



Edible Mushrooms for Sustainable and Healthy Human Food: Nutritional and Medicinal Attributes

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Abstract: Global food production faces many challenges, including climate change, a water crisis, land degradation, and desertification. These challenges require research into non-traditional sources of human foods. Edible mushrooms are considered an important next-generation healthy food source. Edible mushrooms are rich in proteins, dietary fiber, vitamins, minerals, and other bioactive components (alkaloids, lactones, polysaccharides, polyphenolic compounds, sesquiterpenes, sterols, and terpenoids). Several bioactive ingredients can be extracted from edible mushrooms and incorporated into health-promoting supplements. It has been suggested that several human diseases can be treated with extracts from edible mushrooms, as these extracts have biological effects including anticancer, antidiabetic, antiviral, antioxidant, hepatoprotective, immune-potentiating, and hypocholesterolemic influences. The current study focuses on sustainable approaches for handling edible mushrooms and their secondary metabolites, including biofortification. Comparisons between edible and poisonous mushrooms, as well as the common species of edible mushrooms and their different bioactive ingredients, are crucial. Nutritional values and the health benefits of edible mushrooms, as well as different biomedical applications, have been also emphasized. Further research is needed to explore the economic sustainability of different medicinal mushroom bioactive compound extracts and their potential applications against emerging diseases such as COVID-19. New approaches such as nano-biofortification are also needed to supply edible mushrooms with essential nutrients and/or to increase their bioactive ingredients.

Keywords: anticancer; antidiabetic; antioxidants; phenolics; poisonous mushroom; biomolecules

1. Introduction

More than 14,000 mushroom species have been identified, about 10% of which are macro-fungi. Edible mushrooms are macro-fungi that can be seen with the naked eye, i.e., fleshy fruit bodies of many species of mushrooms, and they have already been widely used in food and medicine due to their delicious taste and diverse physiological activities [1]. The fruiting bodies of edible mushrooms, which include about 700 species, can be safely consumed and are considered beneficial to human health [2]. Edible mushrooms are seen as an important source of food because of their high content of polysaccharides, dietary fiber, proteo-glucans, and vitamins such as riboflavin and thiamine [3–5]. Edible mushrooms also have many bioactive ingredients that are beneficial for human health such as antioxidants [6], terpenoids [7], lectins [8], phenolics/polyphenolics [9], polysaccharides [10], and



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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). ergosterols [11,12]. Not much is known regarding the capability of mushrooms to treat and/or prevent chronic diseases. However, several chronic diseases have been treated by consuming edible mushrooms (e.g., *Coriolus versicolor, Ganoderma lucidum, Grifola frondose, Phellinus linteus, Pleurotus eryngii*, and *Poria cocos*) such as cancer [13], diabetes mellitus [14], obesity [15,16], hyperlipidemia [10], cardiovascular and neurodegenerative diseases [17], and hypercholesterolemia [2].

Whether edible mushrooms are considered a sustainable healthy human food source mainly depends on the mushroom species and their chemical composition as well as the growing media. The safety and health of a mushroom is the main factor that controls its edibility. Many studies have confirmed that mushrooms grown in polluted soils threaten human health [13,18–23]. These studies focused on pollutants (e.g., heavy metals, organic toxicants, radioactive pollutants, or radionuclides) in mushrooms grown in polluted soils as reported in China [20,23], Iran [18,21], Poland [22,24,25], Spain [26], and Turkey [27,28]. However, further investigations on the consumption of edible mushrooms cultivated in polluted soils are needed before the association between pollutants and edible mushrooms can be more clearly understood [19].

Therefore, this review focuses on edible mushrooms and the differences between them and poisonous mushrooms. Common species of edible mushrooms will be discussed, including their bioactive ingredients content, nutritional values, and health benefits. The biomedical applications of edible mushrooms will also be reported.

2. Methodology of the Review

This review is an attempt to focus on the edible mushrooms and the difference between them and poisonous mushrooms. The methodology that was followed in this study depended on the collected materials from the common scientific websites or engines such as the databases of ScienceDirect, SpringerLink, PubMed, and MDPI. This is work based on combinations of key terms to identify useful documents, including edible mushrooms, poisonous mushrooms, nutritional value, and medicinal attributes. The collected information included original articles, review articles, and chapters in the English language, and more than 200 articles finally were selected. The collected information was analyzed and listed in tables and drawn in figures. Tables summarize much of the information by surveying the nutritional and medicinal attributes in collected articles on edible mushrooms, whereas figures include photos of edible and poisonous mushrooms along with comparisons between them. The studies were collected from the main places for mushroom production such as China, Iran, Poland, India, Brazil, Ireland, Taiwan, and Malaysia.

3. Sustainable Production of Edible Mushrooms

More than 100 countries cultivate edible mushrooms commercially using different systems and on different scales. The global production of mushrooms increases annually at growth rate of about 7%. The current global consumption of mushrooms is around 12.74 million tonnes, and it is predicted that the global production of mushrooms will scale to 20.84 million tonnes by 2026 [29]. Mushrooms can be classified into some categories including (1) cultivated mushrooms (which can be grown commercially by farmers using various strategies to produce for sale at supermarkets; these include enoki and oyster mushrooms), (2) wild mushrooms (which can grow on the root systems of trees in forests and are harvested by mushroom hunters—lots of wild mushrooms are poisonous), (3) medicinal mushrooms (several mushrooms have medicinal benefits but might not always be pleasant to consume), and (4) poisonous mushrooms, which have toxic substances or toxins [30]. Based on the growing method of mushrooms, they can be classified into saprotrophic mushrooms (sapro = rot; troph = eating), which grow on dead matter; mycorrhizal mushrooms (mykes = fungus; rhiza = root), which have a symbiotic relationship (sym = together; biosis = way of living) with crops or trees; and parasitic mushrooms, which infect and depend on its host plant and then kill it [30].

Most cultivated mushrooms have a basic life cycle, which includes the following stages (1) sporulation (i.e., production spores not seeds), (2) spore germination and the mating of cells, (3) colonization to complete fruiting initiated, (4) the formation of primordia, and (5) after fruiting or mature of mushrooms, spores release again and the cycle repeats (Figure 1) [31]. The cultivation steps can be summarized in terms of seven stages, as presented in Figure 2 and described in [31]. The sustainable production of mushrooms is important because mushrooms are considered edible foods and are high in protein content. There are many poisonous mushrooms, which must be clear to consumers in order to avoid causing serious ecological and health problems [32]. The huge amount of wastes that result from mushroom cultivation needs to be sustainably recycled for in order to protect the environment and to produce the bioenergy as well. Therefore, edible mushrooms can be promoted as an important agri-business activity to address many environmental issues, especially the ecological degradation [29,33]. The cultivation of mushrooms can be used to manage farm wastes by recycling them, as well as to dispose of spent mushroom substrate "SMS" (i.e., wastes remaining after harvesting mushrooms). On the other hand, the cultivation of mushrooms should protect from many competitor microorganisms and promote hygiene, which are controlled through the environmental conditions as presented in Table 1 [34].

Table 1. The environmental conditions controlling the most commonly cultivated species as ideal values, but certain strains may exceed them.

Environmental Conditions	Spawn Run	Primordia Formation	Fruitbody Development
Temperature	21–27 °C	10–21 °C	10–24 °C
Relative Humidity	85–95%	95–100%	80–90%
Light	50–100 lux	1000–1500 lux	1000–1500 lux
CO_2 level	5000–20,000 ppm; 1 FAE/h	500–2000 ppm; 4–8 FAE/h	<1000–2000 ppm; 4–8 FAE/h
Duration	2–8 weeks	3–12 days	5–8 days

Source: [34] Fresh Air Exchange (FAE).



Figure 1. The industry of mushroom cultivation is considered an important industry, which needs certain steps to produce the edible mushrooms as presented in these photos. The first group of photos (1) includes mushroom fungi (*Pleurotus ostreatus*) culture, which should first be ready on the surface of agar plate beside the cultivation substrates, as well as tools for propagation of mushroom and poured media (heat treated at 95 °C, for 1 day). The inoculant and the millet spawn in a jar should be also prepared. The second and third group of photos (2,3) include the industrial preparing and filling of spawn in the factory, whereas the group of photos in (4) represent oyster mushroom production. These steps have been photographed from the factory of "Magyar Gomba Kertész Kft", and all photos were taken by Gréta Törős, Debrecen University, Hungary.

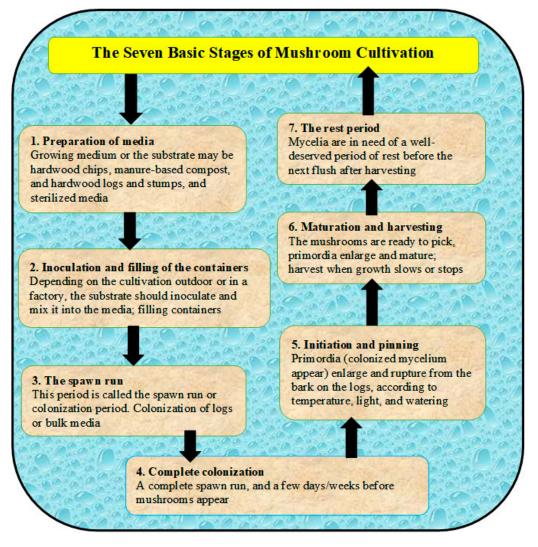


Figure 2. Different stages of mushroom cultivation starting from preparation of media till harvesting.

4. Edible vs. Poisonous Mushrooms

There are many categories of mushrooms, such as edible, non-edible, and poisonous mushrooms; wild and cultivated mushrooms; or medicinal and industrial mushrooms. Mushroom by-products, which may be generated during production and processing, represent a disposal problem. However, these by-products may be promising sources for several applications because of their nutritional and functional properties [35,36]. There may be many sustainable applications for these by-products, including the production of bioactive compounds for pharmaceutical and nutraceutical formulations, as well as several other applications such as animal feeds, fertilizers, energy production, bioremediation, bio-based materials, cosmetics, and cosmeceuticals. Many applications of edible mushrooms are presented in Figure 3, according to Kumar et al. [37], Zhang et al. [38], and Lopez-Hortas et al. [39].



1-Food consumption (ready to eat/cook or as prebiotics for food supplementation)

2- Cosmetics like skin care formulations (because of lentinan, carotenoids, ceramides, etc.)

3- Biosorbent or bio-degradator through biorem ediation of polluted environments

4- Green synthesis of metal nanoparticles (e.g., Ag, Au, Cu, Se, TiO2, ZnO)

5-Bio- or organic-fertilizers (recycling of agro-wastes or spent mushroom substrates)

6- Therapeutic properties (bioactive compounds like polysaccharides, antioxidants, etc.)

7- Production of cellulolytic enzymes (e.g., laccase, xylanase, mannanase, etc.)

8- Bioethanol production through the bio-fermentation for agro-industrial or agro-wastes

9- Edible mushrooms based-films/coatings for food packaging industries

10- Production biochar (pollutants removing) and carbon dots (for biomedical applications)

Figure 3. Potential applications of different mushrooms and their by-products, which include using bioactive compounds in developing the pharmaceutical and nutraceutical formulations, in addition to applications such as animal feeds, bioremediation, fertilizers, energy production, bio-based materials, cosmetics, and cosmeceuticals.

Some poisonous species of mushrooms have toxins that are not destroyed under the high temperatures reached during cooking [40]. Several studies have been conducted on the identification of mushrooms, including their taxonomy, and naming indices can be found on many websites such as Index Fungorum (http://www.indexfungorum.org/, accessed on 15 January 2022), Myco-Bank Database (http://www.mycobank.org/, accessed on 15 January 2022), the British Mycological Society (https://www.britmycolsoc.org.uk/library/english-names, accessed on 15 January 2022), International Mycological Association, (https://www.ima-mycology.org/, accessed on 15 January 2022), Fungal databases (https://nt.ars-grin.gov/fungaldatabases/, accessed on 15 January 2022), NCBI or National Center for Biotechnology Information (https://www.ncbi.nlm.nih.gov/taxonomy, accessed on 15 January 2022), and the Global Biodiversity Information Facility (https://www.gbif.org/species, accessed on 16 December 2021).

FAO has stated that reports on the identification of edible or poisonous mushroom species are based on named sources, and there is no test or characteristic to distinguish edible from poisonous mushrooms [41]. The edibility of mushrooms was simplified into the following categories based on the available information: (1) confirmed edible mush-

rooms (E1), (2) confirmed edible mushrooms with conditions (E2), (3) unconfirmed edible mushrooms (E3), and poisonous mushrooms (P) [41]. It is worth noting that some edible mushrooms are very similar in their appearance to the poisonous types and may grow in the same habitat; an example is *Entoloma sarcopum* (an edible mushroom) and *Entoloma rhodopolium* (a poisonous mushroom) [42] (Table 2; Figure 4). The edibility of mushrooms must be accurately identified based on different advanced methods such as sensory identification methods (e.g., morphological and odor methods), instrumental analysis methods (e.g., mass spectrometry, chromatographic, and spectral technology), and molecular biology methods (e.g., isothermal amplification technology, molecular marker technology, endogenous reference gene method, and sequencing technology). A review of this topic was provided by Wei et al. [43]. Edible and non-edible or poisonous mushrooms have recently been discussed in reviews such as Wu et al. [40], Li et al. [44], Ramírez-Terrazo et al. [45], Zhang et al. [46], and Wei et al. [43].

Table 2. A list of some selected non-edible or poisonous mushroom species including the common English name and their family.

Mushroom Species Name	Common English Name	Family
Agaricus pilatianus (Bohus) Bohus	Basionym	Agaricaceae
Agaricus phaeolepidotus F.H. Møller	Agaric	Agaricaceae
Agaricus praeclaresquamosus A.E. Freeman	Ink-smelling mushroom	Agaricaceae
Agaricus xanthoderma var. xanthoderma	Carbolic mushroom	Agaricaceae
Amanita gemmate (Fr.) Gillet	Yellow agaric	Amanitaceae
Amanita muscarina	Fly agaric	Amanitaceae
Amanita pantherine (DC ex Fr.) Secr.	Panther	Amanitaceae
Amanita phalloides	Killer agaric	Amanitaceae
Boletus calopus Fr.	Farkino	Boletaceae
Boletus radicans Pers.	Rooting bolete	Boletaceae
Boletus satanas Lenz	Devil's bolete	Boletaceae
<i>Clitocybe dealbata</i> (Sowerby) P. Kumm	Field or ivory funnel	Tricholomataceae
Clitocybe cerussata (Fr.) P Kumm	Wax white funnel	Tricholomataceae
Cortinarius orellanus Fr.	Fool's webcap	Cortinariaceae
Entoloma sinuatum	Livid pinkgill	Entolomataceae
Entoloma rhodopolium (Fr.) P. Kumm.	Wood pinkgill	Entolomataceae
Gyromitra fastigiata (Krombh.) Rehm	Red-brown priest mushrooms	Discinaceae
Gyromitra esculenta (Pers.) Fr.	False Morel	Discinaceae
Galerina marginata (Batsch) Kühner	Funeral Bell	Hymenogastraceae
Helvella crispa Scop.	Curly paprika mushrooms	Helvellaceae
Helvella leucopus Pers.	Pale foot saddle	Helvellaceae
<i>Hygrocybe conica</i> (Schaeff.) P. Kumm	Blackening waxcap	Hygrophoraceae
Hypholoma fasciculare (Huds.) P. Kumm	Basionym	Strophariaceae
Hebeloma synapizans (Paulet) Gillet	Bitter poisonpie	Hymenogastraceae
Inocybe asterospora Quelet	Star spore susula	Inocybaceae
Inocybe fastigiate (Schaeff.) Quél.	Kerti susulyula	Inocybaceae
Inocybe patouillardii Bres.	Brick red susula	Inocybaceae
Lepiota cristata (Bolton) P. Kumm	Stinky dapperling	Agaricaceae
Lepiota brunneoincarnata	Meat brown venison	Agaricaceae
Lepiota pseudohelveola Kühner ex Hora	Roe deer mushrooms	Agaricaceae
<i>Mycena pura</i> (Pers.) P. Kumm	Lilac Bonnet	Mycenaceae
Omphalotus olearius (DC.) Singer	Illuminated funnel (Basionym)	Omphalotaceae
<i>Psilocybe semilanceata</i> (Fr.) P. Kumm	Magic mushroom	Hymenogastraceae
Paxillus involutus (Fr.) Fr.	Brown rollrim	Paxillaceae
Tricholoma sulphureum (Bull.) P. Kumm	Stinky Knight	Tricholomataceae
Ramaria Formosa (Pers.) Quél	Salmon coral	Gomphaceae
Russula emetica (Schaeff.) Pers.	Sickener	Russulaceae
Scleroderma citrinum Pers.	Common Earthball	Sclerodermataceae
Sarcosphaera eximia var. nivea M.M. Moser	Tulip cup mushrooms	Pezizaceae
Tricholoma pardinum (Pers.) Quél.	Panther (Leopard Knight)	Tricholomataceae
Tricholoma saponaceum (Fr.) P. Kumm	Soap scent	Tricholomataceae

Note: Sources: http://xn--gombahatroz-r7a1v.hu/, accessed on 16 December 2021, [47,48]. https://www.plantlife.org.uk/application/files/6714/8240/8340/recommended-english-names-for-fungi.pdf, accessed on 15 January 2022.



Amanita muscaria



Galerina marginata



Omphalotus olearius



Russula emetica



Agaricus phaeolepidotus



Gyromitra fastigiata



Hypholoma fasciculare



Tricholoma sulphureum

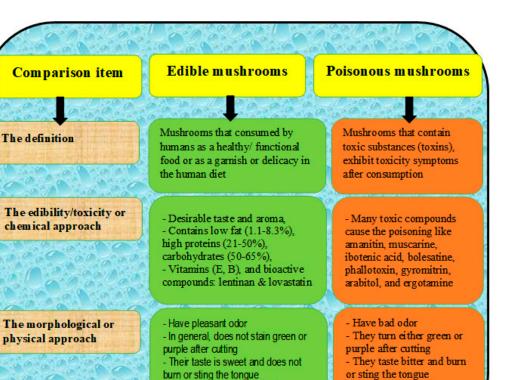
Figure 4. List of some poisonous mushrooms including the scientific names for each one. Sources: by user Strobilomyces, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=1091222; by Onderwijsgek, CC BY-SA 3.0 nl, https://commons.wikimedia.org/w/index.php?curid=1428517; by Gerhard Koller (Gerhard), CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=18730680; by Alan Rockefeller, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=95423433; by Alan Rockefeller, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=61680344; by Renier van Rensburg, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=61680344; by Strobilomyces, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=63737437, accessed on 16 January 2022.

Several taxa of poisonous mushrooms have been reported particularly among the most common wild mushrooms, such as *Amanita*, *Chlorophyllum*, *Cantharocybe*, *Inocybe*, *Entoloma*, *Leccinellum*, *Russula*, and *Xerocomus* [49–51]. Poisonous mushrooms have toxic compounds that usually cause problems due to unintentional ingestion, with these problems including endocrine toxicity, neurotoxicity, cytotoxicity, myotoxicity, and gastrointestinal disturbances (Table 3) [52]. Many poisonous species produce neurotoxic secondary metabolites such as muscarine or psilocybin [51], alpha-amanitin and amanitin [53], coprine [50], gyromitrin [52], ibotenic acid [54], orellanine [55], phallotoxin [56], and russuphelins [57]. Differences between edible and poisonous mushrooms are of important concern for human health, which mainly depends on the following criteria: the edible mushrooms should have a pleasant odor and sweet taste and not be stained green or purple under cutting; the should not burn or sting the tongue when a piece is tasted; and there should be no scales on the cap [58]. A comparison between edible and poisonous mushrooms can be found in Figure 5 [58].

Table 3. A list of main toxins, clinical features, and their relationships to poisonous mushrooms based on the classification of poisonous mushrooms.

Toxins	Poisonous Mushrooms	Clinical Features
Group 1: Cytotoxic mushroom p	oisoning	
α-amanitin	Amanita phalloides, A. virosa, A. verna, A. exitialis	Liver damage 1–3 days after ingestion due to hepatotoxic and nephrotoxic effects
Amanitin	Amanita verna, A. virosa, A. phalloides, Lepiota helveola, Galerina marginata	Gastrointestinal disturbances; liver and renal failure
Orellanine	Amanita smithiana, A. pseudoporphyria Cortinarius orellanus, C. rubellus	Kidney failure (early primary nephrotoxicity) Delayed primary nephrotoxicity
Group 2: Neurotoxic mushroom		
Muscarine	Omphalotus, Clitocybe cerussata, C. dealbata, Inocybe fibrosa, I. hystrix, I. geophylla, I. rimosa, I. sambucina	Respiratory failure, bradycardia, miosis, salivation, lacrimation, diarrhea and bronchospasm perspiration, lachrymation
Psilocybin and psilocin	Psilocybe caerulescens, P. cubensis, P. semilanceata, Panaeolus cinctulus	Euphoria, hallucinations, tachycardia and blood pressure, mydriasis, tremors, and fever
Ibotenic acid	Amanita muscaria, A. pantherina, A. gemmate, A. ibotengutake,	Neurotoxicity, continuous periods of excitation and inhibition in the nervous system
Muscinol	Amanita muscaria, A. pantherina, A. gemmate, A. cothurnata, A. regalis	Central nervous system depression and hallucinations
Group 3: Myotoxic mushroom pe		
Bolesatine	Rubroboletus satanas (Lenz), R. lupinus, R. legaliae	Non-lethal; causes gastrointestinal irritation, vomiting, nausea
Russuphelins Saponaceolide	Russula sübnigricans Tricholoma equestre, T. terreum nd related toxicity mushroom poisoning	Gastrointestinal disturbances, and renal failure Delayed onset myotoxicity
-	Coprinopsis alopecia, C. atramentaria,	Flushing, headache, dyspnea, sweating, arrhythmia,
Coprine	C. romagnesiana	hypotension, and confusion
Gyromitrin	Gyromitra esculenta, G. californica, G. ambigua, G. gigas, G. infula	Neurotoxicity, gastrointestinal upset, and destruction of blood cells
Polyporic acid	Hapalopilus rutilans	Abdominal pain, nausea, vomiting, diarrhea
Trichothecenes	Podostroma cornu-damae	A multi-organ illness, often fatal
Group 5: Gastrointestinal irritan		
	Chlorophyllum molybdites, Entoloma sinuatum, Tricholoma pardalotum	Gastrointestinal effects without causing other significant effects
Group 6: Miscellaneous adverse		Ū.
Ergotamine	Claviceps spp.	Deadly can affect the vascular system and lead to loss of limbs and/or cardiac arrest
Acromelic acid	Paralepistopsis amoenolens, Clitocybe acromelalga	An erythromelalgia-like syndrome; reddening, swelling, and burning pain in the extremities
Hydro-Cyanic Acid	Pleurocybella porrigens, Grifola frondose, Pleurotus eringii	Delayed onset with cramps and coma; re-existing chronic renal failure
Lentinan (Shiitake) Phallotoxin	Lentinola edodes, Auricularia auricular-judae Amanita phalloides	Dermatitis, linear rash/whiplike lesions, photosensitivity Gastrointestinal upset
Paxillus syndrome	Paxillus involutus	Abdominal pain, nausea, vomiting, and acute respiratory failure

Sources: [50,51,53,55,57-60].



They do not contain

worms; the cap has scale

Figure 5. A comparison between edible and poisonous mushrooms, including morphological and chemical approaches.

They contain worms and the cap

has no scale

5. Common Species of Edible Mushrooms

Edible mushrooms are the fleshy fruit bodies of many species of macro-fungi that can be used in the human diet (Table 4). The edibility criteria of mushrooms may depend on the absence of poisonous substances or toxins that are detrimental to human health. Edible mushrooms are mainly consumed for their nutritional value, medicinal features, and sweet taste. Several species of edible mushrooms are found the wild and raised for harvest, but some species are difficult to cultivate. Several articles or reviews have reported about edible mushrooms from different points of view:

- (1) Studies on edible mushrooms harvested from polluted areas with a focus on Africa [13], China [20,23,61,62], Greece [63], Iran [18,21], Poland [22,24,25,64–66], Turkey [27,28,67–72], and Spain [26] or on Europe as a whole, e.g., Świsłowski et al. [73], or on the global level, e.g., Dowlati et al. [18].
- (2) A study focusing on locals' perspective concerning the changing of the abundance of wild edible mushrooms, which has decreased due to direct exploitation by 31% and land use change by 38% of all taxa [74].
- (3) Studies on the bioactive properties of different edible mushrooms, including total phenolic content, phenolic acid, antioxidant capacities, and antimicrobial activity in Pleurotus sajor-caju wild edible mushroom [75], in *Agaricus bisporus, Cantharellus cibarius, Boletus edulis, Lactarius deliciosus, Lentinus edodes, Ganoderma lucidum, Hericium erinaceus, Morchella* spp., and *Pleurotus ostreatus* [76], and in *Pleurotus ostreatus* [77]; polysaccharide in many edible mushrooms [78]; and bioactive components in several species of edible mushrooms [79].
- (4) Studies on determining the amount of potentially bioavailable compounds such as phenolic compounds in mycelia of *Agaricus bisporus*, *Cantharellus cibarius*, and *Lentinula edodes* [80].

- (5) Studies on integrated methods (morphological and molecular approaches) for the identification of bioactive compounds [81], or using only molecular strategies for identification [82].
- (6) Studies on the mineral and nutritional composition of wild edible mushrooms [82–85] and the nutritional value and biological properties of some edible mushrooms [86].
- (7) Studies on using mushroom-derived bioactive compounds against SARS-CoV-2 infection [87,88].

Table 4. List of selected edible mushroom species as reported in the literature.

Mushroom Species Name	Common English Name	Family
Agaricus arvensis Schaeff.	Horse mushroom	Agaricaceae
Agaricus bitorquis (Quél.) Sacc.	Pavement mushroom	Agaricaceae
Agaricus bisporus (J.E. Lange) Imbach, white	White cultivated mushroom	Agaricaceae
Agaricus bisporus (J.E. Lange) Imbach, brown	Brown cultivated mushroom	Agaricaceae
Agaricus sylvaticus Schaeff.	Blushing wood mushroom	Agaricaceae
Agrocybe cylindracea (Brig.) Fayod	Poplar mushroom	Strophariaceae
Amanita ovoidea (Bull.) Link	Bearded amanita	Amanitaceae
Amanita vaginata (Bull.) Lam.	Grisette	Amanitaceae
Armillaria mellea (Vahl) P. Kumm.	Honey fungus	Physalacriaceae
Auricularia auricula-judae (Fr.) Quél	Black wood ear	Auriculariaceae
Cantharellus cibarius Fr.	Chanterelle	Cantharellaceae
Clavariadelphus pistillaris (L.) Donk	Giant club	Clavariadelphaceae
<i>Clitocybe nebularis</i> (Batsch) P. Kumm.	Clouded funnel	Tricholomataceae
	The Miller	Entolomataceae
Clitopilus prunulus (Scop.) P. Kumm.		
Cordyceps militaris (L.) Fr.	Scarlet caterpillar club	Cordycipitaceae
Coprinus comatus (O.F. Müll.) Gray	Shaggy inkcap/lawyer's wig	Agaricaceae
Gyroporus castaneus (Bull.) Quél.	Chestnut bolete	Gyroporaceae
Helvella acetabulum (L.) Quél.	Vinegar cup	Helvellaceae
Hygrophorus marzuolus (Fr.) Bres.	March mushroom	Hygrophoraceae
Hygrophorus russula (Schaeff. ex Fr.) Kauffman	Pinkmottle woodwax	Hygrophoraceae
Lactarius pubescens Fr.	Bearded milkcap	Russulaceae
Lactarius repraesentaneus Britzelm.	Yellow bearded milkcap	Russulaceae
Lactarius rufus (Scop.) Fr.	Rufous milkcap	Russulaceae
Lactarius scrobiculatus (Scop.) Fr.	Spotted milkcap	Russulaceae
Lactarius sanguifluus (Poulet) Fr	Bloody milkcap	Russulaceae
Lactarius volemus (Fr.) Fr.	Fishy milkca	Russulaceae
Lentinus edodes (Berk.) Pegler	Shiitake	Marasmiaceae
Lentinus tigrinus (Bull.) Fr	Tiger sawgill	Hygrophoraceae
Lepista irina (Fr.) H. E. Bigelow	Flowery blewit	Tricholomataceae
<i>Lepista nuda</i> (Bull.) Cooke	Wood blewit	Tricholomataceae
Leucoagaricus leucothites (Vittad.) Wasser	White dapperling	Agaricaceae
Lycoperdon molle Pers.	Soft puffball	Lycoperdaceae
Lyophyllum decastes (Fr.) Singer	Clustered domecap	Tricholomataceae
Pleurotus citrinopileatus Singer	Golden oyster mushroom	Pleurotaceae
Pleurotus ostreatus (Jacq. ex Fr.) P. Kumm	Oyster mushroom	Pleurotaceae
Polyporus squamosus (Huds.) Fr.	Dryad's saddle	Hygrophoraceae
Macrolepiota mastoidea (Fr.) Śinger	Slender parasol	Agaricaceae
Neoboletus luridiformis (Rostk.)	Basionym	Boletaceae
Neolentinus lepideus (Fr.) Redhead & Ginns	Scaly sawgill	Polyporaceae
Otidea cochleata (L.) Fuckel	Brown ear	Pyronemataceae
Pluteus petasatus (Fr.) Gillet	Scaly shield	Pĺuteaceae
Pluteus salicinus (Pers.) P. Kumm	Willow shield	Pluteaceae
Russula albonigra (Krombh.) Fr.	Menthol brittlegill	Russulaceae
Russula delica Fr.	Milk White brittlegill	Russulaceae
Russula fellea (Fr.) Fr.	Geranium brittlegill	Russulaceae
Russula viscida Kudřna	Viscid brittlegill	Russulaceae
Strobilomyces strobilaceus (Scop.) Berk.	Old man of the woods	Boletaceae
Suillus bellinii (Inzenga) Kuntze	Champagne bolete	Suillaceae
Suillus bovinus (L.) Roussel	Bovine bolete	Suillaceae
Suillus luteus (L.) Roussel	Slippery jack	Suillaceae
Tricholoma focale (Fr.) Ricken	Booted knight	Tricholomataceae
Tricholoma focule (Fr.) Ricken Tricholoma terreum (Schaeff.: Fr.) Kumm		Tricholomataceae
Valuentaria alajaamkalua (DC)	Grey knight Basispum	
Volvopluteus gloiocephalus (DC.)	Basionym	Pluteaceae
<i>Volvariella volvacea</i> (Bull.) Singer	Straw mushroom	Pluteaceae
Xerocomus subtomentosus (L.) Fr.	Homotypic synonym	Boletaceae

Selected references: [1,10,12,22,25,27,28,44,46,69,89–93], English name from [47,48].

6. Bioactive Ingredients of Edible Mushrooms

Edible mushrooms contain various bioactive ingredients such as proteins, polysaccharides, polyunsaturated fatty acids (PUFA), dietary fibers, amino acids, vitamins, and minerals (Table 5). They have essential health effects, such as antioxidant, antimicrobial, immune-stimulatory, and anticancer, cholesterol-lowering properties (Figure 6) [12,37–39]. Several significant components and secondary metabolites dominate their biological activity. Lectins are carbohydrate-binding proteins that can be found in many types of edible mushrooms such as *Phaseolus vulgaris*, *Agaricus campestris*, *Agaricus bisporus*, *Grifola frondosa*, *Boletus satanus*, *Flammulina velutipes*, *Tricholoma mongolicum*, *Ganoderma lucidum*, and *Volvariella volvacea*. Lectins have been shown to increase insulin secretion, activate the immune system, and have anticancer effects [8]. Lectins can also play essential roles in physiological processes such as dormancy, growth, morphogenesis, morphological changes, and molecular recognition in the early stages of mycorrhization. Lectins isolated from the edible mushroom *Clitocybe nebularis* exhibit immunostimulatory effects on the most potent antigen-presenting cells, dendritic cells [94].

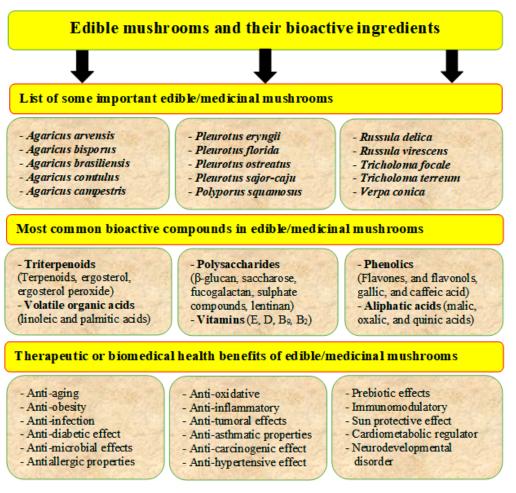


Figure 6. Edible mushrooms are an important source of human food and have several bioactive ingredients (phenols, lectins, terpenoids, flavonoids, etc.) and bio-medicinal activities such as anticancer, antidiabetic, antiaging, antiviral, antioxidant, and anti-inflammatory.

Glucans are one of the unique ingredients in mushrooms that have immune-stimulatory, anticancer, anti-inflammatory, and antioxidant effects. They can be found in different types of edible mushrooms such as Jelly ears (*Auricularia auricular*), Reishi (*Ganoderma lucidum*), Shiitake (*Lentinula edodes*), and Oyster (*Pleurotus ostreatus*) [95]. For example, beta-glucan, isolated from Pleurotus pulmonarius, has potent anti-inflammatory and antinociceptive properties that inhibit pro-inflammatory cytokines [96]. Glucans isolated from Pleurotus

pulmonarius also suppressed colon carcinogenesis associated with colitis by regulating cell proliferation, inducing apoptosis, and suppressing inflammation [97]. Beta-glucan is a high-molecular-weight polysaccharide of glucose bound by glycosidic bonds.

Table 5. A list of some phenolic compounds, polysaccharides, proteins, and triterpenoids found in selected edible mushrooms species.

Edible Mushrooms	Phenolics	Polysaccharides	Proteins	Triterpenoids	Refs.
Agaricus bisporus Boletus edulis Cordyceps aegerita Coprinus comatus	Gallocatechin Gallic acid Proto-catechuic acid Flavones, and flavonols	Heteropoly-saccharide ABP Polysaccharides (BEBP-1) Fucogalactan Modified polysaccharide	Protein type FIIb-1 β-Trefoil lectin Ageritin Laccases	Ergosterol Boledulins A-C Bovistols A-C Terpenoids	[98–101] [98,102–104] [105–108] [109–111]
Lactarius deliciosus	Syringic acid, vanillic acid	Polysaccharide (LDG-M)	Laccase	Azulene-type sesquiterpene	[112–115]
Pleurotus ostreatus Pleurotus eryngii Pleurotus cornucopiae Macrolepiota procera Russula virescens Tuber melanosporum	Caffeic acid, and ferulic acid Cinnamic acid Gallic acid Proto-catechuic acid Quercetin Flavonoids, phenols	Mycelium polysaccharides PEPE-A1 and PEPE-A2 β-glucan Polysaccharides SRVPs Exo-poly-saccharides (TP1)	Concanavalin A Laccase Oligopeptides β-Trefoil lectin Laccase	Ergosterol Ergosterol Ergostane-type sterols Lanostane triterpenoids Ergosterol	[116] [117,118] [119–122] [103,123–125] [126–128] [101,120–129]

Abbreviations: FIP (Immunomodulatory proteins); PEPE (*Pleurotus eryngii* purified polysaccharides); PSK (Polysaccharide K); PSP (Polysaccharide peptide); RVP (*Russula virescens* polysaccharide); LDG m (*Lactarius deliciosus* polysaccharides); BEPF (crude polysaccharides isolated from *B. edulis*).

Phenolic compounds are secondary metabolites of edible mushrooms. Polyphenols have been extensively studied and shown to be effective against a variety of health complications. Phenolic acids such as p-hydroxybenzoic, cinnamic, gallic, salicylic, p-coumaric acids, syringic acids, caffeic, ferulic, chlorogenic, and flavonoid can be found in mushrooms [130]. Gallic, caffeic, and p-coumaric acids are the main phenolic groups and play an essential role in the biological activity of mushrooms [131]. Phenolic compounds have high antioxidant activity. Polyphenols from edible mushrooms such as *Meripilus giganteus*, *Agaricus hydnum*, and *Rufescens silvaticus* have high antioxidant capacity [80]. Phenolic compounds have also shown anticancer activity against kidney cancer cell lines and human ovarian cancer cell lines [6]. Flavonoid compounds, including myricetin, rutin, naringenin, quercetin, morin, and hesperetin, are included in the polyphenol content, and they exhibit antiproliferative effect [132].

Terpenoids such as monoterpenoids, sesquiterpenoids, diterpenoids, and triterpenoids, are essential components in mushrooms. They have been shown to have antimicrobial, anticancer, anticholinesterase, anti-inflammatory, antimalarial, and antioxidant properties [106]. Currently, about 285 types of terpenoids have been discovered in mushrooms and have medicinal properties. For example, ganoderic acids are a lanastanoid type triterpenoid and have been isolated from *Ganoderma amboinense*, *Ganoderma lucidum*, etc. Ergosterol, the principal sterol in most edible mushrooms, is a valuable dietary precursor of vitamin D2 and a natural antioxidant [133]. Phytosterols, such as ergosterols and ergosterol peroxide, have been shown to be more potent than the nonsteroidal anti-inflammatory drug indomethacin, as shown by their 50% inhibitory effect. High levels of ergosterols can be found in *Agaricus bisporus*, *Lentinus edodes*, *Grifola frondose*, *Pleurotus ostreatus*, *Agaricus bisporus*, and *Agaricus bisporus* [12].

7. Nutritional Values and Health Benefits of Edible Mushrooms

As a crucial source of food for humans for thousands of years, the medicinal and organoleptic properties provided by the chemical composition and nutritional value of edible mushrooms have been reported by several researchers (Figure 7). The consumption of edible and medicinal mushrooms in Eastern and Western countries has gradually increased in recent decades [134]. *Agaricus bisporus, Lentinus edodes,* and *Pleurotus* spp. are presently the most common cultivated edible mushrooms, with China as the largest producer of these mushrooms in the world [86]. Edible mushrooms are known for their high contents of carbohydrates, protein, and crude fibers, as well as different bioactive compounds, which provide both nutritional and health benefits for humans [86,135]. The relative content of these nutritional components differs by species and between countries, as reported in Table 6.



Cantharellus cibarius



Agaricus bisporus



Morchella esculenta



Lactarius volemus



Lentinula edodes



Pleurotus ostreatus



Boletus edulis



Flammulina velutipes

Figure 7. Photos of some common edible mushrooms and their scientific names. Sources: by frankenstoen from Portland, CC BY 2.0, https://commons.wikimedia.org/w/index.php?curid=7304 024; CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=191739; by Dan Molter (shroomydan), CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=9822537; by TOMMES-WIKI, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=27753655; by Strobilomyces, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=179148; by Archenzo, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=24474; by voir ci-dessous, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=3330811; by Мыць Денис, Public Domain, https://commons.wikimedia.org/w/index.php?curid=1334049, accessed on 16 January 2020.

The main nutritional compounds that edible mushrooms are rich in include proteins, carbohydrates, crude fiber, total phenolic compounds, and vitamins and many minerals. Several studies have discussed the nutritional value of edible mushrooms from different locations such as Argentina [136], Bangladesh [85], China [136,137], Chile [86], India [83,138], and Turkey [9,76]. Many reports have also focused on one or more edible mushrooms such as *Agaricus bisporus* [24,139]; *Lactarius deliciosus* [140]; *Pleurotus citrinopileatus* [91]; *Helvella leucopus* and *Morchella pulchella* [9]; *Pleurotus sajor-caju* and *Calocybe indica* [141]; *Agaricus bisporus*, *Cantharellus cibarius*, and *Lentinula edodes* [80]; some studies have focused on several species, e.g., Altaf et al. [83], Das et al. [135], and Taskın et al. [6]. Several myco-chemical structures and compositions can be found in edible mushrooms, including phenolic compounds, fatty acids, terpenoids, lipids, polysaccharides, and proteins, which are important compounds for human health. Saini et al. [11] reported the biologically active nutraceutical compounds present in edible mushrooms, including ergosterol, proteins, and fatty acids content (388 mg/100 g DW, 4.5–37.4%, and 1.75–15.5%, respectively).

Table 6. General nutritional values (based on dry weight) of some common edible mushrooms from different sources.

Mushroom Species Used in the Study	Moisture (%)	Total Protein (%)	Total Carbo-Hydrate (%)	Crude Fiber (%)	Ash (%)	Total Phenols (%)	Refs.
I. Studied many species							
Agaricus bisporus, Agrocybe							
cylindracea, Boletus loyo, Cortinarius	86–96	8.56-23.88	62.97-83.65	7–15	5-13	0.75-4.72	[86]
lebre, Cyttaria espinosae							
Apioperdon pyriforme, Helvella		11 5 04 5		0 (10	0 5 14 5	F 0 10 0	[00]
elastica, Morchella conica and	-	11.5-24.5	-	2.6-4.8	9.5–14.7	5.0-12.3	[83]
Rhizopogon luteolus) Auricularia auricula-judae, A.							
polytricha, Lactifluus piperatus,	49-88	19-56	7-18	5-11	3–8	7.3-10.2	[138]
Laetiporus sulphureus	47 00	17 50	7 10	5 11	5.0	7.5 10.2	[150]
Auricularia auricular, Ganoderma							
lucidum, Pleurotus citrinopleatus, P.	4 11	20.45	11 (1	F 40	(10	1.0	[05]
djamor, P. eryngii, P. ostreatus, and P.	4-11	20-45	11–61	5-40	6-10	1–8	[85]
ostreatus							
Agaricus bisporus, Pleurotus ostreatus,	88-92	1.7-2.11	3–9	20-37	0.8-1.15	1.1-1.5	[136]
Lentinula edodes	00 72	1.7 2.11	0 9	20 07	0.0 1.10	1.1 1.0	[100]
Tricholoma, Shiitake mushroom,	(0 1 F F	0 - 0(0	0 5 05 0	111 50 0	10 10 1		[107]
Pleurotus eryngii, Dictyophora	6.9–15.5	8.5-36.9	0.5-37.3	14.4-70.2	1.3-10.1	-	[137]
indusiata Agaricus bisporus, Boletus edulis,							
Cantharellus cibarius, Lactarius	82.6-91	1.5-3.6	3.2-8.3	_	_	_	[5]
deliciosus, Leccinum rufom	02.0 71	1.5 5.6	3.2 0.5				
Astraeus odoratus, Craterellus aureus,							
Lentinus edodes, Phaeogyroporus	-	13.1-32.8	2.79-44.3	77.1	-	-	[142]
portentosus							
Agaricus bisporus, Boletus edulis,							
Calocybe indica, C. gambosa, Grifola	-	18.1-62.8	31.1-70.6	7.81-32.3	3.5-19.7	-	[135]
frondosa, Flammulina velutipes	07 00	1 = 4 - 5 - 4	2 27 2 22		10.10		[4,44]
Pleurotus sajor-caju; Calocybe indica	87-89	1.74-3.4	3.37-3.33	-	1.2–1.3	-	[141]
II. Studied only one species	<u>81 70</u>	29.29	20.57	24.56	7.12		[143]
Agaricus bisporus Flammulina velutipes	81.79	18.42	20.57 56.37	24.56 7.81	6.33	-	[143]
Grifola frondosa	83.06	21.1	58.8	10.1	7.0	-	[144]
Hericium erinaceus	95.69	23.3	57.0	7.8	9.4	-	[145]
Lactarius deliciosus	92	17.19	66.61	31.81	8.62	4.5-13.6	[140]
Lyophyllum decastes	-	18.31	34.36	29.02	14.20	-	[146]
Pleurotus florida	87.05	34.56	31.59	11.41	7.40	-	147
Pleurotus ostreatus	85.55	30.92	31.40	12.10	7.05	-	[147]
Russula delica	-	26.25	34.88	15.42	17.92	-	[146]
Tremella fuciformis	91.73	4.6	94.8	1.4	0.4	-	[148]
Tricholoma giganteum	-	16.1	70.1	4.5	5.0	-	[149]
Volvariella volvacea	-	30.1	50.9	11.9	12.6	-	[149]

The biofortification approach can be defined as a method by which pollutants and/or biodegradation from the environment can be removed or blocked from microorganisms such as bacteria, fungi, or algae. It is considered a sustainable agricultural strategy and a cost-effective tool to increase the bioavailability or content of essential nutrients in the edible parts of cultivated plants and reduce malnutrition [150]. Some edible mushrooms have been biofortified with nutrients, particularly selenium [151], which is applied to produce Se enrichment and increase bioactive metabolites of *Pleurotus ostreatus* [152], *Cordyceps militaris* [153], *Hericium erinaceus* [154], and *Ganoderma lucidum* [155]. Nano-biofortification is also an important approach that recently has been confirmed for using nano-selenium as anti-COVID-19 nanoparticles [156,157].

8. Biomedical Applications of Edible Mushrooms

Medicinal mushrooms can be defined as mushrooms that are used to modulate human immune responses such as antimicrobial, anticancer, and antioxidant (Table 7). These mushrooms have important compounds such as alkaloids, polyphenols, polysaccharides, sesquiterpenes, terpenoids, and metal chelating agents for treatment different human diseases [17]. Medicinal mushrooms are gaining more recognition. Consequently, this is creating new paths for researchers to understand how these types of mushrooms can play a role against human diseases such as neurodegenerative diseases (i.e., Alzheimer's disease, Huntington's disease, multiple sclerosis, Parkinson's disease, motor neuron disease, and prion disease) through mechanisms such as regulating neurotrophins synthesis, reducing oxidative stress, neuroinflammation, protecting neurons, and modulation of acetylcholinesterase activity [17,158]. These strategies may include roles of mushrooms such as (1) antibacterial antibiotics, (2) antimycotics, (3) biofilm inhibitors, (4) anticancer agents, (5) antidiabetes, (6) improving nerve functioning, (7) cardiovascular disease control, (8) antiviral agents, (9) prebiotic, and (10) immunosuppressive and immunomodulatory agents [158,159].

Table 7. A survey of some pharmacological or medicinal activities in selected edible mushrooms species according to published studies, study model, and the suggested disease being treated.

Mushroom Species	Study Model	Pharmacological or Medicinal Activities (Disease)	Place	Refs.
Agaricus blazei	Animal/cell line	Tumoricidal, anticarcinogenic activity and antimetastatic activity (cancer)	Brazil	[160]
Russula griseocarnosa	Not available	Antioxidation, immune regulation, hypoglycemic/hypolipidemic activities (diabetes)	China	[161]
Macrolepiota procera, Gymnopus dryophilus	Not available	Anticancer, anti-inflammatory, and reducing cardiovascular diseases (cancer)	Poland	[12]
Lentinus edodes and Hypsizygus tessellatus	Cell line	Immunomodulatory activity (inflammatory lung conditions)	Ireland	[96]
Sanghuangprous vaninii Russula virescens	Cell line In vitro	Anticancer particularly gynecological cancers (cervical cancer) Anticancer, hypoglycemia and immune activities (cancer)	China China	[162] [163]
Ganoderma lucidum, G. artum and G. tsugae	Cell line	Anti-inflammatory, antitumor, antioxidation, anti-hyperglycemic or hyperlipidemic effects (diabetes)	China	[164,165]
Sanghuangporus sanghuang	Cell line	Antioxidant activities and anti-coronavirus (SARS-CoV-2) activity	China	[166]
Ganoderma lucidum	Not available	Arthritis, bronchitis, hypertension, gastric ulcer, and nephritis (tumorigenic diseases)	China/Iran	[167]
Agaricus spp., Pleurotus spp., Lentinus spp.	Cell line	Antitumor and anticancer agents (cancer)	India	[168]
Ganoderma lingzhi, Ĝ. applanatum, G. lucidum, and G. tsugae	Simulated gastrointestinal condition	For immunological diseases (gastrointestinal diseases)	Hungary	[169]
Pleurotus citrinopileatus, P. djamor, P. eryngii, and P. ostreatus Armillaria mellea, Antrodia	In vitro	Anti-atherosclerotic properties (high lovastatin content) (cardiovascular diseases and cancers)	Poland	[170]
camphorata, Hericium erinaceus, Ganoderma spp.	In vitro/in vivo	Anti-neuroinflammatory activities (Alzheimer's disease)	Malaysia	[171]
Calvatia gigantea, Fomes fomentarius, Phallus impudicus	Cell culture	Anti -bacterial, antitumor, antioxidative and anti-inflammatory (cancer)	European Union	[172]
Agaricus bisporus, Ganoderma frondosa, Lentinula edodes	Cell line	Anticancer (cancer)	Mauritius	[173]
Antrodia salmonea	Cell line	Antioxidant, anti-inflammatory, antitumor, and antiatherosclerosis activity (atherosclerosis)	Taiwan	[174]
Lignosus rhinocerus, L. tigris, L. cameronensis	Cell line	Anticancer, anti-inflammatory, and antioxidative activity (cancer)	Malaysia	[175]
Species of Agaricus, Ganoderma, Pleurotus	Animal	Anticancer, alleviation of osteoarthritis (cancer and osteoarthritis)	Cameroon/ Nigeria	[176]
Ganoderma applanatum, Pleurotus eryngii, Lentinula edodes	Clinical trials on human and animals	Antioxidant, antibacterial activity, antitumor, and antiproliferative activity (Alzheimer's disease, and human colon cancer)	Italy	[177]

Several studies have been published about different therapeutic applications of medicinal mushrooms [178]. These studies depend on the kind of bioactive compounds and mushroom species, which can be divided into the following groups:

(1) Anticancer group

This group includes many kinds of cancers such as colorectal, oral, renal, and cervical cancers besides leukemia, as well as breast, liver, lung, and prostate cancer. The main bioactive mushroom extracts that can be used against cancers may include methanol, polysaccharides, ganoderic acid, and ethanol extracts. Medicinal mushrooms that have these bioactive compounds include *Agaricus brasiliensis*, *Boletus edulis*, *Ganoderma lucidum*,

Pleurotus ostreatus, P. pulmonarius, Ophiocordyceps sobolifera, Sanghuangprous vaninii, and *Tremella mesenterica* [93,158,162,163,179,180].

(2) Antidiabetic group

This includes many mushroom species such as *Grifola frondose* and *Phellinus linteus*, which have different polysaccharides as bioactive compounds [14,158,181,182].

(3) Cardiovascular diseases group

This includes species such as *Agaricus bisporus* and *Tricholoma matsutakei*. The crude extract of peptides found in these mushrooms may be useful in treating these diseases [158,183].

(4) Immune-function group

This includes many species such as *Pleurotus ostreatus* and *Trametes pubescens*. The lectine extracts from these mushrooms may boost immune function [15,158,159,163].

(5) Rheumatoid arthritis group

This includes some mushroom species such as *Grifola frondose* and *Psilocybin* spp. The active metabolite psilocin or polysaccharides extracts may help with rheumatoid arthritis [15,184].

(6) Antiviral group

Major human viral diseases include human immunodeficiency virus (HIV), herpes simplex virus (HSV), hepatitis B and C viruses (HBV, HCV), and influenza. There are many antiviral compounds that can be extracted from various mushroom species [10,158,159,185]. Medicinal mushrooms can be divided into following groups based on three items mushroom species, extract of bioactive compounds, and virus disease group [186].

(i) Antiviral mushrooms against HIV

This group includes mushrooms that have bioactive compounds that are active against human immunodeficiency virus (HIV), which include *Lentinus edodes* (polycarboxylated water-solubilized lignin), *Pleurotus ostreatus* (ubiquitin-like protein), *Ganoderma lucidum* (several triterpenoids), and *Ganoderma colossus* (lanostane triterpenes).

(ii) Antiviral mushrooms against HSV

This group includes mushrooms that have bioactive compounds that act against Herpes simplex virus (HSV), which includes *Agaricus brasiliensis* (sulfated polysaccharide HSV-1), and *Ganoderma lucidum* (GLPG or Ganoderma lucidum proteoglycan).

(iii) Antiviral mushrooms against influenza

This group includes mushrooms that have bioactive compounds that act against influenza virus (H5N1), which includes *Phellinus baumii* (hispidin), *Inonotus hispidus* (phenolic extracts), and *Phellinus igniarius* (sesquiterpenoid).

(iv) Antiviral mushrooms against hepatitis virus

This group includes mushrooms that have bioactive compounds that act against hepatitis virus B or C (HBV, HCV), which include *Antrodia camphorate* (polysaccharides for HBV), *Ganoderma lucidum* (ganoderic acid), *Lentinula edodes* (mycelia solid culture extract for HCV), and *Pleurotus ostreatus* (lectin HBV). Recently, some published studies have reported about the biological role of bioactive compounds from mushrooms against COVID-19 such as polysaccharides [87,187], colossolactones, and ergosterol [88].

(v) Antiviral mushrooms against other viruses

This group includes mushrooms that have bioactive compounds that act against other viruses, which include *Hypsizygus marmoreus* (sterols for Epstein–Barr virus), *Auricularia auricular* (polysaccharides for Newcastle disease virus), and *Agaricus blazei* (Murill extract for foot-and-mouth disease virus).

(7) Group of neurodegenerative diseases

Some medicinal mushrooms such as *Grifola frondosa*, *Hericium erinaceus*, *Lignosus rhinocerotis*, *Paxillus panuoides*, *Pleurotus giganteus*, and *Sarcodon scabrosus* can improve human cognitive functions. Many bioactive ingredients can be used from this group of mushrooms against many diseases such as hericenones, scabronines, ganoderic acids, and aqueous and ethanolic extracts [17,188].

(8) DNA damage group

This group includes mushrooms such as *Agaricus blazei* and *Ganoderma lucidum*, which have extracts such as polysaccharides that may work against DNA damage [189].

(9) Antiaging group

This includes Tricholoma lobayense and *Ganoderma lucidum*, which could supply polysaccharide TLH-3 Ergosterol ganodermasidase, which acts against aging [10,15].

(10) Antiobesity group

Many bioactive compounds can be extracted from mushroom species and used against obesity, including *Pleurotus eryngii*, *P. sajor-caju*, and *Ophiocordyceps sinensis*. These compounds may include β -glucan water extract and Cordyceps sinensis polysaccharide [16,142,190,191].

9. Bioactive Compounds from Edible Mushrooms and Toxic Dose

In general, the link between medicinal edible mushrooms and the impacts of their bioactive compounds in preventing human diseases (mycotherapy) is still in need of more investigation. Thus, a growing concern in mycotherapy is required from the scientific community to expand clinical trials to explore the potential benefits of the safe consumption of these mushrooms [192]. The bioactive compounds found in mushrooms may have important effects on human health. Mushrooms are most often taken into the body through ingestion, but their mechanisms need to be studied in both in vivo and in vitro clinical studies in order for their actions to be fully understood. Research should also be undertaken to standardize all production stages of edible mushrooms from cultivation through the extraction process, commercial preparation, regulation, and precise monitoring for high quality level [192], as set by the European Food Safety Authority (EFSA). This issue has been discussed by many studies, as reported by [74,79].

The bioactive compounds and their efficiency depend on several factors, from cultivation to the handling or processing of these bioactives to protect them from any harsh environments and to improve their bio-availability and biological activities upon human digestion [193]. The characterization of these bioactive components also depends on the kind of methodology and instrumentation used during their measurement, such as biochemical and high-performance liquid chromatography (HPLC) [194] or UHPLC-Mass Spectrometry-(MS)/MS [12], as well as all processing and extraction tools such as the drying temperature during processing [195] and hot water during extraction [196]. Therefore, it is difficult to establish the standardized doses for each edible mushroom for each bioactive compound required to achieve its desired biological effect.

It is assumed that up to 3.8 million fungal species inhabit the Earth. Around 120,000 of those are currently known, and more than 27,000 are macromycetes. Only about 500 species of macromycetes are known to be poisonous for humans [197]. As mentioned above, several studies have confirmed the beneficial attributes of consuming edible mushrooms. On the other hand, several potential risks to human health may occur when edible mushrooms grow in polluted soils and are ingested [13,198]. These risks mainly depend on the kind of pollutants, their consumed concentration, and the mushroom species [64,199]. The levels of pollutants, especially toxic elements in mushrooms before marketing, should be continually evaluated to assess the human health risk [21]. Poisonous mushrooms are considered a significant cause of "emergency medicine" when they cause mycotoxicity [198]. Poisonous mushrooms contain a variety of various toxins such as satratoxins [200], muscarine, amanitin, gyromitrin, ibotenic acid, orellanine, and russuphelins, which can differ markedly in

their toxicity (Table 2). It is not easy to demarcate between edible and poisonous mushroom species because there are several cultivated and edible wild species that have dual potential health benefits and toxic compounds [198]. Some edible species may cause cardiac toxicity, allergic reactions, rhabdomyolysis, and mutagenic effects, as observed in laboratory rodents or in assays on cell cultures [198].

The mechanisms of interactions of nutritional or toxic compounds with the human body is of crucial concern. These mechanisms may include their toxic or harmful effects on the human endocrine, metabolic, and nervous systems. The recent increase in global consumption of edible mushrooms, with fresh mushroom of up to 300 g per day, may represent a public health concern [201]. Many studies using tumor-bearing animals, cultured cancer cells, and clinical trials are required to investigate these mechanisms [202]. Several poisoning cases resulting from deadly toxic mushrooms such as Trichoderma cornudamae have been reported (Table 3), but toxicological analyses of these poisonings are still rare [200]. Cytotoxic mushroom poisoning may result from toxins of α -amanitin, amanitin, and orellanine, and their mechanisms may include (1) liver damage 1-3 days after ingestion due to hepatotoxic and nephrotoxic effects (such as mushrooms of Amanita phalloides, A. virosa, A. verna, A. exitialis); (2) gastrointestinal disturbances and liver and renal failure (such as Amanita verna, Lepiota helveola, and Galerina marginata); (3) kidney failure or early primary nephrotoxicity (Amanita smithiana, and A. pseudoporphyria); and (4) delayed primary nephrotoxicity (Cortinarius orellanus, and C. rubellus). More mechanisms and the mushrooms involved are listed in Table 2. The most distinguished poisonous mushrooms in Tables 1 and 2 may include some species of Agaricus, Amanita, Gyromitra, Tricholoma, and *Russula*. In this context, a comprehensive review of the activity of bioactivities in *Pleurotus* spp. and their mechanism of action was reported by Cateni et al. [10].

10. Antinutritional Properties of Mushrooms

Apart from the many advantages resulting from the consumption of plant foods, some plants (e.g., legumes) and mushrooms possess potential deleterious effects due to their content of toxins or antinutrients [203–205]. Antinutrients are defined as natural or synthetic compounds, which can interfere with the uptake/absorption of nutrients by humans, and limit the bioavailability of essential nutrients causing a serious harmful impact on human health [203,205]. Antinutrients may include chitin, glucosinolates, lectins, phytates, oxalates, saponins, or tannins, which plants need in order to protect themselves from the surrounding stressful conditions. On the other hand, these antinutrients have become well-known to possess many beneficial effects and therapeutic potential on many human diseases [206].

Although several benefits of edible mushroom have been reported in different fields, as discussed earlier, including nano-biotechnology [33,207] and the production of bioactive compounds [79], some reports discussed how mushroom products can be hard to digest due to their content of antinutrients such as chitin (e.g., [203,208]). Some other reports have confirmed that edible mushroom consumption may be associated with a lower risk of mortality [209]. In general, edible mushrooms contain about 1.87–7.25% chitin, and many published studies involve the chitin in mushrooms from different points of view such as the production of chitinase [210], wound treatment [211], isolation of chitin–glucan complex [212,213], production of chitin/cellulose nanofiber [214], and production of chitin nanopaper [215].

11. General Discussion

The main intent of this review was to summarize the information related to edible mushrooms with a focus on their nutritional and medicinal applications. Mushroom by-products, which may be generated during their production and processing, may represent a disposal problem. However, these by-products may be promising sources for several applications because of their nutritional and functional properties [35,36]. There may be many sustainable applications for these by-products, including the production of bioac-

tive compounds for pharmaceutical and nutraceutical formulations, as well as several other applications such as animal feeds, fertilizers, energy production, bioremediation, bio-based materials, cosmetics, and cosmeceuticals [33,91,216]. The sustainable productivity of edible/medicinal mushrooms has been reported by many researchers such as Shirur et al. [29], which could be used in industrial applications (Kumar et al. [37]), for the production of healthy food products (Zhang et al. [38]), for healthy and more sustainable foods (Das et al. [135], and for promising strategies of sustainable and novel food production (Lopez-Hortas et al. [39]).

On the other hand, toxic or poisonous mushrooms are considered an important issue, which still needs more exploration in terms of their toxins. Despite the health problems associated with poisonous mushrooms, the use of their main bioactive substances in such mushrooms in clinical applications is possible, as reported by many researchers (e.g., Patocka et al. [217]). These toxins could be applied in many respects, including biotechnology, biological control, and anticancer medicine. There is a need also for the discovery of more toxic species of mushrooms, and their toxins, which are expected to be increasingly known based on toxicological analyses.

12. Conclusions

Mushrooms are seen as an important source of food and are thought to play a crucial role in a healthy diet. The nutritional values of edible mushrooms results from their low content of calories, fat, and sodium and their high content of dietary fiber, proteins, vitamins, and essential nutrients, such as Cu, Mn, Se, and Zn. Several secondary metabolites (i.e., bioactive compounds) can be extracted from many edible medicinal mushrooms such as β-glucan, calcaelin, ergosterol, ganoderic acid, flavonoids, hispolon, laccase, lectins, lentinan, phenolics, proteoglycan, nucleotides, nucleosides, and triterpenoids. These compounds could offer various health benefits such as those provided by antioxidant, antiaging, anticancer, antimicrobial, anti-inflammatory, antiobesity, and immunomodulatory agents. These biological activities can reduce heart disease and hypertension, regulate metabolic disorders and body functions, improve gut health, boost the immune system, and help in weight loss. Edible mushrooms have become more popular as health promoters, with great concern given to different research activities looking into bioactive ingredients in several mushroom species. These bioactive compounds are needed to fortify or supply various staple food products. Although these bioactive components of edible mushrooms are crucial for human health, there is also an urgent need for testing such compounds against recent diseases such as coronavirus disease (COVID-19). Further investigations are needed on the nano-biofortification of different mushrooms, their bioactive compounds and therapeutic properties, and the health benefits of edible mushrooms for a healthy lifestyle.

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