cultivated edible mushrooms, as well as their by-products, are an excellent source of essential microelements, although special care should be taken when consuming large quantities of wild mushrooms.-

### 3. Human health

Edible mushroom by-products are highly valued for their polysaccharides, with beneficial effects on human health. While some non-digestible polysaccharides promote a diverse and healthy intestinal microbiota, as they are fermented by some of these bacteria, others have been shown to have an antiglycemic effect, decreasing blood glucose absorption. Despite their benefits, the risks of consuming edible mushrooms, such as allergies, presence of heavy metals or microbiological contamination of the raw material, must also be considered.

#### 3.1. Prebiotic potential of edible mushroom by-products

Prebiotics, natural compounds that stimulate the growth of healthy intestinal microbiota, have gained considerable interest for their application in functional foods that can manipulate the composition of the microbiome and protect it from the proliferation of pathogenic bacteria [75]. Examples of prebiotics, such as inulin and  $\beta$ -glucans, belong to a group of carbohydrates that are indigestible by the host but can be used by specific groups of intestinal bacteria. Fermentation of these prebiotics by the intestinal microbiota produces short-chain fatty acids (SCFAs) (Table 4), which have beneficial effects at the immune, physiological, and metabolic levels [76]. It is important to note that the concept that bacterial species are always beneficial or detrimental is not straightforward, as microbial diversity plays a key role. A poorly diverse microbiome has been linked to diseases such as obesity and diabetes [77]. Therefore, promoting a diverse and balanced microbiome through the consumption of prebiotics can maintain overall health and prevent certain diseases.

**Table 4**

Short chain fatty acids (SCFAs) produced during fermentation by probiotic bacteria and their correlation with some clinical disorders.

Name	Molecular formula	Their disruption can be a sign of
Acetic acid (C2:0) *	CH <sub>3</sub> COOH	Cancer[78], constipation[79], and unhealthy aging[80].
Propionic acid (C3:0) *	CH <sub>3</sub> CH <sub>2</sub> COOH	Constipation[79], Multiple Sclerosis Disease[81], autism spectrum disorder [82], and obesity and type 2 diabetes[83]. Obesity and type 2 diabetes[83].
Butyric acid (C4:0) *	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> COOH	Allergy[84].
Valeric acid (C5:0)	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> COOH	No fermentation of indigestible proteins [85].
Isobutyric acid (C4:0)	(CH <sub>3</sub> ) <sub>2</sub> CHCOOH	Depression[86], mucosal immunity in broilers[87] and ovariectomy-induced osteoporosis[88].
Isovaleric acid (C5:0)	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub> COOH	

\* -more abundant

Edible mushrooms are a great source of polysaccharides with a potential prebiotic effect because they contain indigestible polysaccharides such as glucans, chitin, hemicellulose, mannans, xylans and galactans. Polysaccharides from edible mushrooms are able to reach the colon uncorrupted and, once there, stimulate the growth of bacterial strains such as *Lactobacillus* [5]. Furthermore, the addition of fungal polysaccharides to probiotic foods increases the probability of bacteria surviving the digestive process [89].

Numerous studies have focused on comparing the prebiotic activity of different edible fungi species (Fig. 5). For example, in the study by Sawangwan et al. (2018), water-ethanol extracts (1:4) of different mushrooms (*Auricularia auricula-judae*, *L. edodes*, *Pleurotus citrinopileatus*, *Pleurotus djamor*, *P. ostreatus* and *Pleurotus pulmonarius*) were supplemented to MRS broth for cultivation of *Lactiplantibacillus plantarum* and *Lactobacillus acidophilus* [90]. The supernatant of the bacterial culture was then used to measure the inhibition of pathogenic bacteria such as *Bacillus cereus* and *Staphylococcus aureus*. The results showed that the *P. ostreatus* extract had higher levels of total sugars, whereas the media supplemented with *L. edodes* and *P. pulmonarius* stimulated the growth of probiotic bacteria the most. In addition, the supernatant of *A. auricula-judae* with *L. plantarum* excelled in inhibiting *B. cereus*. Finally, a digestive survival assay was performed against an incubation with hydrochloric acid, and it was observed that fungal extracts could increase the percentage survival of probiotic bacteria. Most positively, these results far outperformed the positive control (fructooligosaccharides and inulin).

The microorganisms of the human intestinal microbiota dedicate a significant part of their genetic material to the expression of carbohydrate-active enzymes (CAZymes), which degrade part of the non-digestible dietary fiber [91]. Among them, bacteria of the phyla Bacteroidetes (genus: *Bacteroides*, *Parabacteroides*, *Prevotella*), Firmicutes (genus: *Clostridium*, *Eubacterium*, *Lactobacillus*, *Faecalibacterium*) and Actinobacteria (genus: *Bifidobacterium*) were mainly found [92]. The study by Temple et al. (2017) demonstrated the ability of *Bacteroides thetaiotaomicron*, present in the human microbiota, to degrade  $\beta$ -glucans present in the fungal cell wall via PUL 1,6- $\beta$ -glucan [6]. It was previously hypothesized that this PUL targets 1,3- and 1,4- $\beta$ -glucans present in vegetables. This was disproved by deleting the enzyme BT3312 (encoded by PUL) from *B. thetaiotaomicron* and finding that without it, the bacterium was unable to grow with 1-6- $\beta$ -glucans as a carbon source. This ability of some bacteria to degrade fungal polysaccharides, which are abundant in the stalks and unmarketable parts of edible mushrooms, opens a window for their use in functional foods to modulate the human gut microbiota.

Among all cultivated edible mushrooms, those of the *Pleurotus* genus have shown a significant prebiotic character. In a study conducted by Synytsya et al. (2009), different polysaccharide extracts of *P. ostreatus*

## Effects of fungal polysaccharides in the gut

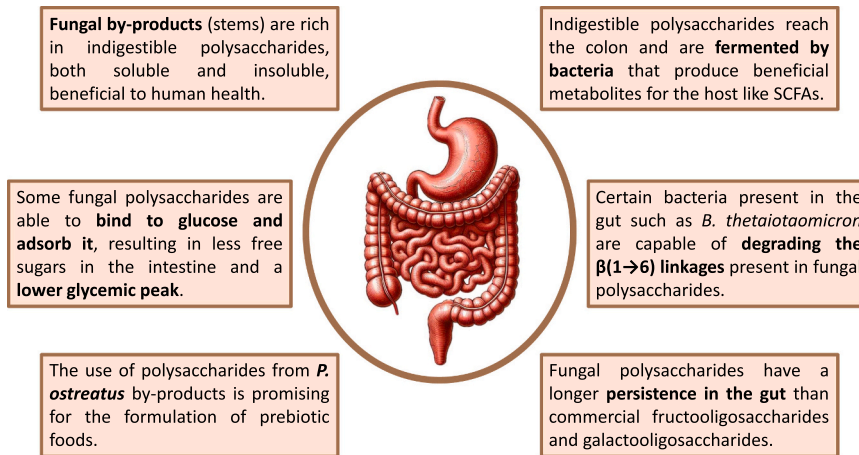


Fig. 5. Effect of fungal polysaccharides in the gut, highlighting their prebiotic and antiglycemic effects.

and *P. eryngii* stems were formulated [93]. The prebiotic potential of these extracts was then evaluated *in vitro* by culturing *Lactobacillus* spp., *Bifidobacterium* spp. and *Enterococcus faecium* strains on Man-Rogosa-Sharpe medium without glucose supplemented with *Pleurotus* polysaccharides. Bacterial growth, SCFAs production and biomass were monitored. The alkaline extract of *P. eryngii* stimulated the growth of *Lactobacillus* and *Enterococcus*, whereas aqueous extracts increased the total biomass of *E. faecium*. For *Bifidobacterium*, the results were more variable, as the same extract stimulated some strains while others did not grow. Recent studies have linked the microbiota-modulating potential of these fungi as a target for the treatment of various diseases. For example, the study by Kerezoudi *et al.* (2021) explored the *in vitro* effect of the fungi *G. lucidum* and *P. ostreatus* as beneficial prebiotics for bone health [94]. Gut microbiota samples from healthy and osteopenic women were used as inoculum for a fermenter supplemented with fungal extract. The fermentation products were evaluated on osteoblast cell cultures and were found to stimulate their metabolic activity.

In line with these studies, Lam *et al.* (2018) evaluated the potential of glucans to mimic human milk oligosaccharides and their effect on infant bacterial communities *in vitro* [4]. Faecal samples were collected from 3-month-old breastfed infants and used to compare the fermentation rate of 13 carbohydrates, including  $\beta$ -glucans from oats and *Pleurotus tuber-regium*. The results showed that of the 3  $\beta$ -glucans tested, the higher molecular weight from barley and *P. tuber-regium* had a lower maximum population increase for total anaerobic bacteria and *Lactobacillus* than the lower molecular weight oat  $\beta$ -glucan. On the contrary the latter glucan had a longer persistence time of population growth for total anaerobic bacteria and *Lactobacilli*. In general, complex carbohydrates could provide a longer fermentation period to sustain the growth of infant faecal bacteria, in contrast to fructooligosaccharides and galactooligosaccharides present in commercial formulations. Sucrose and xylitol were more selective for bifidobacteria, whereas glucose, xylooligosaccharides,  $\beta$ -glucans, starch and inulin were more selective for *Lactobacillus*. Further human studies are needed to assess the real benefits of *Pleurotus* consumption, although *in vitro* and animal studies are quite optimistic [95].

### 3.2. Glycemic load control

Consumption of foods high in sugar and calories is directly linked to obesity, type 2 diabetes, cardiovascular disease, metabolic syndrome, and cancer. Edible mushrooms, on the other hand, have been shown to have a high hypoglycemic and therefore anti-diabetic potential, as fiber promotes the slow release of sugars into the bloodstream (Fig. 5). For instance, the study by Hosseini *et al.* (2022) demonstrated that the

consumption of dry white mushroom powder significantly reduced the concentration of fructosamine in the blood of diabetic patients [96]. This effect is attributed to its polysaccharides, which can attenuate the effects of diabetes by inhibiting glucose absorption and increasing intestinal viscosity [97]. In addition, polysaccharides have been shown to have the ability to bind and adsorb glucose, which helps to maintain a lower concentration of free sugars in the small intestine [98], thus controlling the glycemic index.

Considering the antiglycemic effect of fungal polysaccharides, numerous studies have used fungal fiber to formulate functional foods. In addition to being satiating and nutritious, these products are an ideal complement to special diets such as diabetic and obesity diets. For example, in the study by Wang *et al.* (2021), wheat flour noodles were fortified with *P. ostreatus* and *A. bisporus* powders (cap, stem and whole mushrooms) [99]. It was found that the noodles fortified with edible mushroom stems significantly limited the amount of easily digestible carbohydrates in wheat flour. The number of simple sugars released was found to be indirectly proportional to the levels of insoluble fiber. This, as discussed above, may protect simple carbohydrates from the action of  $\alpha$ -amylases. In addition, it has been hypothesized that insoluble fiber has a higher antioxidant potential than soluble fibre because it contains a higher amount of phenolic acids. A similar study by Owheruo *et al.* (2023) used a mixture of wheat and *P. ostreatus* flours to develop low glycaemic index/load cookies [100]. *In vitro* tests showed that the cookie inhibited the  $\alpha$ -amylases and  $\alpha$ -glucosidases responsible for carbohydrate degradation, and it was demonstrated in a rat model that the higher the concentration of fungal flour in the diet, the lower the post-prandial blood glucose response. The results of these studies show that supplementation of mushroom flour from mushroom products could be a key ingredient in the formulation of satiating, low-calorie products suitable for people with diabetes or other metabolic disorders.

### 3.3. Risks of mushroom consumption

Despite the remarkable health benefits of consuming edible mushrooms, there are some aspects to consider before incorporating them widely into the diet. One of the risk factors is that mushrooms are excellent bioaccumulators of heavy metals such as Cu, Pb, Fe, Zn, Cd, Mn, Ni, Cr, Hg and Co [101,102]). Despite this, the health risk is minimal except through the consumption of mushrooms that have been grown on heavily contaminated substrates. Furthermore, a number of studies have discovered notable variations in the levels of heavy metals in fruit bodies' caps and stems, with the latter showing a lower concentration [103–105]. García *et al.* (2009) analyzed the lead content of different wild mushrooms cultivated in the province of Lugo (Spain) and

concluded that the concentrations obtained were similar to those of other food products, such as cereals, with a low risk to human health [106]. Despite this, in other regions, such as in Yunnan province (China), soil contamination is a serious problem resulting in wild mushrooms with concentrations above the safe limits of toxic metals such as As, Cd and Pb [107]. The intake of the same mushroom species that has been farmed with substrates coming from a part of the globe with high levels of hazardous chemicals can lead to major health problems, which should be taken into account in today's globalized world. Another potential problem with the consumption of edible mushrooms is the presence of some organic compounds harmful to human health. The presence of formaldehyde, a potential carcinogen, has been described at dangerous levels (119–494 µg/g wet weight) in samples of *L. edodes* [108]. A more recent study by Shao et al. (2024) analyzed the formaldehyde concentration of 2000 samples of different edible mushrooms cultivated in China, including *A. bisporus*, *P. ostreatus* and *L. edodes* [109]. The results showed that the latter mushroom presented the highest levels (0 mg/kg - 270 mg/kg), which is slightly lower than the maximum values allowed for export to Japan (300 mg/kg). To address this issue, numerous pretreatments have been reported that can reduce the concentration of formaldehyde in by-products, such as high-temperature pre-drying [110] or non-thermal treatments based on enzymatic inhibition [111]. In line with these hazards, it is necessary for the industry to optimize its protocols so that both the mushrooms marketed and the by-products are safe for human or animal consumption. Therefore, Pardo et al. (2013) carried out a Hazard analysis and critical control points (HACCP) where they found that the main risks were microbiological contamination of the raw material, the presence of heavy metals in the compost and the application of unauthorized insecticides during cultivation [112]. The actions that need to be considered are eliminating batches that have a larger microbial load than permitted; examining the compost's microbial composition and heavy metal content; and conducting analysis to ensure that no unauthorized compounds were employed during cultivation.

Once the product has reached the consumer, there are still some health risks to be considered, such as allergies and digestive problems. Mushroom allergies are rare, as well as the potential allergens. Despite this, there are documented cases such as a 36 kDa *A. bisporus* porin that caused vomiting, urticaria and abdominal pain in a female patient [113]. *In silico*, Singh et al. (2023) identified Putative heat shock hsp70 protein (A0A172B3E0), potentially allergenic, in *A. bisporus* [114]. In addition, cases of gastrointestinal problems due to the consumption of mushrooms or their extracts have been described. An example of this is the trial by Spierings et al. (2007) in which the effect of a shiitake extract was tested in humans [115]. Fifteen percent of the patients did not adequately tolerate the minimum doses of the treatment, presenting with adverse effects such as nausea and fatigue. Despite this, the consumption of fresh mushrooms and their by-products is generally harmless and efforts are being made by the scientific community to obtain safe and beneficial foods.

#### 4. Use of edible mushroom by-products in the food industry

The health benefits of consuming edible mushrooms, as well as their high production volume, make their by-products ideal candidates for application in the food industry. The use of shiitake peptides as a flavor enhancers, the use of fungal polysaccharides to improve texture and bacterial viability in dairy products and the use of extracts to improve the organoleptic properties of meat have been described.

##### 4.1. Flavor enhancers

Excessive salt consumption is a major global health concern, largely because of the consumers' strong preference a salty taste. This has led to its widespread use in meat products. However, research has revealed that the addition of umami flavors to low-sodium foods can effectively

enhance the perception of saltiness, thus providing a healthier alternative [116]. While monosodium glutamate (MSG) has traditionally been used as a popular umami enhancer, there is an increasing shift toward the use of natural compounds. Several fungal peptides such as Gly-Cys-Gly, Glu-Pro-Glu, Cys-Met, Val-Phe and Gly-Glu found in *L. edodes* have been identified as responsible for umami flavor [117]. Mushrooms have emerged as a valuable source of umami flavor enhancers, with applications in a wide range of products, including broths, meat products, and snacks (Table 5). Among the various mushroom species, shiitake stands out for its remarkable umami properties. For example, a study by Harada-Padermo et al. (2021) successfully replaced MSG in corn snacks with the by-product mushroom stipes, resulting in a significant improvement in flavor [118]. Similarly, in meat products, França et al. (2022) demonstrated the potential of mushroom stipes as a flavor enhancer in low-sodium hamburgers, with promising results [119].

##### 4.2. Fortification of dairy products with mushroom polysaccharides

Lactic acid bacteria such as *Lactobacillus* spp. and *Bifidobacterium* spp. are present in the healthy gut microbiota and are used in various fermented foods with probiotic effects. These include many dairy products such as yoghurts or kefir. As part of this review, the study by Chou et al. (2013) showed a correlation between the viability of probiotic bacteria in yoghurt and the addition of polysaccharides from edible mushroom by-products [89]. A concentration between 0.1% and 0.5% of polysaccharides from *L. edodes* stem, *P. eringii* base and *F. velutipes* base increased the survival of *L. acidophilus*, *L. casei* and *Bifidobacterium longum* during cold storage. This is because the polysaccharides act synergistically with the peptides and amino acids in yoghurt to maintain bacterial concentrations of 10<sup>7</sup> CFU/mL. These polysaccharides not only provide a greater probiotic effect, but also help to improve the organoleptic qualities of dairy products. For example, a recent study by Kondyli et al. (2022) analysed the effect of *P. ostreatus* β-glucans in the production of ovine spreadable cheese (Table 5). The results showed that cheese supplemented with polysaccharides had better moisture retention after 21 days of storage without affecting the taste of the product [122].

Among all the extracts used in dairy formulations, the most promising is the aqueous extract of *P. ostreatus* (Table 5). This extract has been extensively evaluated for yogurt formulation since it provides viscosity, increases the viability of probiotic bacteria, and provides phenolic compounds that increase antioxidant capacity. In a study conducted by Vital et al. (2015), the structure of different yogurts supplemented with various concentrations of *P. ostreatus* aqueous extract was analysed by scanning electron microscopy [126]. A reticular structure with large empty spaces was observed in the control yogurt, whereas a more compact structure was noted in the supplemented yogurts. The higher the extract concentration, the smaller the voids in the structure, which almost disappeared at concentrations of 0.75% and 1% extract. This resulted in a yogurt with better rheological properties and a less firm but more cohesive texture, as well as greater adhesiveness, elasticity and less syneresis. In the commercial context, consumer acceptance of the product is almost as important as the health benefits it may provide. Therefore, the study by Antontceva et al. (2019) complements these investigations by performing a sensory evaluation of different yogurts supplemented with increasing concentrations of ethanolic extract (low molecular weight compounds), aqueous (soluble β-glucans) and a precipitate of insoluble compounds (polysaccharides such as chitin or insoluble β-glucans) [127]. It was found that the ethanolic extract and the insoluble fraction had a negative effect on the colour of the sample, while the aqueous extract slightly changed to a light beige color. In terms of consistency, the yoghurt with the aqueous extract was more homogeneous than the yogurt supplemented with the insoluble polysaccharides. Finally, a sensory test was carried out with the following parameters: taste, aroma, color, consistency, and appearance. From all

**Table 5**  
Benefits described in food products based on mushrooms mentioned in this review.

Product	Mushroom	By-product	Benefits	Authors
3D printed vegan meat	<i>P. ostreatus</i> <i>L. deliciosus</i> <i>G. lucidum</i>	Caps	Meat replacer.	[120]
Cookies	<i>P. ostreatus</i>	Whole mushroom	Reduces postprandial glycemia.	[100]
Corn snacks	<i>L. edodes</i>	Stipes	Low-sodium flavor enhancer.	[118]
Goat meat nuggets	<i>F. velutipes</i>	Stem	Reduced lipid oxidation.	[29]
Hamburger	<i>L. edodes</i>	Stipes	Low-sodium flavor enhancer	[119]
Hamburger	<i>Pleurotus sapidus</i>	Base	Better appearance and color.	[121]
Noodles	<i>P. ostreatus</i> and <i>A. bisporus</i>	Cap, stems, and whole mushroom	Reduces postprandial glycemia.	[99]
Ovine spreadable cheese	<i>P. ostreatus</i>	Whole mushroom polysaccharides	Maintains moisture longer.	[122]
Pork meat sausage	<i>L. edodes</i>	Whole mushroom	Reduced meat content.	[123]
Pork meat sausage	<i>P. ostreatus</i>	Cap	Reduced lipid oxidation.	[124]
Vegan nuggets	<i>P. sajor-caju</i>	Stems	Meat replacer.	[125]
Yogurt	<i>F. velutipes</i> , <i>L. edodes</i> and <i>P. eringii</i>	Polysaccharides from stems and base	Increases the viability of probiotic bacteria.	[89]
Yogurt	<i>P. ostreatus</i>	Aqueous extract	Increases the viability of probiotic bacteria and improves their rheological properties.	[126]
Yogurt	<i>P. ostreatus</i>	Aqueous extract	Fortification with $\beta$ -glucans.	[127]

the yogurts supplemented, the one with the aqueous extract scored higher in all areas. These results show that the application of aqueous *P. ostreatus* extract to various functional foods would be able to improve their prebiotic properties without neglecting their palatability.

#### 4.3. Stabilizer in low-fat ice cream

Ice cream, as a complex and heterogeneous food product, presents distinctive characteristics throughout its production and storage process. Notably, the formation of large ice crystals can negatively affect the sensory properties of the ice cream, so it is crucial to control the free water crystallisation process. It is recommended that the size of ice crystals in ice cream should be between 20–50  $\mu\text{m}$ , with crystal formation of 10–20  $\mu\text{m}$  being an important requirement for achieving a creamy consistency [128].

Currently, there are several modern integrated ice cream stabilization systems that use emulsifiers and food stabilizers. For example, Cremodan® functional complex systems are well known and contain high melting fatty acid mono- and diglycerides (E471) together with hydrocolloids. However, consumers are showing an increasing preference for products made exclusively from natural ingredients and without food additives. In this context,  $\beta$ -glucan stands out as a natural stabilizer that can increase the viscosity of ice cream mixes, improve their melting strength, promote uniform distribution of the air phase, and influence the growth and distribution of ice crystals during product production and storage [128,129]. However, it is important to note that an excess of  $\beta$ -glucan can negatively affect ice cream texture and other physicochemical parameters [130].

Oat-derived  $\beta$ -glucans are increasingly being used in low-fat ice cream formulations [129]. These polysaccharides can mimic the fatty acids present in dairy products, making them particularly suitable for application in ice cream. In addition, due to their high molecular weight, both fungal  $\beta$ -glucans (2–3 g/mol [131]) and plant derivatives, exhibit a high thickening effect. Consumer demand for low-fat products has led to a continuous search for healthy and tasty alternatives. In this regard, edible mushroom by-products have emerged as a promising source for the formulation of low-fat foods and ice creams while providing a high fiber content.

#### 4.4. Meat products

Edible mushrooms are being investigated for their ability to improve the organoleptic properties of processed meat products and to develop new vegan foods that mimic them (Table 5). The fibrous texture of the stems and bases of edible mushrooms, their health benefits, and low cost

make them ideal for the production of hamburgers, sausages and nuggets, among other products. Regarding the use of mushrooms to supplement meat products, the study by Wan-Mohtar *et al.* (2020) supplemented chicken hamburgers with *P. sapidus* base [121]. The organoleptic qualities were analyzed, and the results showed that the burgers supplemented with 10% mushroom base had a better color and appearance than the control. However, in terms of taste, they could not surpass them, since the mushroom had a slightly bitter taste, as seen in the hamburgers fortified with 20% and 30% of *P. sapidus*.

One of the most interesting properties when using fungal by-products to formulate meat products is their capacity to reduce lipid oxidation. Banerjee *et al.* (2020) studied the effect of adding *F. velutipes* stem waste on the lipid oxidation of goat meat nuggets during 9 days of storage [29]. The results showed that this by-product increased the antioxidant potential due to the strong reducing power, scavenging activity and metal chelating ability of the extracts. Other authors have shown similar results in the formulation of different meat products. In the work of Wu *et al.* (2022), pork meat sausages were produced supplemented with *P. ostreatus* puree at concentrations ranging from 0 to 40% [124]. To analyze the differences in lipid peroxidation of the samples, thiobarbituric acid reactive substances (TBARS), a by-product of these reactions, were analyzed. It was found that the higher the concentration of *P. ostreatus* in the formulation, the lower the formation of TBARS, possibly due to the chemical composition of the mushroom (phenols,  $\alpha$ -tocopherol and flavonoids such as rutin and chrysin). Such a property is interesting because it could be used to reduce the concentration of nitrites in meat [132]. The best formulation was the one with 20% mushroom, although at this concentration the gel production of the pork myofibril protein was reduced, resulting in a lower cohesion of the sausage. In the study by Wang *et al.* (2019), similar results were obtained by supplementing pork sausages with *L. edodes* [123]. The best formulation was obtained when 25% of the pork lean meat was replaced with this mushroom. *L. edodes* increased moisture content, total dietary fiber, DPPH radical scavenging activity due to phenols, and the concentration of the amino acid methionine, glutamic acid, and cysteine. However, darker sausages with softer texture were produced. Therefore, further research will have to address the loss of organoleptic properties, such as consistency and flavor, so that the benefits of edible mushrooms can reach consumers through meat.

In recent years, the demand for vegan products that simulate meat has increased considerably. In response, researchers have taken advantage of the properties of edible mushrooms to formulate new products. These include the development of vegan nuggets from *P. sajor-caju* stems and chickpea flour [125] and 3D-printed vegan meat using *G. lucidum*, *Lactarius deliciosus*, and *P. ostreatus* [120]. In the latter promising study,

it was found that fungal fortification positively affected the maximum printed layer and that the gel-like consistency of the ink contributed to successful 3D printing. On the product side, *P. ostreatus* fortification reduced hardness, stiffness and chewiness and increased juiciness with good palatability. In addition, the fungi improved the nutritional value and contributed to the umami taste of the vegan meat. Although the texture of these foods still needs to be improved, using edible mushroom by-products to prepare vegan foods would reduce costs, provide nutrient-rich foods, and help implement a circular economy model.

## 5. Animal feed

Numerous benefits have been described when fungal by-products are added to animal feeds. In aquaculture, fungal polysaccharides help maintain a healthy microbiome and increase growth in shrimp. In terrestrial vertebrates such as broilers and pigs, they improve health and meat quality. Fungal by-products could be a cheap and abundant source to supplement the diets of species as diverse as sheep and shrimp [133].

### 5.1. Aquaculture

Mushroom powder has been used in numerous feed formulations due to its prebiotic potential (Table 6). Diets enriched with edible mushroom powder have been shown to promote growth in commercial species. Fungal polysaccharides, once ingested by the animal, stimulate its beneficial microbiota, and improve its intestinal health [133]. A sector that has benefited most from the potential of edible fungal by-products is aquaculture, both crustacean and fish farming. A study by Huynh et al. (2018) showed that the administration of polysaccharides as prebiotics to shrimp (*Litopenaeus vannamei*) farms promoted the growth of beneficial bacteria (*L. plantarum*) [134]. However, the isolation and purification of polysaccharides is a costly process. Therefore, the use of agricultural by-products as a prebiotics would be a more cost-effective source. Specifically, in the work of Prabawati et al. (2022), a combination of probiotics (*L. plantarum*) with prebiotics from king oyster mushroom by-products was administered to farmed shrimp [95]. The treated animals showed increased disease resistance compared to the control, and enhanced growth.

### 5.2. Livestock farming

The results for terrestrial vertebrates vary considerably with respect to aquaculture. While growth is usually not affected, meat quality parameters as well as animal health show positive variations (Table 6). In

**Table 6**  
Animal feed supplementation with edible mushrooms and their health benefits.

Animal	Mushroom	By-product	Benefits	Authors
Broiler	<i>F. velutipes</i>	Stems	Improved antioxidant status and lipid metabolism.	[135]
Dog	<i>L. edodes</i>	Whole mushroom	Food attractant; increased palatability.	[136]
Japanese quail	<i>P. ostreatus</i>	Dried whole mushroom	Reduced lipid oxidation in meat.	[137]
Lamb	<i>A. bisporus</i>	Stipe	Cheap and nutritious substrate for alfalfa supplementation.	[138]
Pig	<i>F. velutipes</i>	Stem	SCFA increase and promote of microbiome diversity.	[139]
Sheep	<i>A. bisporus</i>	Cap and stipe	Cheap and nutritious substrate for alfalfa supplementation.	[140]
Shrimp	<i>P. eryngii</i>	Hot-water extract of stem and volva	Increased growth performance and health status. Synergia with <i>L. plantarum</i> .	[95]

the study by Vargas-Sánchez et al. (2018), the effect of supplementing the diet of Japanese quail (*Coturnix japonica*) with *P. ostreatus* was investigated [137]. This bird is highly valued in Europe and Latin America for its meat and eggs. The problem with this species is that its fatty acids are very susceptible to oxidation, which causes discoloration of the meat, formation of toxic compounds and reduced its shelf life. To combat this situation, synthetic antioxidants are often used, some of which have recently been restricted due to their harmful effects on human health. In this study, it was found that supplementing quails with a diet rich in *P. ostreatus* did not increase their weight or feed intake, but it did improve meat quality. Supplementation with 10 or 20 g *P. ostreatus*/kg of feed was sufficient to delay lipid oxidation and maintain color and texture due to the antioxidant potential of the fungus. These results are consistent with those of other poultry species and other fungal by-products. Mahfuz et al. (2020) monitored the growth, meat quality and health status of broilers supplemented with *F. velutipes* stem residues [135]. The results showed that a 2% dietary supplement improved the antioxidant status and lipid metabolism in broilers. This antioxidant effect could be due to the fact that copper, zinc and selenium present in mushrooms could stimulate the synthesis of enzymes responsible for scavenging free radicals and degrading superoxide anions, such as SOD (enzyme complex with copper and zinc) [141].

Regarding mammals, several studies have evaluated the effect of supplementing different farm species with edible mushrooms (Table 6). In the study by Moradzadeh-Somarin et al. (2021), the effect of using button mushroom waste as feed for sheep along with alfalfa was studied [140]. The results showed that animals supplemented with up to 21% fungal waste had better digestibility of organic matter, as well as a higher abundance of short-chain fatty acids due to the higher fermentative activity of intestinal bacteria. These concentrations did not affect the production of purine derivatives or excreted nitrogen, although they had a negative effect on crude protein digestibility. As a follow-up, the study by Yousefi et al. (2022) evaluated the effect of the use of button mushroom by-products on lamb performance [138]. The results matched those of the earlier studies. Although there is little breakdown of the by-product in the rumen, it has been observed to be an excellent source of crude protein. The application of button mushrooms in amounts of 20% together with alfalfa could be a good way to provide an outlet for this by-product and increase meat production in countries with fewer resources. Supplementation had no adverse effect on nutrient assimilation and even reduced rumen ammonium concentration. The use of edible fungi in animal feed is being widely studied in other mammals such as pigs [139], promoting a diverse microbiome. Moreover, they have even been used as attractants in dog feed as a substitute for chicken liver [136]. Much more research is required to bring the benefits of mushrooms to domestic animals, which could be a good field of study in the future.

## 6. Conclusions

World mushroom production is expected to grow strongly in the coming years due to high demand. This crop generates a large amount of waste, such as stems, bases and mushrooms that are not suitable for commercialization. These by-products have the potential to be used in the food industry. The high fiber content of mushroom by-products, their micronutrient content, their antioxidant content, and their low caloric value make them ideal candidates to become a widely used ingredient. It is relevant to highlight the use of aqueous extracts with high levels of  $\beta$ -glucans as functional components capable of providing foods with prebiotic polysaccharides and improved texture. Likewise, the inclusion of insoluble polysaccharides can promote a more gradual absorption of sugars, counteracting the effects of increasingly high-calorie diets. Numerous studies support these benefits *in vitro*, although *in vivo* evidence is less abundant. Nevertheless, many authors have developed various functional foods, from yogurts to cookies, with great potential to improve human health. Incorporating these by-

products into feed formulations can enable mushroom producers to fully optimize crop use and pave the way toward establishing a zero-waste paradigm within the industry.

### Funding sources

This work was supported by grant 230025CONV from the Junta de Comunidades de Castilla-La Mancha (co-financed European Union FEDER funds).

### Ethics statement

Not applicable.

### CRedit authorship contribution statement

**Oussama Ahrazem:** Writing – review & editing, Validation, Funding acquisition, Conceptualization. **Lourdes Gómez-Gómez:** Writing – review & editing, Supervision, Conceptualization. **Ángela Rubio-Moraga:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Pablo Navarro-Simarro:** Writing – original draft, Conceptualization.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability

No data was used for the research described in the article.

### References

- [1] Atallah E, Zeaiter J, Ahmad MN, Leahy JJ, Kwapinski W. Hydrothermal carbonization of spent mushroom compost waste compared against torrefaction and pyrolysis. *Fuel Process Technol* 2021;216. <https://doi.org/10.1016/j.fuproc.2021.106795>.
- [2] Ahmed M, Abdullah N, Ahmed K, Bhuyan MHMB. Yield and nutritional composition of oyster mushroom strains newly introduced in Bangladesh. *Pesqui Agropecu Bras* 2013;48:197–202. <https://doi.org/10.1590/s0100-204x2013000200010>.
- [3] Oyetayo FL, Akindahuns AA, Oyetayo VO. Chemical profile and amino acids composition of edible mushrooms *Pleurotus sajor-caju*. *Nutr Health* 2007;18:383–9. <https://doi.org/10.1177/026010600701800407>.
- [4] Lam K, Keung H, Ko K, Kwan H, Cheung PC. *In vitro* fermentation of beta-glucans and other selected carbohydrates by infant fecal inoculum: An evaluation of their potential as prebiotics in infant formula. *Bioact Carbohydr Diet Fibre* 2018;14:20–4. <https://doi.org/10.1016/j.bcdf.2017.07.009>.
- [5] Nowak R, Nowacka-Jechalke N, Juda M, Malm A. The preliminary study of prebiotic potential of Polish wild mushroom polysaccharides: the stimulation effect on *Lactobacillus* strains growth. *Eur J Nutr* 2017;57:1511–21. <https://doi.org/10.1007/s00394-017-1436-9>.
- [6] Temple MJ, Cuskin F, Basle A, Hickey N, Speciale G, Williams SJ, et al. A Bacteroidetes locus dedicated to fungal 1,6-β-glucan degradation: Unique substrate conformation drives specificity of the key endo-1,6-β-glucanase. *J Biol Chem* 2017;292:10639–50. <https://doi.org/10.1074/jbc.M117.787606>.
- [7] Falandyz J. Selenium in edible mushrooms. *J Env Sci Health* 2008;26:256–99. <https://doi.org/10.1080/10590500802350086>.
- [8] Yahia EM, Gutierrez-Orozco F, Moreno-Perez MA. Identification of phenolic compounds by liquid chromatography-mass spectrometry in seventeen species of wild mushrooms in Central Mexico and determination of their antioxidant activity and bioactive compounds. *Food Chem* 2017;226:14–22. <https://doi.org/10.1016/j.foodchem.2017.01.044>.
- [9] Taofiq O, Heleno SA, Calhela RC, Alves MJ, Barros L, Barreiro MF, et al. Development of mushroom-based cosmeceutical formulations with anti-inflammatory, anti-tyrosinase, antioxidant, and antibacterial properties. *Molecules* 2016;21:1372. <https://doi.org/10.3390/molecules21101372>.
- [10] Ahn H, Jeon E, Kim JC, Kang SG, Yoon SI, Ko HJ, et al. Lentinan from shiitake selectively attenuates AIM2 and non-canonical inflammasome activation while inducing pro-inflammatory cytokine production. *Sci Rep* 2017;7:1314. <https://doi.org/10.1038/s41598-017-01462-4>.
- [11] Morales D, Rutckevskis R, Villalva M, Abreu H, Soler-Rivas C, Santoyo S, et al. Isolation and comparison of alpha- and β-D-glucans from shiitake mushrooms (*Lentinula edodes*) with different biological activities. *Carbohydr Polym* 2020;229. <https://doi.org/10.1016/j.carbpol.2019.115521>.
- [12] Kozarski M, Klaus A, Niksic M, Jakovljevic D, Helsen J, Van Griensven L, et al. Antioxidative and immunomodulating activities of polysaccharide extracts of the medicinal mushrooms *Agaricus bisporus*, *Agaricus brasiliensis*, *Ganoderma lucidum* and *Phellinus linteus*. *Food Chem* 2011;129:1667–75. <https://doi.org/10.1016/j.foodchem.2011.06.029>.
- [13] Doğan HH, Akbas G. Biological activity and fatty acid composition of Caesar's mushroom. *Pharm Biol* 2013;51:863–71. <https://doi.org/10.3109/13880209.2013.768272>.
- [14] Morales D, Tabernero M, Largo C, Polo G, Piris AJ, Soler-Rivas C. Effect of traditional and modern culinary processing, bioaccessibility, biosafety and bioavailability of eritadenine, a hypocholesterolemic compound from edible mushrooms. *Food Funct* 2018;9:6360–8. <https://doi.org/10.1039/c8fo01704b>.
- [15] Rathore H, Prasad S, Sharma S. Mushroom nutraceuticals for improved nutrition and better human health: a review. *PharmaNutrition* 2017;5:35–46. <https://doi.org/10.1016/j.phanu.2017.02.001>.
- [16] Dimopoulou M, Kolonas A, Mourtakos S, Androutsos O, Gortzi O. Nutritional Composition and Biological Properties of Sixteen Edible Mushroom Species. *Appl Sci* 2022;12:8074. <https://doi.org/10.3390/app12168074>.
- [17] Lesa KN, Khandaker MU, Iqbal FMR, Sharma R, Islam F, Mitra S, et al. Nutritional value, medicinal importance, and health-promoting effects of dietary mushroom (*Pleurotus ostreatus*). *J Food Qual* 2022;2022. <https://doi.org/10.1155/2022/2454180>.
- [18] Santos-Neves JC, Pereira MI, Carbonero ER, Gracher AHP, Alquini G, Gorin PAJ, et al. A novel branched α-D-glucan isolated from the basidiocarps of the edible mushroom *Pleurotus florida*. *Carbohydr Polym* 2008;73:309–14. <https://doi.org/10.1016/j.carbpol.2007.11.030>.
- [19] Zavadinack M, de Lima Bellan D, da Rocha Bertage JL, da Silva Milhorini S, da Silva Trindade E, Simas FF, et al. An α-D-galactan and a β-D-glucan from the mushroom *Amanita muscaria*: Structural characterization and antitumor activity against melanoma. *Carbohydr Polym* 2021;274:118647. <https://doi.org/10.1016/j.carbpol.2021.118647>.
- [20] Abreu H, Simas FF, Smiderle FR, Sovrani V, Dallazen JL, Maria-Ferreira D, et al. Gelling functional property, anti-inflammatory and antinociceptive bioactivities of β-D-glucan from the edible mushroom *Pholiota nameko*. *Int J Biol Macromol* 2019;122:1128–35. <https://doi.org/10.1016/j.ijbiomac.2018.09.062>.
- [21] Wu T, Zivanovic S, Draughon FA, Sams CE. Chitin and chitosan - value-added products from mushroom waste. *J Agric Food Chem* 2004;52:7905–10. <https://doi.org/10.1021/jf0492565>.
- [22] Aguiló-Aguayo I, Walton J, Viñas I, Tiwari BK. Ultrasound assisted extraction of polysaccharides from mushroom by-products. *LWT* 2017;77:92–9. <https://doi.org/10.1016/j.lwt.2016.11.043>.
- [23] Akram K, Shahbaz HM, Kim GR, Farooq U, Kwon JH. Improved extraction and quality characterization of water-soluble polysaccharide from gamma-irradiated *Lentinus edodes*. *J Food Sci* 2017;82:296–303. <https://doi.org/10.1111/1750-3841.13590>.
- [24] Chen J, Lai P, Shen H, Zhen H, Fang R. Effect of extraction methods on polysaccharide of *Clitocybe maxima* Stipe. *Adv J Food Sci Technol* 2013;5:370–3. <https://doi.org/10.19026/ajfst.5.3273>.
- [25] Zhang J, Wen C, Gu J, Ji C, Duan Y, Zhang H. Effects of subcritical water extraction microenvironment on the structure and biological activities of polysaccharides from *Lentinus edodes*. *Int J Biol Macromol* 2019;123:1002–11. <https://doi.org/10.1016/j.ijbiomac.2018.11.194>.
- [26] Palacios I, Lozano M, Moro C, D'arrigo M, Rostagno MA, Martínez JA, et al. Antioxidant properties of phenolic compounds occurring in edible mushrooms. *Food Chem* 2011;128:674–8. <https://doi.org/10.1016/j.foodchem.2011.03.085>.
- [27] Çayan F, Deveci E, Tel-Çayan G, Duru ME. Identification and quantification of phenolic acid compounds of twenty-six mushrooms by HPLC-DAD. *J Food Meas Charact* 2020;14:1690–8. <https://doi.org/10.1007/s11694-020-00417-0>.
- [28] Nowacka N, Nowak R, Drozd M, Olech M, Los R, Malm A. Antibacterial, antiradical potential and phenolic compounds of thirty-one polish mushrooms. *PLOS ONE* 2015;10:e0140355. <https://doi.org/10.1371/journal.pone.0140355>.
- [29] Banerjee DK, Das AK, Banerjee R, Pateiro M, Nanda PK, Gadekar YP, et al. Application of Enoki Mushroom (*Flammulina Velutipes*) Stem Wastes as Functional Ingredients in Goat Meat Nuggets. *Foods* 2020;9. <https://doi.org/10.3390/foods9040432>.
- [30] Ojeaburu SI, Oriakhi K. Hepatoprotective, antioxidant and, anti-inflammatory potentials of gallic acid in carbon tetrachloride-induced hepatic damage in Wistar rats. *Toxicol Rep* 2021;8:177–85. <https://doi.org/10.1016/j.toxrep.2021.01.001>.
- [31] Naveed M, Hejazi V, Abbas M, Kamboh AA, Khan GJ, Shumzaid M, et al. Chlorogenic acid (CGA): a pharmacological review and call for further research. *Biomed Pharm* 2018;97:67–74. <https://doi.org/10.1016/j.biopha.2017.10.064>.
- [32] Huang XY, Shan ZJ, Zhai HL, Su L, Zhang XY. Study on the anticancer activity of coumarin derivatives by molecular modeling. *Chem Biol Drug Des* 2011;78:651–8. <https://doi.org/10.1111/j.1747-0285.2011.01195.x>.
- [33] Zhao L, Mehmood A, Soliman MM, Iftikhar A, Iftikhar M, Aboelenin SM, et al. Protective effects of ellagic acid against alcoholic liver disease in Mice. *Front Nutr* 2021;8:744520. <https://doi.org/10.3389/fnut.2021.744520>.
- [34] Jiang X, Zuo S, Ye L, Hong W. Nano-fumed silica as a novel pollutant that inhibits the algicidal effect of p-hydroxybenzoic acid on *Microcystis aeruginosa*. *Env Technol* 2017;40:693–700. <https://doi.org/10.1080/09593330.2017.1404135>.
- [35] Zhang J, Cui X, Zhang M, Bai B, Yang Y, Fan S. The antibacterial mechanism of perilla rosmarinic acid. *Biotechnol Appl Biochem* 2021;69:1757–64. <https://doi.org/10.1002/bab.2248>.

- [36] Hu Y, Zhou Y, Liu J, Wang Q, Lin J, Shi Y. Effect of 4-methoxycinnamic acid on the postharvest browning of mushrooms (*Agaricus bisporus*). *J Food Process Preserv* 2020;44. <https://doi.org/10.1111/jfpp.14735>.
- [37] Sharma N, Biswas S, Al-Dayani N, Alhegaili AS, Sarwat M. Antioxidant Role of Kaempferol in Prevention of Hepatocellular Carcinoma. *Antioxidants* 2021;10. <https://doi.org/10.3390/antiox10091419>.
- [38] Gonzalez-Arceo M, Gomez-Lopez I, Carr-Ugarte H, Eseberri I, Gonzalez M, Cano MP, et al. Anti-obesity effects of isorhamnetin and Isorhamnetin Conjugates. *Int J Mol Sci* 2022;24. <https://doi.org/10.3390/ijms24010299>.
- [39] Nithya R, Subramanian S. Antioxidant properties of sinapic acid: in vitro and in vivo approach. *Asian J Pharm Clin Res* 2017;10. <https://doi.org/10.22159/ajpcr.2017.v10i6.18263>.
- [40] Joshi R, Gangabagirathi R, Venu S, Adhikari S, Mukherjee T. Antioxidant activity and free radical scavenging reactions of gentisic acid: in-vitro and pulse radiolysis studies. *Free Radic Res* 2011;46:11–20. <https://doi.org/10.3109/10715762.2011.633518>.
- [41] Medina ME, Galano A, Trigos Á. Scavenging ability of homogentisic acid and ergosterol toward free radicals derived from ethanol consumption. *J Phys Chem B* 2018;122:7514–21. <https://doi.org/10.1021/acs.jpcc.8b04619>.
- [42] Lima VN, Oliveira-Tintino CDM, Santos ES, Morais LP, Tintino SR, Freitas TS, et al. Antimicrobial and enhancement of the antibiotic activity by phenolic compounds: Gallic acid, caffeic acid and pyrogallol. *Micro Pathog* 2016;99: 56–61. <https://doi.org/10.1016/j.micpath.2016.08.004>.
- [43] Song X, Tan L, Wang M, Ren C, Guo C, Yang B, et al. Myricetin: A review of the most recent research. *Biomed Pharm* 2021;134. <https://doi.org/10.1016/j.biopha.2020.111017>.
- [44] Gotvaldova K, Borovicka J, Hajkova K, Cihlarova P, Rockefeller A, Kuchar M. Extensive collection of psychotropic mushrooms with determination of their tryptamine alkaloids. *Int J Mol Sci* 2022;23. <https://doi.org/10.3390/ijms232214068>.
- [45] 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. <https://doi.org/10.1016/j.procbio.2022.06.021>.
- [46] Zhao ZZ, Zhang F, Ji BY, Zhou N, Chen H, Sun YJ, et al. Pyrrole alkaloids from the fruiting bodies of edible mushroom *Lentinula edodes*. *RSC Adv* 2023;13:18223–8. <https://doi.org/10.1039/d3ra02672h>.
- [47] Sugiyama K, Akachi T, Yamakawa A. Hypocholesterolemic action of eritadenine is mediated by a modification of hepatic phospholipid metabolism in rats. *J Nutr* 1995;125:2134–44. <https://doi.org/10.1093/jn/125.8.2134>.
- [48] Gutierrez-Rodelo C, Ochoa-Lopez A, Luis Balderas-Lopez J, Reyes-Ramirez A, Millan-Pacheco C, Favela-Rosales F, et al. Eritadenine as a regulator of anxiety disorders: an experimental and docking Approach. *Neurosci Lett* 2023;813: 137413. <https://doi.org/10.1016/j.neulet.2023.137413>.
- [49] Sánchez-Minutti L, López-Valdez F, Rosales-Pérez M, Luna-Suárez S. Effect of heat treatments of *Lentinula edodes* mushroom on eritadenine concentration. *LWT* 2019;102:364–71. <https://doi.org/10.1016/j.lwt.2018.12.054>.
- [50] Kim J-A, Lau E, Tay D, De Blanco EJC. Antioxidant and NF- $\kappa$ B inhibitory constituents isolated from *Morchella esculenta*. *Nat Prod Res* 2011;25:1412–7. <https://doi.org/10.1080/14786410802425746>.
- [51] Kim JA, Tay D, de Blanco EC. NF-kappaB inhibitory activity of compounds isolated from *Cantharellus cibarius*. *Phytother Res PTR* 2008;22:1104–6. <https://doi.org/10.1002/ptr.2467>.
- [52] Das M, Gurusiddaiah SK. Ergosterol fraction from *Agaricus bisporus* modulates adipogenesis and skeletal glucose uptake in high fat diet induced obese C57BL/6 mice. *Life Sci* 2023;315:121337. <https://doi.org/10.1016/j.lfs.2022.121337>.
- [53] Kikuchi T, Motoyashiki N, Yamada T, Shibatani K, Ninomiya K, Morikawa T, et al. Ergostane-Type Sterols from King Trumpet Mushroom (*Pleurotus eryngii*) and Their Inhibitory Effects on Aromatase. *Int J Mol Sci* 2017;18:2479. <https://doi.org/10.3390/ijms18112479>.
- [54] Development of a Novel Methodology for the Analysis of Ergosterol in Mushrooms. *Food Anal Methods* 2014;7:217–223. <https://doi.org/10.1007/s12161-013-9621-9>.
- [55] Kim J-A, Lau E, Tay D, De Blanco EJC. Antioxidant and NF- $\kappa$ B inhibitory constituents isolated from *Morchella esculenta*. *Nat Prod Res* 2011;25:1412–7. <https://doi.org/10.1080/14786410802425746>.
- [56] Yi C, Sun C, Tong S, Cao X, Feng Y, Firempong CK, et al. Cytotoxic effect of novel *Flammulina velutipes* sterols and its oral bioavailability via mixed micellar nanoformulation. *Int J Pharm* 2013;448:44–50. <https://doi.org/10.1016/j.ijpharm.2013.03.020>.
- [57] Kalogeropoulos N, Yanni AE, Koutrotsios G, Aloupi M. Bioactive microconstituents and antioxidant properties of wild edible mushrooms from the island of Lesbos, Greece. *Food Chem Toxicol Int J Publ Br Ind Biol Res Assoc* 2013;55:378–85. <https://doi.org/10.1016/j.fct.2013.01.010>.
- [58] Guan W, Zhang J, Yan R, Shao S, Zhou T, Lei J, et al. Effects of UV-C treatment and cold storage on ergosterol and vitamin D2 contents in different parts of white and brown mushroom (*Agaricus bisporus*). *Food Chem* 2016;210:129–34. <https://doi.org/10.1016/j.foodchem.2016.04.023>.
- [59] Gao J-M, Wang M, Liu L-P, Wei G-H, Zhang A-L, Draghici C, et al. Ergosterol peroxides as phospholipase A(2) inhibitors from the fungus *Lactarius hatsudake*. *Phytomedicine Int J Phytother Phytopharm* 2007;14:821–4. <https://doi.org/10.1016/j.phymed.2006.12.006>.
- [60] Rivero A, Benavides OL, Rios-Motta J. (22E)-Ergosta-6,22-diene-3beta,5alpha,8alpha-triol: a new polyhydroxysterol isolated from *Lentinus edodes* (Shiitake). *Nat Prod Res* 2009;23:293–300. <https://doi.org/10.1080/14786410802038671>.
- [61] Krzyczkowski W, Malinowska E, Suchocki P, Kleps J, Olejnik M, Herold F. Isolation and quantitative determination of ergosterol peroxide in various edible mushroom species. *Food Chem* 2009;113:351–5. <https://doi.org/10.1016/j.foodchem.2008.06.075>.
- [62] Meza-Menchaca T, Suárez-Medellín J, Del Ángel-Piña C, Trigos Á. The amoebicidal effect of ergosterol peroxide isolated from *Pleurotus ostreatus*. *Phytother Res PTR* 2015;29:1982–6. <https://doi.org/10.1002/ptr.5474>.
- [63] Meza-Menchaca T, Ramos-Ligonio A, López-Monteón A, Vidal Limón A, Kaluzhskiy LA, V Shkel T, et al. Insights into Ergosterol Peroxide's Trypanocidal Activity. *Biomolecules* 2019;9:484. <https://doi.org/10.3390/biom9090484>.
- [64] Merdivan S, Lindequist U. Ergosterol peroxide: a mushroom-derived compound with promising biological activities-a review. *Int J Med Mushrooms* 2017;19: 93–105. <https://doi.org/10.1615/IntJMedMushrooms.v19.i2.10>.
- [65] Kikuchi T, Isobe M, Uno S, In Y, Zhang J, Yamada T. Strophasterols E and F: Rearranged ergostane-type sterols from *Pleurotus eryngii*. *Bioorg Chem* 2019;89: 103011. <https://doi.org/10.1016/j.bioorg.2019.103011>.
- [66] Kora AJ. Nutritional and antioxidant significance of selenium-enriched mushrooms. *Bull Natl Res Cent* 2020;44. <https://doi.org/10.1186/s42269-020-00289-w>.
- [67] Wrobel JK, Power R, Toborek M. Biological activity of selenium: revisited. *IUBMB Life* 2016;68:97–105. <https://doi.org/10.1002/iub.1466>.
- [68] Vetter J, Lelley J. Selenium level of the cultivated mushroom *Agaricus bisporus*. *Acta Aliment* 2005;33:297–301. <https://doi.org/10.1556/aalim.33.2004.3.10>.
- [69] Peng S, Yan J, Li M, Yan Z, Wei H, Xu D, et al. Preparation of polysaccharide-conjugated selenium nanoparticles from spent mushroom substrates and their growth-promoting effect on rice seedlings. *Int J Biol Macromol* 2023;253:126789. <https://doi.org/10.1016/j.ijbiomac.2023.126789>.
- [70] Kanchi S, Inamuddin, Khan A. Biogenic synthesis of selenium nanoparticles with edible mushroom extract: evaluation of cytotoxicity on prostate cancer cell lines and their antioxidant, and antibacterial activity. *Biointerphase Res Appl Chem* 2020;10:6629–39. <https://doi.org/10.33263/BRIAC106.66296639>.
- [71] Sotek Z, Stasińska M, Malinowski R, Pilarczyk B, Pilarczyk R, Bąkowska M, et al. The role in the human diet of bioaccumulation of selenium, copper, zinc, manganese and iron in edible mushrooms in various habitat conditions of NW Poland—a case study. *Sustainability* 2023;15:13334. <https://doi.org/10.3390/su151813334>.
- [72] Golian M, Hegedúsová A, Mezeyová I, Chlebová Z, Hegedús O, Urmínská D, et al. Accumulation of selected metal elements in fruiting bodies of oyster mushroom. *Foods* 2022;11:76. <https://doi.org/10.3390/foods11010076>.
- [73] Siwulski M, Niedzielski P, Budka A, Budzyńska S, Kuczyńska-Kippen N, Kalač P, et al. Patterns of changes in the mineral composition of *Agaricus bisporus* cultivated in Poland between 1977 and 2020. *J Food Compos Anal* 2022;112: 104660. <https://doi.org/10.1016/j.jfca.2022.104660>.
- [74] Koyyalamudi SR, Jeong S-C, Manavalan S, Vysetti B, Pang G. Micronutrient mineral content of the fruiting bodies of Australian cultivated *Agaricus bisporus* white button mushrooms. *J Food Compos Anal* 2013;31:109–14. <https://doi.org/10.1016/j.jfca.2013.03.007>.
- [75] Karakan T, Tuohy KM, Janssen-van Solingen G. Low-Dose Lactulose as a Prebiotic for Improved Gut Health and Enhanced Mineral Absorption. *Front Nutr* 2021;8.
- [76] Bindels LB, Delzenne NM, Cani PD, Walter J. Towards a more comprehensive concept for prebiotics. *Nat Rev Gastroenterol Hepatol* 2015;12:303–10. <https://doi.org/10.1038/nrgastro.2015.47>.
- [77] Delzenne NM, Neyrinck AM, Cani PD. Gut microbiota and metabolic disorders: How prebiotic can work? *Br J Nutr* 2013;109:81–5. <https://doi.org/10.1017/S0007114512004047>.
- [78] Haghshenas B, Nami Y, Abdullah N, Radiah D, Rosli R, Khosroushahi AY. Anticancer impacts of potentially probiotic acetic acid bacteria isolated from traditional dairy microbiota. *LWT* 2015;60:690–7.
- [79] Wang L, Cen S, Wang G, Lee Y, Zhao J, Zhang H, et al. Acetic acid and butyric acid released in large intestine play different roles in the alleviation of constipation. *J Funct Foods* 2020;69. <https://doi.org/10.1016/j.jff.2020.103953>.
- [80] Ma J, Liu Z, Gao X, Bao Y, Hong Y, He X, et al. Gut microbiota remodeling improves natural aging-related disorders through *Akkermansia muciniphila* and its derived acetic acid. *Pharm Res* 2023;189. <https://doi.org/10.1016/j.phrs.2023.106687>.
- [81] Duscha G, Gisevius B, Hirschberg S, Yissachar N, Stangl GI, Dawin E, et al. Propionic acid shapes the multiple sclerosis disease course by an immunomodulatory mechanism. *e16 Cell* 2020;180:1067–80. <https://doi.org/10.1016/j.cell.2020.02.035>.
- [82] Frye RE, Rose S, Chacko J, Wynne R, Bennuri SC, Slattery JC, et al. Modulation of mitochondrial function by the microbiome metabolite propionic acid in autism and control cell lines. *Transl Psychiatry* 2016;6:e927. <https://doi.org/10.1038/tp.2016.189>.
- [83] Heimann E, Nyman M, Degerman E. Propionic acid and butyric acid inhibit lipolysis and de novo lipogenesis and increase insulin-stimulated glucose uptake in primary rat adipocytes. *Adipocyte* 2015;4:81–8. <https://doi.org/10.4161/21623945.2014.960694>.
- [84] Gio-Batta M, Sjöberg F, Jonsson K, Barman M, Lundell AC, Adlerberth I, et al. Fecal short chain fatty acids in children living on farms and a link between valeric acid and protection from eczema. *Sci Rep* 2020;10:22449. <https://doi.org/10.1038/s41598-020-79737-6>.
- [85] Heimann E, Nyman M, Palbrink AK, Lindkvist-Petersson K, Degerman E. Branched short-chain fatty acids modulate glucose and lipid metabolism in primary adipocytes. *Adipocyte* 2016;5:359–68. <https://doi.org/10.1080/21623945.2016.1252011>.

- [86] Szczesniak O, Hestad KA, Hanssen JF, Rudi K. Isovaleric acid in stool correlates with human depression. *Nutr Neurosci* 2016;19:279–83. <https://doi.org/10.1179/1476830515Y.0000000007>.
- [87] Wang X, Hu Y, Zhu X, Cai L, Farooq MZ, Yan X. Bacteroides-derived isovaleric acid enhances mucosal immunity by facilitating intestinal IgA response in broilers. *J Anim Sci Biotechnol* 2023;14:4. <https://doi.org/10.1186/s40104-022-00807-y>.
- [88] Cho KM, Kim YS, Lee M, Lee HY, Bae YS. Isovaleric acid ameliorates ovariectomy-induced osteoporosis by inhibiting osteoclast differentiation. *J Cell Mol Med* 2021;25:4287–97. <https://doi.org/10.1111/jcmm.16482>.
- [89] Chou WT, Sheih IC, Fang TJ. The applications of polysaccharides from various mushroom wastes as prebiotics in different systems. *M1041-8 J Food Sci* 2013;78. <https://doi.org/10.1111/1750-3841.12160>.
- [90] Sawangwan T, Wansanit W, Pattani L, Noysang C. Study of prebiotic properties from edible mushroom extraction. *Agric Nat Resour* 2018;52:519–24. <https://doi.org/10.1016/j.anres.2018.11.020>.
- [91] Wardman JF, Bains RK, Rahfeld P, Withers SG. Carbohydrate-active enzymes (CAZymes) in the gut microbiome. *Nat Rev Microbiol* 2022;20:542–56. <https://doi.org/10.1038/s41579-022-00712-1>.
- [92] Oliphant K, Allen-Vercos E. Macronutrient metabolism by the human gut microbiome: major fermentation by-products and their impact on host health. *Microbiome* 2019;7:91. <https://doi.org/10.1186/s40168-019-0704-8>.
- [93] Synytsya A, Mícková K, Synytsya A, Jablonský I, Spěváček J, Erban V, et al. Glucans from fruit bodies of cultivated mushrooms *Pleurotus ostreatus* and *Pleurotus eryngii*: Structure and potential prebiotic activity. *Carbohydr Polym* 2009;76:548–56. <https://doi.org/10.1016/j.carbpol.2008.11.021>.
- [94] Kerezoudi EN, Mitsou EK, Gioti K, Terzi E, Avgousti I, Panagiotou A, et al. Fermentation of *Pleurotus ostreatus* and *Ganoderma lucidum* mushrooms and their extracts by the gut microbiota of healthy and osteopenic women: potential prebiotic effect and impact of mushroom fermentation products on human osteoblasts. *Food Funct* 2021;12:1529–46. <https://doi.org/10.1039/d0fo02581j>.
- [95] Prabawati E, Hu S, Chiu S, Balantyne R, Risjani Y, Liu C. A synbiotic containing prebiotic prepared from a by-product of king oyster mushroom, *Pleurotus eryngii* and probiotic, *Lactobacillus plantarum* incorporated in diet to improve the growth performance and health status of white shrimp, *Litopenaeus vannamei*. *Fish Shellfish Immunol* 2022;120:155–65. <https://doi.org/10.1016/j.fsi.2021.11.031>.
- [96] Hashemi Yusefabad H, Hosseini SA, Zakerkish M, Cheraghian B, Alipour M. The effects of hot air-dried white button mushroom powder on glycemic indices, lipid profile, inflammatory biomarkers and total antioxidant capacity in patients with type-2 diabetes mellitus: A randomized controlled trial. *J Res Med Sci* 2022;27:49. <https://doi.org/10.4103/jrms.JRMS.513.20>.
- [97] Aramabasic Jovanovic J, Mihailovic M, Uskokovic A, Grdovic N, Dinic S, Vidakovic M. The Effects of Major Mushroom Bioactive Compounds on Mechanisms That Control Blood Glucose Level. *J Fungi* 2021;7. <https://doi.org/10.3390/jof7010058>.
- [98] Hu JL, Nie SP, Xie MY. Antidiabetic Mechanism of Dietary Polysaccharides Based on Their Gastrointestinal Functions. *J Agric Food Chem* 2018;66:4781–6. <https://doi.org/10.1021/acs.jafc.7b05410>.
- [99] Wang L, Brennan MA, Guan W, Liu J, Zhao H, Brennan CS. Edible mushrooms dietary fibre and antioxidants: Effects on glycaemic load manipulation and their correlations pre-and post-simulated *in vitro* digestion. *Food Chem* 2021;351. <https://doi.org/10.1016/j.foodchem.2021.129320>.
- [100] Owheruo JO, Edo GI, Oluwajuyitan DT, Faturoti AO, Martins IE, Akpogheli PO, et al. Quality evaluation of value-added nutritious biscuit with high antidiabetic properties from blends of wheat flour and oyster mushroom. *Food Chem Adv* 2023;3. <https://doi.org/10.1016/j.focha.2023.100375>.
- [101] Isildak O, Turkekel I, Elmastas M, Aboul-Enein HY. Bioaccumulation of Heavy Metals in Some Wild-Grown Edible Mushrooms. *Anal Lett* 2007;40:1099–116. <https://doi.org/10.1080/00032710701297042>.
- [102] Ostos C, Pérez-Rodríguez F, Moreno Arroyo B, Moreno-Rojas R. Study of mercury content in wild edible mushrooms and its contribution to the Provisional Tolerable Weekly Intake in Spain. *J Food Compos Anal* 2015;37:136–42. <https://doi.org/10.1016/j.jfca.2014.04.014>.
- [103] Saba M, Falandysz J, Nnorom IC. Accumulation and distribution of mercury in fruiting bodies by fungus *Stullius luteus* foraged in Poland, Belarus and Sweden. *Env Sci Pollut Res* 2015;23:2749–57. <https://doi.org/10.1007/s11356-015-5513-4>.
- [104] Szymańska K, Strumińska-Parulska D. Atmospheric fallout impact on (210)Po and (210)Pb content in wild growing mushrooms. *Env Sci Pollut Res* 2020;27:20800–6. <https://doi.org/10.1007/s11356-020-08559-w>.
- [105] Šnirc M, Jančo I, Hauptvogel M, Jakabová S, Demková L, Árvay J. Risk assessment of the wild edible leccinum mushrooms consumption according to the total mercury content. *J Fungi* 2023;9. <https://doi.org/10.3390/jof9030287>.
- [106] Garcia MA, Alonso J, Melgar MJ. Lead in edible mushrooms: levels and bioaccumulation factors. *J Hazard Mater* 2009;167:777–83. <https://doi.org/10.1016/j.jhazmat.2009.01.058>.
- [107] Liu B, Huang Q, Cai H, Guo X, Wang T, Gui M. Study of heavy metal concentrations in wild edible mushrooms in Yunnan Province, China. *Food Chem* 2015;188:294–300. <https://doi.org/10.1016/j.foodchem.2015.05.010>.
- [108] Liu JF, Peng JF, Chi YG, Jiang BG. Determination of formaldehyde in shiitake mushroom by ionic liquid-based liquid-phase microextraction coupled with liquid chromatography. *Talanta* 2005;65:705–9. <https://doi.org/10.1016/j.talanta.2004.07.037>.
- [109] Shao Y, Liu H, Huang L, Zhao X, Zhao Z, Yang X, et al. Formaldehyde levels and formaldehyde-exposure-related health risk levels of edible mushrooms cultivated in China. *J Food Compos Anal* 2024;126. <https://doi.org/10.1016/j.jfca.2023.105905>.
- [110] Xu L, Fang X, Wu W, Chen H, Mu H, Gao H. Effects of high-temperature pre-drying on the quality of air-dried shiitake mushrooms (*Lentinula edodes*). *Food Chem* 2019;285:406–13. <https://doi.org/10.1016/j.foodchem.2019.01.179>.
- [111] Wang X, Yang S, Li H, Ren Y, Wang Y, Huang J, et al. Non-thermal treatments for the control of endogenous formaldehyde from *Auricularia auricula* and their effects on its nutritional characteristics. *Food Control* 2022;142. <https://doi.org/10.1016/j.foodcont.2022.109235>.
- [112] Pardo JE, de Figueiredo VR, Alvarez-Orti M, Zied DC, Penaranda JA, Dias ES, et al. Application of hazard analysis and critical control points (HACCP) to the Cultivation Line of Mushroom and Other Cultivated Edible Fungi. *Indian J Microbiol* 2013;53:359–69. <https://doi.org/10.1007/s12088-013-0365-4>.
- [113] Betancor D, Nunez-Borque E, Cuesta-Herranz J, Escudero C, Freundt N, Pastor-Vargas C, et al. Porin: a new button mushroom (*Agaricus bisporus*) Allergen. *J Invest Allergol Clin Immunol* 2020;30:135–6. <https://doi.org/10.18176/jiaci.0454>.
- [114] Singh A, Garg S, Upadhyay AK. Identification and analysis of allergens in edible mushroom (*Agaricus bisporus*). *Mater Today Proc* 2023. <https://doi.org/10.1016/j.matpr.2023.03.639>.
- [115] Spierings EL, Fujii H, Sun B, Walshe T. A Phase I study of the safety of the nutritional supplement, active hexose correlated compound, AHCC, in healthy volunteers. *J Nutr Sci Vitam* 2007;53:536–9. <https://doi.org/10.3177/jnsv.53.536>.
- [116] Mojet J, Heideima J, Christ-Hazelhof E. Effect of concentration on taste-taste interactions in foods for elderly and young subjects. *Chem Senses* 2004;29:671–81. <https://doi.org/10.1093/chemse/bjh070>.
- [117] Kong Y, Zhang LL, Zhao J, Zhang YY, Sun BG, Chen HT. Isolation and identification of the umami peptides from shiitake mushroom by consecutive chromatography and LC-Q-TOF-MS. *Food Res Int* 2019;121:463–70. <https://doi.org/10.1016/j.foodres.2018.11.060>.
- [118] Harada-Paderno SDS, Dias-Faceto LS, Selani MM, Alvim ID, Floh EIS, Macedo AF, et al. Umami Ingredient: Flavor enhancer from shiitake (*Lentinula edodes*) byproducts. *Food Res Int* 2020;137. <https://doi.org/10.1016/j.foodres.2020.109540>.
- [119] França F, Harada-Paderno SDS, Frasceto RA, Saldaña E, Lorenzo JM, De Souza, et al. Umami ingredient from shiitake (*Lentinula edodes*) by-products as a flavor enhancer in low-salt beef burgers: Effects on physicochemical and technological properties. *LWT* 2022;154. <https://doi.org/10.1016/j.lwt.2021.112724>.
- [120] Demircan E, Aydar EF, Mertdinc Mertdinc Z, Kasapoglu Kasapoglu KN, Ozcelik Ozcelik B. 3D printable vegan plant-based meat analogue: fortification with three different mushrooms, investigation of printability, and characterization. *Food Res Int* 2023;173:113259. <https://doi.org/10.1016/j.foodres.2023.113259>.
- [121] Wan-Mohtar W, Halim-Lim SA, Kamarudin NZ, Rukayadi Y, Abd Rahim MH, Jamaludin AA, et al. Fruiting-body-base flour from an Oyster mushroom waste in the development of antioxidative chicken patty. *J Food Sci* 2020;85:3124–33. <https://doi.org/10.1111/1750-3841.15402>.
- [122] Kondyli E, Pappa EC, Arapoglou D, Metafa M, Eliopoulos C, Israelides C. Effect of fortification with mushroom polysaccharide  $\beta$ -glucan on the quality of ovine soft spreadable cheese. *Foods* 2022;11. <https://doi.org/10.3390/foods11030417>.
- [123] Wang L, Guo H, Liu X, Jiang G, Li C, Li X, et al. Roles of *Lentinula edodes* as the pork lean meat replacer in production of the sausage. *Meat Sci* 2019;156:44–51. <https://doi.org/10.1016/j.meatsci.2019.05.016>.
- [124] Wu X, Wang P, Xu Q, Jiang B, Li L, Ren L, et al. Effects of *Pleurotus ostreatus* on Physicochemical Properties and Residual Nitrite of the Pork Sausage. *Coatings* 2022;12. <https://doi.org/10.3390/coatings12040484>.
- [125] Husain H, Huda-Faujan N. Potential application of grey oyster mushroom stems as Halal meat replacer in imitation chicken nuggets. *Food Res* 2020;4:179–86. [https://doi.org/10.26656/fr.2017.4\(s1\).s18](https://doi.org/10.26656/fr.2017.4(s1).s18).
- [126] Vital ACP, Goto PA, Hanai LN, Gomes-da-Costa SM, Filho BAA, Nakamura CV, et al. Microbiological, functional and rheological properties of low fat yogurt supplemented with *Pleurotus ostreatus* aqueous extract. *LWT - Food Sci Technol* 2015;64:1028–35. <https://doi.org/10.1016/j.lwt.2015.07.003>.
- [127] Antontceva E, Belyakova T, Zabodalova L, Shamtsyan M. Fortification of yogurt with  $\beta$ -glucans from oyster mushroom. *Foodbalt* 2019. <https://doi.org/10.22616/foodbalt.2019.038>.
- [128] Buniowska-Olejnik M, Mykhalevych A, Polishchuk G, Sapiga V, Znamirowska-Piotrowska A, Kot A, et al. Study of water freezing in low-fat milky ice cream with oat  $\beta$ -glucan and its influence on quality indicators. *Molecules* 2023;28. <https://doi.org/10.3390/molecules28072924>.
- [129] Aljewicz M, Florczuk A, Dąbrowska A. Influence of  $\beta$ -Glucan structures and contents on the functional properties of low-fat ice cream during storage. *Pol J Food Nutr Sci* 2020;70:233–40. <https://doi.org/10.31883/pjfn.120915>.
- [130] Nakov G, Jukic M, Simic G, Sumanovac F, Komlenic DK, Lukinac J. Effect of the addition of hullless barley flour on the quality of short-dough cookies. *Foods* 2022;11. <https://doi.org/10.3390/foods11162428>.
- [131] Survas SA, Saudagar PS, Bajaj IB, Singhal RS. Scleroglucan: fermentative production, downstream processing and applications. *Food Technol Biotechnol* 2007;42:107–18.
- [132] Shakil MH, Trisha AT, Rahman M, Talukdar S, Kobun R, Huda N, et al. Nitrites in cured meats, health risk issues, alternatives to nitrites: a review. *Foods* 2022;11. <https://doi.org/10.3390/foods11213355>.
- [133] Cavalcante RB, Telli GS, Tachibana L, De Carla Dias D, Oshiro E, Natori MM, et al. Probiotics, Prebiotics and Synbiotics for Nile tilapia: Growth performance and protection against *Aeromonas hydrophila* infection. *Aquac Rep* 2020;17. <https://doi.org/10.1016/j.aqrep.2020.100343>.

- [134] Huynh T, Chi C, Nguyen T, Hien Tran T, Cheng A, Liu C. Effects of synbiotic containing *Lactobacillus plantarum* 7–40 and galactooligosaccharide on the growth performance of white shrimp, *Litopenaeus vannamei*. *Aquac Res* 2018;49:2416–28.
- [135] Mahfuz SU, Long SF, Piao XS. Role of medicinal mushroom on growth performance and physiological responses in broiler chicken. *Worlds Poul Sci J* 2020;76:74–90. <https://doi.org/10.1080/00439339.2020.1729670>.
- [136] Feng T, Hu Z, Tong Y, Yao L, Zhuang H, Zhu X, et al. Preparation and evaluation of mushroom (*Lentinus edodes*) and mealworm (*Tenebrio molitor*) as dog food attractant. *Heliyon* 2020;6:e05302. <https://doi.org/10.1016/j.heliyon.2020.e05302>.
- [137] Vargas-Sánchez RD, Torrescano-Urrutia GR, Ibarra-Arias FJ, Portillo-Loera JJ, Ríos-Rincón FG, Sánchez-Escalante A. Effect of dietary supplementation with *Pleurotus ostreatus* on growth performance and meat quality of Japanese quail. *Livest Sci* 2018;207:117–25. <https://doi.org/10.1016/j.livsci.2017.11.015>.
- [138] Yousefi M, Malecky M, Zaboli K, Najafabadi HJ. *In vitro* and *in sacco* determining the nutritive value of button mushroom stipe and its application in growing lambs diet. *Ital J Anim Sci* 2022;21. <https://doi.org/10.1080/1828051X.2021.1987847>.
- [139] Liu X, Zhang B, Liu H, Zhang G, Zhao J, Liu L, et al. Determination of the available energy values and amino acid digestibility of *Flammulina velutipes* stem waste and its effects on carcass trait and meat quality fed to growing-finishing pigs. *J Anim Sci Biotechnol* 2020;11:41. <https://doi.org/10.1186/s40104-020-00449-y>.
- [140] Moradzadeh-Somarin Z, Seifdavati J, Yalchi T, Abdi-Benemar H, Seyedsharifi R, Elghandour MM, et al. Valorization of dietary edible mushrooms waste: chemical and physical properties, nutrient digestibility, microbial protein synthesis and nitrogen balance in sheep. *J Sci Food Agric* 2021;101:5574–82. <https://doi.org/10.1002/jsfa.11208>.
- [141] Yang B, Zhao G, Wang L, Liu S, Tang J. Effects of the *Agaricus bisporus* stem residue on performance, nutrients digestibility and antioxidant activity of laying hens and its effects on egg storage. *Anim Biosci* 2021;34:256–64. <https://doi.org/10.5713/ajas.19.0853>.