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Patent review: existing, new, and potential pharmacological agents from mushrooms

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Abstract

Mushrooms are non-photosynthetic organisms produced as distinctive spore bearing fruiting bodies of filamentous macro-fungi. More than 14,000 mushroom species have been recognized, of which around 2,200 are edible. Scientists have extensively studied the extracts of different mushroom fruit bodies over the past few decades to identify the biologically active medicinal and nutraceutical components having different health benefits. Mushroom is also considered a functional food owing to the presence of low-fat and high-fiber contents useful in maintaining metabolic health. An expansive patent search since 2019 was conducted to review the information on mushrooms and their bioactive constituents using multiple patent databases. This review aims to highlight the pharmacological effects and potential therapeutic implications of mushroom bioactive substances as published in patent literature. Such information would assist researchers to explore the detailed processes and interactions involved by which the mushroom chemical components exert different medicinal properties, thereby increasing their credibility in clinical applications.

Keywords

mushroom, fungi, patent, therapeutics, medicinal, cancer, arthritis, bioactive

Introduction

Mushrooms are the reproductive structure produced by some fungi, and are a highly preferred component in next-generation low-caloric functional foods, as value-added products, nutraceuticals, and dietary fibers. Although more than 10,000 varieties of mushrooms are identified, only around 2,000 are known to be edible [1]. Mushrooms have long been known for their use in the traditional medicine in many countries. The *Ganoderma* variety has been a commonly used constituent in traditional Chinese medicine for its restorative effects. While countries like China, Japan, and South Korea are considered the homeland for cultivating medicinal mushroom varieties, more recently, North American companies are also establishing

large-scale mushroom cultivation facilities with newer extraction and formulation techniques to meet the rising awareness and adoption of Eastern herbal medicines among consumers in the West. According to a recent study, per capita consumption of mushrooms is very low in India compared to the rest of the world, making India a potential market for mushroom production and expansion [2]. According to Coherent Market Insights, the global market for medicinal mushrooms is projected to reach 59.41 billion by 2031, at a compounded annual growth rate of 8.2% in the next 6 years [3].

The worldwide popularity of mushroom-based commodities is increasing due to their health benefits, low production costs, and improved technologies. Medicinal mushrooms, characterized by their high content of biologically active compounds, have great potential in the design of innovative new-generation functional foods and medicinal formulations, as reported in a recent review article. The abundance of polysaccharides, amino acids, polyphenols, alkaloids, vitamins, eritadenine, and sterols in medicinal mushrooms contributes to improving immunity, regulating metabolism, and maintaining the overall health and well-being of the body [4]. These secondary metabolites are also reported for a wide range of pharmacological activities being anti-allergic, anti-microbial, anti-inflammatory, anti-hyperlipidemia, osteoprotective and many more [5]. The antioxidants in mushrooms are thought to mitigate the risk of developing hypertension, metabolic disorders, and even more serious conditions like Alzheimer's, heart disease, and diabetes. Mushroom polysaccharides and other secondary metabolites are reported to be crucial for anti-tumor activities [6]. It is suggested that the total metabolite extract of *Ganoderma applanatum* exerts apoptotic anti-tumor properties and can provide promising bioactives as alternative or co-anticancer medications [7]. Another study has shown the potential of *Lentinula edodes* butanol extract as an anti-bacterial drug that can overcome drug resistance [8]. Mushroom-derived compounds have been presently subjected to different stages of clinical studies, and are widely and effectively used in Asia to treat various cancers and other conditions. Detailed mechanistic study of their effects on the human organism, and their long-term clinical studies are needed to confirm their nutraceutical effects, safety, and dosage [9]. Besides the benefits of mushrooms in the health sector, new applications of fungal biomass and composite materials in the packaging, textile, leather, and automotive industries are also reported in a patent survey covering the time period 2009–2018 [10].

With this background, we aim to review the patent literature claiming mushrooms and/or their pharmacologically active bio-constituents in conjunction with the recently published non-patent literature to get an overview of the medicinal potential of mushrooms offering various therapeutic uses. Pharmacological and chemical studies of the bioactive constituents can result in the confirmation of hit molecules and further contribute to chemical lead generation for targeting various illnesses.

Areas covered: Based on an examination of the patents released between January 2019 and December 2024, this review outlines the current knowledge and advancements made in the field of medicinal mushrooms as bioactive/extracts in pharmaceutical formulations.

Method and scope

Patent search strategies were developed using the generic term "mushroom", and different synonyms, scientific and common names as key terms and concepts in combination with Cooperative Patent Classification (CPC) codes related to this technical area. The search strategies were executed, and patents were retrieved and analyzed using various free and paid databases such as Questel Orbit, Chemical Abstracts, Clarivate Analytics, Google Scholar, and Espacenet. Combining hits and de-duplication of around 2,000 unique patent families naming mushrooms and limiting the data to the last six years (earliest publication date 2019–2024) yielded around a thousand patents. Further critical review identified five hundred and thirteen patent documents focusing primarily on mushrooms, of which a major cluster of three hundred and thirty-four patents claim the use of mushroom extract and/or its bioactive constituents for different pharmaceutical applications. Fifty patents claim different processes for the cultivation of mushrooms. While thirty-seven patents mention the application of mushrooms in cosmeceuticals, another ninety-two patents mention their application in food and nutraceuticals. The larger cluster of three hundred and thirty-four patents disclosing mushrooms in pharmaceuticals is further categorized based on

the formulation type, comprising mushroom extract and/or bioactive constituent as a single ingredient or in polyherbal composition. Figure 1 shows the technology catalog for the patent clusters created using Prisma Flow Diagram [11]. The count of patents is rounded up/down for the larger result sets retrieved during the search period.

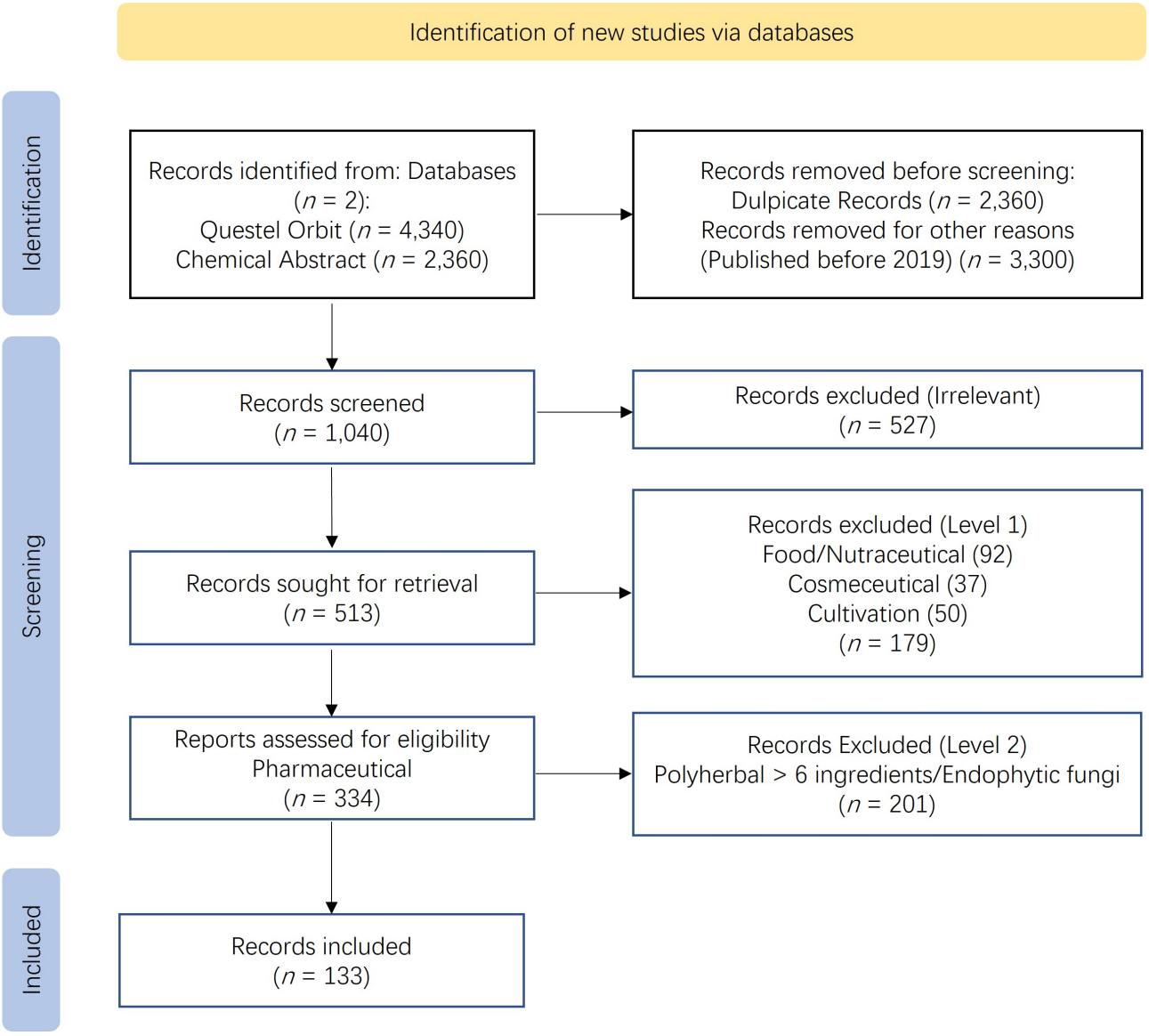

Figure 1. Technology catalog. Adapted from [11]. © Author(s) (or their employer(s)) 2019. CC BY.

Data inclusion and exclusion criteria

This review outlines the current knowledge from the one hundred and thirty-three patent literature centering on the pharmacological potential of mushrooms, including as a single component—extract/powder (51) and/or bioactive ingredient (32) or multiple spp. (35), or in a polyherbal formulation comprising less than or equal to five other herbs (15).

Patents pertaining to methods of mushroom cultivation and extraction, non-therapeutic usage, such as methods of isolating bioactive compounds from mushroom extracts for cosmeceuticals, food, and nutraceuticals, are not included in the scope of this review. A large set of two hundred and one patents, mostly claiming polyherbal formulations comprising six or more other herbs along with a mushroom and/or its bioactive constituent, is not included in the scope of this review. The majority of such patents either broadly disclosed mushrooms as only an optional ingredient in the pharmaceutical composition, or

claimed the therapeutic activity arising particularly from an active ingredient in the composition other than mushrooms. A few patent documents disclosing endophytic fungi are not included in the scope of this review.

Results and discussion—data analysis

The priority country-wise distribution of the one hundred and thirty-three technical inventions disclosed in the patents is shown in Figure 2. An increasing patenting activity trend from the year 2018 onwards suggests developing research interest in the field pertaining to the use of mushroom components as therapeutic agents. The number of patents filed in 2024 would be incompletely represented due to the processing lag, since patent applications are published only after a period of 18 months from the date of filing. The global distribution of the one hundred and thirty-three patents with respect to the priority countries indicates that Korea has the highest number of patent filings (43), followed by China (39), the USA (27), and Japan (9) (Figure 2). While Australia has four patents, India has three patents, Canada, Indonesia, and Italy have two patents each, Thailand and Latvia have a single patent filing. Priority countries for the Patent Cooperation Treaty (PCT) (16) and European (1) filings have been considered for the analysis.

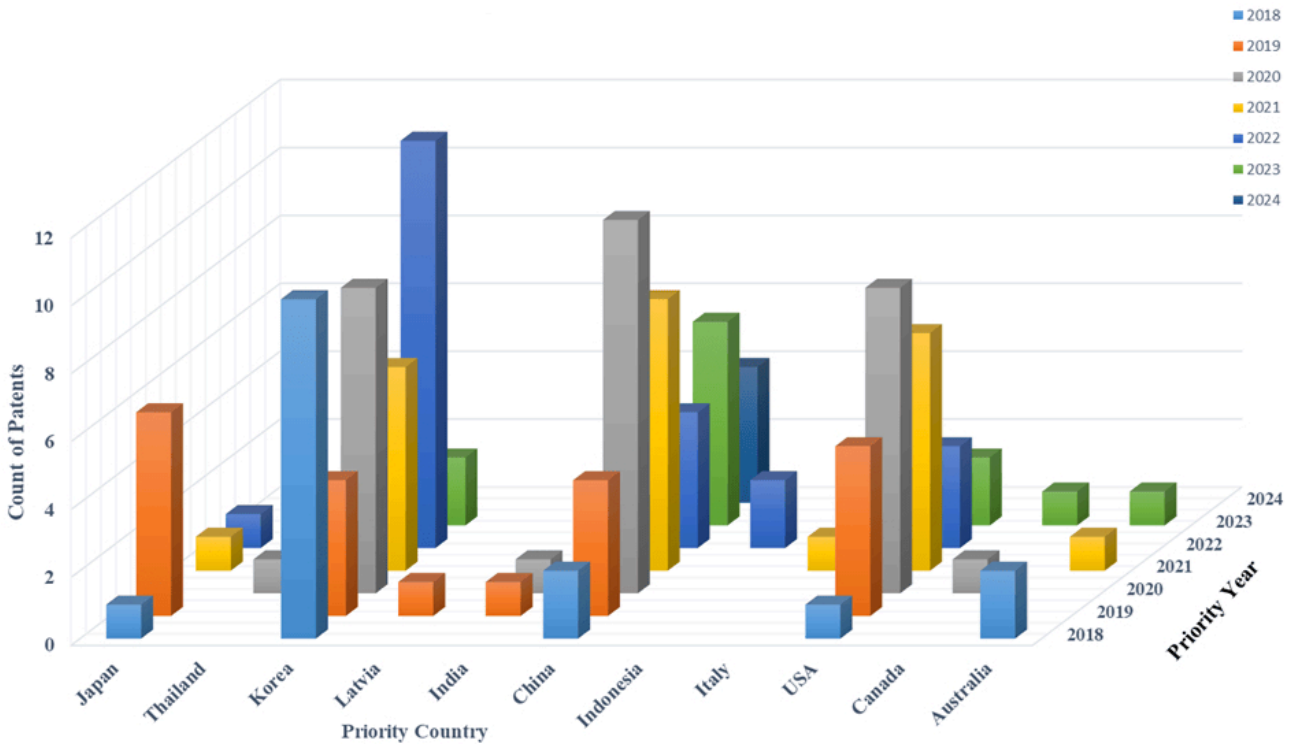

Figure 2. Priority country-wise family distribution of patents.

A critical review and thorough analysis of the shortlisted one hundred and thirty-three patents focusing on the use of mushroom extract and/or its bioactive component for therapeutic applications is conducted and segregated into fourteen therapeutic clusters based on the claimed therapeutic condition and mushroom variety, as shown in Figure 3. A single patent mentioning the treatment of any specific medical condition, or patents claiming the cure of more than one type of illness using mushrooms, are clustered as a "Miscellaneous" category. The analysis reveals that mushroom extracts, powder/residues, and/or the bioactive constituents are either applicable as a single active ingredient in a mono-herbal formulation, or used in synergy with other herbs or bioactive constituents in a polyherbal formulation for the healing of different medical conditions. While the majority of twenty-four inventions have focused on the use of mushrooms for addressing different types of cancers, a significant number of fifteen and sixteen patents have also disclosed their use for preventing and treating various infections and inflammation,

respectively. The data also reflects that the *Ganoderma* mushroom variety has been most commonly claimed for its use in medicinal formulations, followed by the *Phellinus* genus. Mushroom stacking by combining multiple mushroom species has also been extensively exploited for the treatment of diseases like cancer and neurodegenerative disorders, leveraging the synergistic interaction of the unique health benefits of each species. A detailed discussion is included in the following sections.

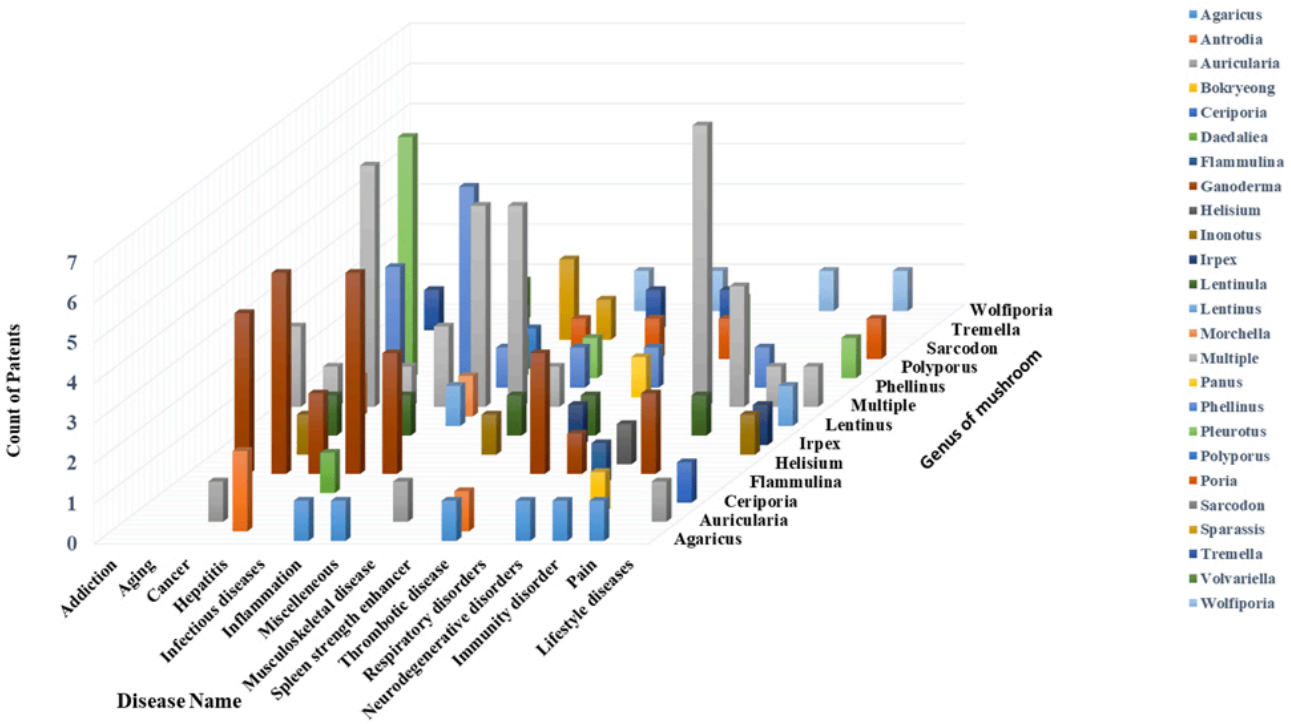

Figure 3. Distribution of mushroom varieties across therapeutic conditions.

The shortlisted one hundred and thirty-three patents analyzed herein have disclosed mushrooms either by their common or scientific names, with or without specifying the species. For uniform representation, we have mentioned all varieties by scientific names corresponding to the common names as listed in Table 1.

Table 1. Scientific and common names of mushrooms used in the review.

Sr. No.	Genus	Species	Common name
1	*Agaricus*	*bisporus*	Champignon Mushroom, Cultivated Mushroom, Button Mushroom, Common Mushroom
		blazei *brasiliensis* *rufotegulis*	Almond Mushroom, Almond Agaricus, Mushroom of The Sun, God's Mushroom, Mushroom of Life, Royal Sun Agaricus, Jisongrong, Himematsutake
2	*Agrocybe*	*cylindracea*	Black Poplar Mushroom, Pioppino
3	*Cyclocybe*	*aegerita*	
4	*Pholiota*		
5	*Cyclocybe*	spp.	Poplar Fieldcap, Poplar Mushroom, Velvet Pioppini
6	*Albatrellus*	*confluens*	Fused Polypore
		spp.	Sheep Polypore, Forest Lamb Mushroom
7	*Amanita*	spp.	Grisette, Grisette Amanita
8	*Antrodia*	*camphorate* *cinnamomea*	Stout Camphor
9	*Astraeus*	*asiaticus* *auricula*	False Earthstar, A Gasteroid Fungus, Wild Edible Mushroom

Table 1. Scientific and common names of mushrooms used in the review. (*continued*)

Sr. No.	Genus	Species	Common name	
10	*Auricularia*	*polytricha*	Wood Ear, Jew'S Ear, Cloud Ear, Jelly Ear, Throat Mushroom	
		cornea		
11	*Imleria*	*badia*	Bay Bolete	
12	*Polyporus*			
13	*Boletus*	*edulis*	Cep, Penny Bun, Porcino, Porcini, Hog Mushrooms	
14	*Calvatia*	spp.	Puffball Mushrooms	
15	*Cantharellus*	*cibarius*	Golden Chanterelle, Girolle	
16	*Caripia*	spp.	Pod Parachute	
17	*Clitocybe*	*maxima*	Great Clitocybe, Large Funnel Cap, Large White Clitocybe, Big Cup Mushroom, Pig Stomach Mushroom, Big Cup Umbrella	
18	*Psilocybe*	spp.	Magic, Hallucinogenic, Psychedelic, Psychoactive, Sacred, Saint Mushrooms, Gilled Mushrooms	
19	*Pluteus*			
20	*Pholiotina*			
21	*Panaeolus*			
22	*Inocybe*	*umbrinella*		
23	*Gymnopilus*	spp.		
24	*Copelandia*			
25	*Coprinus*	*comatus*	Lawyer's Wig	
		spp.	Shaggy Ink Cap, Shaggy Mane	
26	*Cordyceps*	*bassiana*	Beauveria Bassiana	
		cicadicola	Yartsa Gunbu, Yarshagumba, Yarchagumba, Yarsagumba, Keera Jhar, Keeda Jadi, Keeda Ghas, Ghaas Fafoond	
		gunnii	Vegetable Caterpillar	
		liangshanensis	Caterpillar Fungus	Chinese Caterpillar Fungus, Yartsa Gunbu
		militaris		Orange Cordyceps
27	*Coriolus*	*versicolor*	Turkey Tail, Many-Zoned Polypore	
28	*Polyporus*			
29	*Trametes*			
30	*Ceriporia*	*lacerata*	White Rot Fungus	
31	*Coriolopsis*	*trogii*		
32	*Funalia*			
33	*Trametes*			
34	*Pseudosperma*	*umbrinella*		
35	*Craterellus*	*cornucopioides*	Black Chanterelle, Black Trumpet, Trumpet of the Dead	
36	*Cyathus*	spp.	Bird'S Nest Fungi	
37	*Daedalea*	*dickinsii*	Daedalea	
38	*Daldinia*	*concentrica*	King Alfred's Cake, Cramp Balls, Coal Fungus	
39	*Dictyophora*	*indusiata*	Veiled Lady, Bridal Veil Fungus, Bamboo Mushroom, Long Net Stinkhorn, Crinoline, Stinkhorn Basket	
40	*Phallus*	*indusiatus*		
41	*Elaphomyces*	*granulatus*	Deer Truffles	
42	*Flammulina*	*filiformis*	Velvet Shank	
		velutipes		
43	*Fomes*	*fomentarius*	Horseshoe Mushroom, Hoof Fungus, Tinder Fungus, Ice Man Fungus	
44	*Fomitopsis*	*officinalis*	False Tinder Fungus, Hoof Fungus, Tinder Conk, Tinder Polypore, Ice Man Fungus	
45	*Ganoderma*	*applanatum*	Jannabibulocho	
		gibbbosum	Wood-Decay Fungi	
		lucidum	Reishi, Lingzhi, Varnished Conk, Ling Chih	
46	*Geastrum*	spp.	Earthstars	
47	*Grifola*	*frondosa*	Maitake, Hen-Of-The-Woods, Ram'S Head, Sheep'S Head	

Table 1. Scientific and common names of mushrooms used in the review. (*continued*)

Sr. No.	Genus	Species	Common name
48	*Hericium*	*coralloides*	Coral Tooth Fungus, Comb Coral Mushroom
		erinaceus	Lion'S Mane, Yamabushitake, Bearded Tooth Fungus, Bearded Hedgehog
		mollifolium	
49	*Hydnum*	*repandum*	Sweet Tooth, Pig's Trotter, Wood Hedgehog, Hedgehog Mushroom
50	*Hypomyces*	*chrysospermus*	White Moth Mushroom
51	*Hypsizygus*	*ulmarius*	Elm Oyster Mushroom
52	*Inonotus*	*obliquus*	Chaga, Birch Canker Polypore, Clinker Polypore, Birch Conk
53	*Irpex*	*lacteus*	Milk-White Toothed Polypore
54	*Lactarius*	*deliciosus*	Pineflower Mushrooms, Saffron Milk Caps, Red Pine Mushroom
		flavidulus	Yellowish Milkcap, Yellowish Lactarius
55	*Lentinula*	*edodes*	Shiitake Mushrooms
56	*Lentinus*	spp.	Woodcaps, Sawgills
57	*Leucopaxillus*	*Leucopaxillus*	Arge , White Leucopax, Leucopaxillus
58	*Lucid*	*ganoderma*	Reishi, Varnished Conk, Ling Chih
59	*Lyophyllum*	spp.	Fried Chicken Mushroom, Clustered Domecap
60	*Marasmius*	*oreades*	Fairy Ring Mushroom, Scotch Bonnet
61	*Morchella*	*esculenta*	Morel, Yellow Morel, True Morel, Morel Mushroom, Sponge Morel, Guchhi
62	*Ophiocordyceps*	*sinensis*	Chinese Caterpillar Fungus, Yartsa Gunbu
63	*Panus*	*rudis*	Ruddy Panus, Hairy Trumpet
64	*Phellinus*	*igniarius*	Willow Bracket, Fire Sponge, False Tinder Polypore, Punk Ash Polypore, False Tinder Conk
		linteus	Meshimakobu, Sanghuang, Sanghwang, Mesima, Black Hoof Mushroom
65	*Pholiota*	*nameko*	Nameko Mushroom, Pholiota Nameko, Butterscotch Mushroom
		spp.	Shaggy Scalycap, The Shaggy Pholiota, The Scaly Pholiota
66	*Pleurotus*	spp.	Oyster Mushroom, Shaggy Scalycap, The Shaggy Pholiota, The Scaly Pholiota
		citrinopileatus	Golden Oyster
		cornucopiae	Branched Oyster Mushroom, Cornucopia Mushroom
		djamor	Pink Oyster Mushroom
		eryngii	King Trumpet Mushroom, Rench Horn Mushroom, Eryngi, King Oyster Mushroom, King Brown Mushroom, Boletus of The Steppes, Trumpet Royale, Ali'i Oyster
		ostreatus	Oyster Fungus, Hiratake, Pearl Oyster Mushroom
		pulmonarius	Oyster Mushroom, Pollinosis Mushroom, Indian Oyster, Italian Oyster, Phoenix Mushroom, The Lung Oyster
67	*Polyozellus*	*multiplex*	Blue Chanterelle, Clustered Blue Chanterelle, Black Chanterelle
68	*Polyporus*	*umbellatus*	Umbrella Polypore
69	*Poria*	*cocos*	Fu-Ling, Hoelen, Tuckahoe, Indian Bread, China Root, China Tuckahoe, Matsuhodo
70	*Russula*	spp.	Russula, Brittlegills
71	*Sarcodon*	*aspratus*	Sarcodon, Toothed Hydnoid Fungus
72	*Schizophyllum*	*commune*	Split-Gill Mushroom, Common Split-Gill
73	*Sparassis*	*crispa*	Cauliflower Fungus, Wood Cauliflower, Cauliflower Mushroom, Zinnia mushroom
74	*Stropharia*	*rugoso-annulata*	Wine Cap Stropharia, Garden Giant, Burgundy Mushroom, King Stropharia
75	*Suillus*	*placidus*	Slippery White Bolete
		spp.	Slippery Jacks, Larch Boletes
76	*Termitomyces*	spp.	Termite Mushrooms
77	*Naematelia Syn Tremella*	*aurantialba*	Golden Ear Mushroom, Golden Ear
78	*Tremella*	*fuciformis*	Snow Fungus, Snow Ear, Silver Ear Fungus, White Jelly Mushroom, White Cloud Ears

Table 1. Scientific and common names of mushrooms used in the review. (*continued*)

Sr. No.	Genus	Species	Common name
79	*Tricholoma*	*bakamatsutake*	Fool's Matsutake, Baka-Matsutake
		caligatum	True Booted Knight, Brown Matsutake, False Matsutake
		magnivelare	American Matsutake, White Matsutake, Ponderosa Mushroom, Pine Mushroom
		matsutake	Matsutake Mushroom, Pine Mushroom, Songi (Korea), Song-Koumo, Oak-Mushroom, Pine-Fungus (China)
		terreum	Grey Knight, Dirty Tricholoma, Earthy Tricholoma, Mouse Tricholoma
80	*Volvariella*	*volvacea*	Paddy Straw Mushroom, Straw Mushroom, Chinese Mushroom
81	*Wolfiporia*	*extensa*	Hoelen, Poria, Tuckahoe, China Root, Fu Ling, Matsuhodo
82	*Xerocomus*	spp.	Suede Bolete, Brown & Yellow Bolete, Boring Brown Bolete, Yellow-Cracked Bolete

Common genus classification for multiple associated species and vice versa is entered once. Source: https://en.wikipedia.org/wiki/Edible_mushroom; https://www.mssf.org/cookbook/moreedible.html; https://www.first-nature.com/fungi/index1binom.php.

Anti-cancer activity

Latest reports propose the control of cancerous cell proliferation by mushrooms in the treatment of a variety of cancers [12]. Medicinal mushrooms have also been approved as an addition to standard cancer treatments in Japan and China, either alone or combined with radiation or chemotherapy. Varieties such as *Ganoderma lucidum*, *Trametes versicolor* or *Coriolus versicolor*, *L. edodes*, and *Grifola frondosa* are being studied for their effects on the immune system and on tumor cells. According to a recent report, it is thought that the polysaccharides (β-glucans) in mushrooms strengthen the immune system to fight cancer [13]. Twenty-four patents were identified that indicate the use of mushrooms and/or their isolated phytochemicals with anticancer activity. We found that the majority of research on anticancer is carried out using the *Ganoderma* variety. An Indian patent assigned to Amala Cancer Research Center Society has claimed a natural edible chemotherapeutic agent comprising concentrated defatted methanolic extract from *Morchella esculenta* exhibiting tumor inhibition of at least 85% per 500 mg/kg body weight treatment [14]. Pharmaceutical sediments containing ethanol extract of *Auricularia polytricha* are claimed to decrease the proliferation and expression of colon cancer cells and effectively inhibit the growth of tumor cells without any side effects [15]. Two USA patents have claimed the anticancer activity of bioactive compounds of *G. lucidum* extract (GLE) and their selective efficacy against breast cancer [16, 17]. In one patent, the inventor discloses the inclusion of GLE in the range of 100–450 mg per dose in a polyherbal composition. The β-glucan polysaccharides and triterpenoids in the extract not only promote apoptosis in cancer cells, but additionally downregulates estrogen-α receptors, cellular migration and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, provides anti-angiogenic effect through down regulation of vascular endothelial growth factor (VEGF), and inhibits metalloproteinase (MMP-9). Further, the complex synergistic combination with other constituents (quercetin, *Emblica officinalis*, indole-3-carbinol, catechins, *Allium sativum*) and minerals (iodine, selenium) enables curtailed dosage, avoiding the possible adverse effects resulting from use of several of the ingredients [16]. In the other patent, structures of the seven most abundant *G. lucidum* extracted compounds, and their selective efficacy against triple negative breast cancer (TNBC), inflammatory breast cancer (IBC), and other human cancer cell types, including both solid and blood malignancies, are disclosed, thereby confirming their potential as anticancer agents. While 5,6-dehydroergosterol, a bioactive compound purified from the GLE, was demonstrated as the single most biologically active compound against IBC models with promising half maximal effective concentration (EC_{50}) values in the low micromolar range (SUM-149) and ample therapeutic index in normal cells (BJ, HMEC), its sulfonamide derivatives showed improved bioavailability [17]. A Chinese patent has disclosed an injectable formulation using GLE in a traditional Chinese Shuganning preparation showing an additive effect in treating breast cancer when combined with 5-fluorouracil (5-FU) [18]. Many inventors have commonly exploited the synergistic potential of cannabinoids and mushroom-based compositions for effective cancer treatment. An international application by Cannabotech has claimed the combination of cannabinoids and multiple mushrooms used as an adjunctive therapy to a conventional therapy for treating

breast cancer [19]. Another USA patent by Apollon Formularies Plc. has also claimed a composition comprising aqueous or ethanolic extract of one or more of an edible or medicinal mushroom, and at least one cannabinoid, along with additional terpenes, and flavonoids for the treatment of various cancer types [20]. Alvit Lcs Pharma Ltd. has claimed a composition comprising a synergistic combination of medicinal mushroom extracts such as *G. lucidum*, or *Cordyceps sinensis*, and *Cannabis* derived compound tetrahydrocannabinol (THC) for treating pancreatic cancer in mammalian subjects [21]. Another pharmaceutical composition comprising *Phellinus linteus* derived hispidine as an active ingredient, in combination with an anticancer agent selected from the group consisting of gemcitabine, gefintip, cisplatin, paclitaxel, oxaliplatin, and 5-FU in a ratio of 1:(0.004 to 0.02) is reported for treating pancreatic cancer. The synergistic combination can effectively treat pancreatic cancer through growth inhibition and cell death of the cancer cells [22]. Qilu University of Technology has claimed a new *Inonotus hispidus* strain from the wild *Phellinus igniarius* rich in various active ingredients such as polysaccharides, polyphenols, flavones, and triterpenes, and can be useful for preventing and treating cancer [23]. An anticancer pharmaceutical composition containing a mixture of *Coprinus comatus* mushroom extract, along with powder of *G. lucidum*, *L. edodes*, and *Pleurotus ostreatus* varieties is claimed to treat various cancers such as gastric, breast, uterine, colorectal, pancreatic, and liver cancer by suppressing the growth and spread of cancer cells, and increasing the activity of T cells with no side effects [24]. Combination therapy comprising *Lactobacillus plantarum* strain and herbal medicine comprising powder or extract form of *Cordyceps militaris* and *Phellinus linteus* mushrooms for anticancer activity particularly against colon cancer is claimed [25]. Pure active ingredients such as Striatal C, Striatal C', and Striatal D isolated from *Cyathus striatus* (CBS 126585) extract are claimed for their use in the treatment of epithelial cell cancer by combined administration with extracts of other medicinal mushrooms selected from the group consisting of *L. edodes*, *Coprinus*, and *Tremella species* [26]. Medicinal formulations for cancer treatment comprising either recombinant protein from *Ganoderma microsporum* in a dose from 5 μg/mL to 200 μg/mL [27], or betulinic acid derivatives from *Inonotus obliquus* mushroom extract are claimed [28]. Two Chinese patents have claimed the anti-liver cancer potential of mushrooms. The joint application by the two assignees Ganoherb Bio Technology Fujian Co. Ltd., and Fujian Xianzhilou Biological Science & Technology Co. Ltd. disclosed a composition containing GLE and sorafenib (SF) in optimal mass concentration ratio of 112.5:4 after considering the damage caused to liver cancer HepG2 cells, and the attenuating effect on L02 cells, the CI synergy index such that GLE effectively improved the sensitivity of SF by a combined synergistic effect [29]. According to the patent application assigned to Henan University of Traditional Chinese Medicine, a novel bicyclopyrrole aldehyde compound extracted from *L. edodes* can act as a new auxiliary in an anti-liver cancer drug composition. The compound has an in vitro growth inhibitory activity on the liver cancer cell line (SMMC-7721), without any toxic or side effects on the normal human normal liver cell line HL-7702 [30]. Hunan Wanzhen Biotechnology Co. Ltd. has filed six patents claiming the application of the polysaccharide selenoside-II and selenoside-III extracted from *P. ostreatus* mushroom as anticancer active ingredient in preparation of drug composition for treating different cancer types. While the polysaccharide selenoside-II has been demonstrated to inhibit the growth of non-small lung adenocarcinoma cells [31], polysaccharide selenoside-III inhibits the growth of liver cancer cells [32], colon cancer cells [33], breast cancer cells [34], kills gastric [35] and prostate cancer cells [36]. Both polysaccharides can reduce toxic side effects while promoting the metabolism and proliferation of normal cells. In another Chinese patent an effective component of *P. igniarius* mycelia concentrated solution has been claimed for resisting lung cancer cell proliferation on the human lung cancer A549 cell line [37].

The distribution of mushroom varieties for various anticancer applications across the reviewed patent literature is summarized in Table 2.

Anti-infective activity

Scientists have studied the action of mushrooms as a favourable source of natural antibiotics and biofilm-preventing agents. Various species such as *G. lucidum*, *Laetiporus sulphureus*, *and L. edodes*, are reported to

Table 2. Selected research on mushrooms with anticancer activity.

Reference	Name of mushroom	Bioactive	Types of cancer (claimed)	Biological role
[14]	*Morchella esculenta*	-	Cancer*	Inhibits tumor
[15]	*Auricularia polytricha*	-	Colon cancer	Decreases proliferation, expression of cancer cells
[16]	*Ganoderma lucidum*	β-Glucan polysaccharides; triterpenoids	Breast cancer	Downregulates estrogen-α-receptors, NF-κB pathway, cellular migration, VEGF pathway, inhibits MMP-9, promotes anti-angiogenic effect, apoptosis in cancer cells
[17]	*Ganoderma lucidum*	5,6-Dehydroergosterol Ergosterol peroxide	Breast cancer	Decreases cancer cell viability, induces cell cycle arrest and apoptosis, reduces cell migration, invasion, and key signaling pathways in cancer cells
[18]	*Ganoderma lucidum*	-	Breast cancer	Synergistic combination with 5-fluorouracil (5-FU)
[19]	Multiple species[1]	-	Breast cancer	Synergistic combination with cannabinoids, cytotoxic activity
[20]	Multiple species[2]	-	Cancers#	Synergistic combination with cannabinoids induces apoptosis of cancer cells, inhibits the VEGF pathway, migration, adhesion, or invasion of cancer cells, prevents angiogenesis of cancer cells, disrupts cancer cell growth, and restores normal cell cycle in cancer cells
[21]	Multiple species[3]	-	Pancreatic cancer	Synergistic combination with THC, decreases IL-6 secretion, immune-stimulator
[22]	*Pellinus linteus*	Hispidine	Pancreatic cancer	A synergistic combination with gemcitabine, gefintip, cisplatin, paclitaxel, oxaliplatin, and 5-FU inhibits the growth of cancer cells
[23]	*Phellinus igniarius*	-	Lung cancer	Inhibits the proliferation of human lung cancer A549 cells
[24]	Multiple species[4]	-	Cancers#	Inhibits the proliferation of cancer cells and increases the activity of T cells with no side effects
[25]	*Phellinus linteus*, *Cordyceps bassiana*	-	Cancers#	A synergistic combination with *Lactobacillus plantarum* strain inhibits the proliferation of cancer cells and tumors, and reduces side effects
[26]	Multiple species[5]	Striatal C, Striatal C', Striatal D	Cancers#	NA
[27]	*Ganoderma microsporum*	Immunomodulatory protein	Cancers#	Induces a specific active immune response of the immune cells against the tumor cells, enhancing immunogenicity without toxicity
[28]	*Inonotus obliquus*	Betulinic acids I and II	Cancers#	Inhibits cell viability and ATP levels of cancer cells
[29]	*Ganoderma lucidum*	-	Liver cancer	Synergistic combination with sorafenib inhibits the proliferation of HepG2 cells
[30]	*Lentinula edodes*	Bicyclic pyrrole aldehyde [3-ethyl-4-oxo-2,4,5,6-tetrahydrocyclopenta(c)pyrrole-1-carbaldehyde]	Liver cancer	Inhibits the proliferation of liver cancer SMMC-7721 cells
[31]	*Pleurotus ostreatus*	Polysaccharide selenoside-II (heteropolysaccharide compound II modified	Lung cancer	Inhibits the growth of non-small lung adenocarcinoma cells

Table 2. Selected research on mushrooms with anticancer activity. (*continued*)

Reference	Name of mushroom	Bioactive	Types of cancer (claimed)	Biological role
		with organic selenium)		
[32]		Polysaccharide selenoside-III (heteropolysaccharide compound III modified with organic selenium)	Liver cancer	Apoptosis of HepG2 cells without damaging normal hepatocytes
[33]			Colon cancer	Apoptosis of HCT116 cells without damaging the normal colon cell line
[34]			Breast cancer	Apoptosis of MCF-7 cells without damage to normal breast cells
[35]			Gastric cancer	Apoptosis of MGC803 cells without damage to normal cells
[36]			Prostate cancer	Apoptosis of PC-3 cells without damage to normal cells
[37]	*Phellinus igniarius*	-	Cancer	Inhibiting the proliferation of lung cancer A549 cells

*: Cancer type is not specifically claimed; #: includes one or more from the list of cancers: lung, breast, brain, oral, esophageal, stomach, gastric, glioma, colon, liver, cervical, bladder, uterine, colorectal, pancreatic, prostate, cutaneous, ovarian, gallbladder, biliary tract, thyroid, laryngeal, acute myeloid leukemia, neuroblastoma, retinoblastoma, melanoma, etc. 1: *A. bisporus*, *G. lucidum*, *G. frondosa*, *L. edodes*, *T. versicolor*; 2: *A. blazei*, *A. confluens*, *A. camphorate*, *B. badius*, *C. maxima*, *C. militaris*, *C. sinensis*, *C. liangshanensis*, *C. gunnii*, *C. cicadicola*, *F. velutipes*, *F. fomentarius*, *F. trogii*, *G. lucidum*, *G. fondosa*, *H. erinaceus*, *I. umbrinella*, *I. olbiquus*, *L. flavidulus*, *L. edodes*, *P. linteus*, *P. ostreatus*, *S. commune*, *S. placidus*, or *T. versicolor*; 3: *G. lucidum*, *C. sinensis*, *G. frondosa*, *T. versicolor*, *C. versicolor*, *I. obliquus*, *L. edodes*, *A. blaze*i; 4: *C. comatus*, *L. edodes*, *G. lucidum*, *P. ostreatus*; 5: *Cyathus striatus*, *L. edodes*, *Coprinus* spp., *Tremella* spp. IL-6: interleukin-6; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; THC: tetrahydrocannabinol; VEGF: vascular endothelial growth factor; ATP: adenosine triphosphate.

show antimicrobial activity. The methanolic extracts of *Fistulina hepatica*, *Ramaria botrytis*, and *E. delica*, rich in phenolics, are also reported to be effective against multi-resistant microorganisms such as *Proteus mirabilis*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli*. While the phenolic compounds and extract of *Agaricus blazei* is reported for anti-quorum sensing effect, oral biofilm inhibition is known for *L. edodes* extract [38]. Mushroom extracts are known to demonstrate therapeutic effects against pneumonic superinfection and severe lung inflammation that often complicates COVID-19 infection. A recent review at Oslo University has stated that the antimicrobial properties of *A. blazei*, *Hericium erinaceus*, and *G. frondosa* mushrooms could be used to combat COVID-19 [39]. An in-depth analysis of fifteen patents under this subsection reveals that, along with mushroom extract, specific active compounds such as the *P. linteus* polysaccharide also contributes to the antimicrobial effect by the fungus. A USA patent assigned to Mycelium Biotech Assets Ptd. Ltd. has claimed the use of GLE in the manufacture of a medicament for the treatment of viral, bacterial, fungal, and/or protozoal infections in humans [40]. Pharmaceutical composition comprising a dry extract of *G. lucidum* (polysaccharide titer of 50%) is also claimed for the treatment of HPV (papilloma virus) vaginal infections [41]. Bharath Institute of Higher Education & Research in India has claimed the protection of medicinal composition comprising *Ganoderma* extract for antifungal and antibiofilm activity [42]. Studies have been reported for the pharmacological potential of certain mushrooms in managing skin ailments owing to their antioxidant, anti-inflammatory, and antimicrobial properties [43]. Skin care capsule formulations specifically for the treatment of acne comprising GLE in a 2:1 combination with saw palmetto are claimed by Bottled Science Ltd. in two patents. This combination reduces the concentration of dihydrotestosterone in the body and additionally, the *Ganoderma sichuanense* extract also boosts the immune system [44, 45]. Antiacne medicines from the extraction of *L. edodes* is also claimed [46]. Another antibacterial composition containing fruiting body of *P. linteus* mushroom ethanol extract, and more specifically, *L. edodes* mushrooms grown by adding fermented sulfur as an active ingredient, is claimed for broad-spectrum antibacterial activity [47]. Mushroom bioactive compounds such as daedalin A and a derivative isolated from the mycelium culture solution of *Daedalea dickinsii* are claimed for use in a pharmaceutical composition for disinfecting helicobacter [48]. Antiviral pharmaceutical composition with therapeutic agent originated from different edible or medicinal mushroom extracts, along with one or more cannabinoids, is reported in PCT application filed by AI Pharmaceuticals Jamaica Ltd. [49]. In another PCT application, the assignee has claimed an antiviral composition comprising a polar extract

of *Astraeus asiaticus*, along with acyclovir in a weight ratio of 1:1 to 4:1 for use in the treatment of hand, foot and mouth disease (HFMD) [50]. Grape King Bio. Ltd. has claimed an oral composition comprising bioactive components of *P. linteus* mycelia for antiviral efficacy against enterovirus type 71 [51]. Anhui Senbaigu Pharmaceutical Co. Ltd. and Anhui Medical University jointly owns two patents claiming the use of *P. igniarius* for antiviral pharmaceutical composition. In one patent, *P. igniarius* extract is used alone, and in the other patent application it is claimed for use in combination with *Thesium chinense* compound for preparation of therapeutic drugs for treating corona virus respectively [52, 53]. While the *P. igniarius* extract showed significant antiviral effect by inhibiting viral replication, increasing the virus clearance rate demonstrating very low cytotoxicity on Vero cells [half-maximal inhibitory concentration (IC_{50}) of water extract was 3,408.194 μg/mL, and IC_{50} of alcohol extract was 1,398.063 μg/mL] [52], the medicinal composition of *P. igniarius* and *Thesium chinense* compound was ideal for treating coronary pneumonia due to the combined anti-inflammatory effect of *Thesium chinense* and the immunity regulation effect of *P. igniarius* [53]. Oral pharmaceutical compositions comprising *P. linteus* polysaccharide extracts are also protected by Taijian Biotech for preventing the bio-membranes of the periodontal bacteria from adhering to teeth and gums [54]. A PCT application has claimed the antibacterial activity of *Sarcodon aspratus* extract in a composition for inhibiting oral diseases such as periodontitis, periimplantitis, dental caries, gingivitis, halitosis, etc. [55].

Anti-inflammatory activity

Mushroom bioactive metabolites, including peptides, polysaccharides, terpenes, sterols, fatty acids, phenols, and many other low molecular weight molecules, have been well reviewed for their mechanisms of action as potent anti-inflammatory agents [56]. It is well demonstrated that these compounds possess a significant inhibitory effect on the major pro-inflammatory biomarkers and associated signaling pathways both in the in vivo and in vitro settings [57]. Eight patents under this category were analyzed to evaluate the anti-inflammatory potential of mushroom materials as claimed by inventors. Therapeutic compositions comprising extracts or isolates of edible or medicinal mushroom species such as *Polyporus umbellatus*, and *M. esculenta* alone or in combination with other natural extracts are reported for enhancing the anti-inflammatory function for a variety of different inflammatory diseases including inflammatory bowel and skin disease, retinitis, gastritis, hepatitis, enteritis, arthritis, tonsillitis, laryngopharyngitis, bronchitis, pneumonia, pancreatitis and nephritis [58, 59]. The polyherbal composition comprising *P. umbellatus* water extract exhibited a high inhibitory effect against nitric oxide and the catalyzing enzymes inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) [58]. Another patent has claimed the anti-inflammatory action of *M. esculenta* extract by increasing superoxide dismutase activity, and glutathione concentration [59]. In another invention, a composition comprising aqueous or ethanolic extract of one or more edible or medicinal mushrooms along with an extract from *Cannabis* spp. has been claimed for the treatment of inflammatory diseases [60]. A Chinese patent has provided an effective method for extracting *L. edodes* dregs and its use in medicament showing higher in vitro inhibition of lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 cells [61]. In another invention, a composition is claimed for treating neuroinflammation which comprises 0.01% to 99.99% of a red ginseng extract cultured from fermented complex mushroom-grain aged strain obtained by co-cultivating the fermented complex mushroom-grain ripening strain and red ginseng and extracting them with water, alcohol, or a mixed solvent [62]. Compounds in medicinal mushrooms have been reported to act in the early inflammatory phase of wound healing by promoting growth and multiplication of keratinocytes [63]. Two Korean patents have claimed a pharmaceutical composition comprising extracts of *M. esculenta* in combination with bentonite for wound healing [64, 65]. The compositions operate on the immune system by removing harmful bacteria and restoring the affected areas. In another Chinese application by Zhuhai Weimei Biotechnology Co. Ltd., a polysaccharide-containing biomedical dressing comprising β-glucan and chitosan from *G. lucidum* as the key active ingredients, along with glycerol and carbomer as auxiliary, is claimed for treating burns, and nursing of non-chronic wounds [66].

Inflammation and skin disorders

Mushrooms are thoroughly researched to identify valuable new drug candidates for skin diseases and disorders (SDDs) that vary greatly in symptoms and severity [67]. A pharmaceutical composition comprising a complex extract of *Pleurotus cornucopiae* and *Rehmannia glutinosa* as active ingredients is claimed for treating inflammatory skin diseases. Combination of the complex extract not only reduces nitric oxide production, but also effectively inhibits the expression of inflammatory cytokines tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), IL-6, prostaglandin E2 (PGE2), iNOS, and COX-2 [68]. Atopic dermatitis (AD) is a persistent inflammatory condition of the skin that often leads to allergic disorders along with pruritic and eczematous skin lesions. Inherited predisposition, environmental host factors, bacterial infection, skin barrier dysfunction, and immunological factors appear to play a significant role in its development. Recent research in herbal medicines, such as the use of *C. militaris* mushroom extract in the treatment of AD-like skin lesions is reported for better efficiency and reduced side effects [69]. Compositions containing composite extracts of *Sparassis crispa*, *C. militaries*, and truffles as active ingredients are claimed in a Korean patent for treatment of AD, pruritus, and inflammation [70]. Patents claiming a medicinal composition comprising either ganoderic acid or its derivative isolated from an GLE, or polyozellin or its pharmaceutically acceptable salt isolated from extracts of *P. multiplex* as active ingredients is claimed for the prevention and treatment of AD by inhibiting the expression of IL-6, psoriasin, and concentration of immunoglobulin E (IgE) [total IgE and *Dermatophagoides farinae* extract (DFE)-specific IgE] and IgG2a in serum [71, 72]. Psoriasis is a chronic skin inflammatory disease affecting 2–3% of the world's population, including approximately 0.5–1% of children. It is mainly caused by the interactions between epidermal keratinocytes, dermal vascular cells, and immunocytes [73]. An individual inventor has claimed a method for treating or alleviating psoriasis by administering a pharmaceutical composition comprising an effective amount of an immunomodulatory protein derived from the *Ganoderma* genus, or a recombinant or fragment [74]. A Chinese patent application filed by Shanghai Zhina Biotechnology Co. Ltd. has claimed the preparation of a keratinocyte function protective agent for repairing skin damage caused by sodium dodecyl sulfate by combining *Agaricus bisporus* extract with a composition of wild chrysanthemum, orientalis leaves, and sophora flavescens in 15–40% each, and 10–35% liquorice. The agent can effectively promote the expression of cell ELOVL1 mRNA in skin, thereby maintaining the skin barrier function [75].

Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a chronic inflammatory disease that impairs the gastrointestinal tract. The effects and putative mechanisms of action of various natural polysaccharides, more particularly the glucans harvested from mushrooms, are being researched for the treatment of IBD [76]. Two patents claiming pharmaceutical compositions comprising mushroom extracts for treating IBD were identified within this study period. A Korean patent has claimed the use of *P. linteus* extract in 0.01–1 g/L for treating IBD, by promoting the growth of intestinal beneficial *Lactobacillus* spp., and inhibiting the growth of intestinal harmful bacteria [77]. In another patent, mushroom bioactive components such as psilocybin, psilocin, along with extracts from *Hericium* mushroom, together with one or more cannabinoids, are claimed for treating irritable bowel syndrome (IBS). The inventors have further demonstrated that psilocybin, alone or in combination, provides superior benefits in treating the 5-hydroxytryptamine serotonin 2A (5-HT2A) receptor-associated IBS [78].

Immuno-enhancer

The amelioration and treatment of diseases associated with immune dysfunction, such as immunodeficiency and/or autoimmunity, pose significant medical and economic challenges. Mushrooms and/or their extracts have been advocated as potential immune modulators for immunotherapy and autoimmunity [79]. Mushroom constituents, including polysaccharides (β-glucans), triterpenoids, lectins, and proteins, are also reported to manifest immunomodulatory effects in the treatment of immune conditions such as multiple sclerosis (MS), rheumatoid arthritis (RA), and thyroid conditions [80]. An

individual inventor has claimed a method for extracting active ingredients from mushroom species including *Fomes fomentarius*, *G. lucidum*, and dried *L. edodes* and further developed a formulation for enhancing immune function while minimizing side effects [81]. In another invention, a composition comprising a complex of red ginseng extract and *L. edodes* mycelium extract is claimed for enhancing immunity by inducing activity of B cells or T cells which are responsible for the immune system, and promoting antibody formation in splenocytes [82]. Integria Healthcare has claimed a composition comprising stacked mushroom extracts from *G. lucidum*, *L. edodes*, and/or *G. frondosa* for a combined synergistic effect in the treatment of conditions associated with immunological dysfunction by immunostimulation of one or more pro-inflammatory cytokines [83]. A therapeutic composition comprising the bioactive compounds styrylpyrone, thyryllorone (hypholomine B), and davarialactone derived from *P. linteus* (KACC93057P) is claimed for enhancing immune function by manifesting the expression of IL-6 and TNF-α of macrophages in vitro [84]. Chinese patents have also emphasized the activity of mushroom-derived polysaccharides in pharmaceutical products for enhancing immunity. In one patent the inventors have shown the improved immunoregulatory activity of three polysaccharides derived from *A. bisporus* namely, microbial polysaccharide (MP), and two high-purity uniform polysaccharides—polysaccharide MP-1 and MP-2 in recovering the body weight of immunocompromised mice by increasing spleen and thymus indexes, improving spleen lesion conditions, and enhancing the expression of TNF-α, NO, and IL-6 in serum of the mice [85]. Similar effect is also claimed in another Chinese patent assigned to Zhejiang Johncan Biotechnology Co. Ltd., wherein β-glucan component of average molecular weight 32,589–36,584 daltons and total polysaccharide content greater than 95% extracted from *G. lucidum* is shown to enhance the immunocompetence of mice by increasing the thymus and the spleen index, enhancing the NK cell killing activity, and increasing the content of IL-2 and IL-4 in serum [86].

Arthritis

RA is a systemic autoimmune disease that affects 0.5–1.0% of the world's population, causing chronic symptoms such as joint swelling, stiffness, and immune senescence, particularly posing increased risk of disability in the elderly population. Researchers have studied the anti-inflammatory, immunomodulatory, anti-angiogenic, and osteoprotective effects of *G. lucidum* polysaccharides on RA [87, 88]. Jeju National University, Korea, in a recent PCT application, has claimed a composition comprising a supercritical extract of *G. lucidum* spores for preventing or treating arthritis [89]. Other assignees have also claimed pharmaceutical compositions wherein active ingredients from extracts of one or more mushrooms, such as *Wolfiporia extensa*, *S. aspratus*, *L. edodes* along with other herbal extracts are used for treating RA [90, 91]. The claimed compositions containing the active extracts effectively treat RA by promoting IL-10 or IL-12 secretion, inhibiting proliferation and migration of synoviocyte lines, and inhibiting production of inflammatory cytokines IL-6, IL-1β, TNF-α, C-C motif chemokine ligand 2 (CCL2), and C-X-C motif chemokine ligand 2 (CXCL2).

Neurodegenerative & mental disorders

Neurodegenerative diseases (ND) are represented by progressive damage to the brain or the nervous system. Scientific research has proposed the beneficial effects of edible mushrooms in preventing age-based neuronal dysfunctions such as Parkinson's and Alzheimer's diseases. Mushroom species such as *G. frondosa*, *Lignosus rhinocerotis*, *H. erinaceus* are reported for improving cognitive functions and ND treatments [92]. Grape King Bio. has claimed a pharmaceutical composition prepared by using *H. erinaceus* mycelium extract, containing erinacin S as an active ingredient for improving central nervous system myelination [93]. Synergistic and entourage enhanced combinations of psilocybin from the extract of psychedelic mushroom *Psilocybe cubensis*, psychoactive tryptamines, and cannabinoids are also claimed for developing compositions to treat central nervous system disorders [94]. A similar composition comprising a combination of major and minor tryptamines from *Psilocybe* spp., such as psilocybin or a structurally similar analog, and norbaeocystin, respectively, for treating a neurological or psychological disorder is claimed by the inventors from the University of Miami [95]. Recent studies have suggested that

microdosing the hallucinogenic drugs psilocybin and psilocin, belonging to the mushroom genus *Psilocybe*, resulted in greater improvements in the mental health of individuals by acting via 5-HT2A serotonin receptors, and can be a new treatment option for depression. While Psilocybin itself is not psychoactive, the rapidly dephosphorylated derivative psilocin, formed upon ingestion in the mucosa by alkaline phosphatases and nonspecific esterases, causes the hallucinogenic effect as it is structurally similar and binds to over 15 human signaling serotonin-related receptors [96, 97]. Optimi Health Corp. has filed two patents wherein a transdermal pharmaceutical composition comprising psilocybin and psilocin from *Psilocybe* mushrooms in deep eutectic solvent is claimed for the treatment of anxiety, depression, and other mental health conditions [98, 99]. In another patent, the assignee Mydecine Innovations Group Inc. has claimed a pharmaceutical composition comprising the combination of the serotonin receptor agonist psychedelic compound psilocybin, along with a suitable uridine 5'-diphospho-glucuronosyltransferase (UGT) inhibitor for not only inhibiting the metabolic breakdown and clearance of psilocin by glucuronidation, but also modulating the physiological response of the psychedelic compound in the subject [100]. Two patents assigned to Korea University Industrial & Academic Collaboration Foundation have claimed antidepressant compositions containing ethanolic extract of *Pleurotus eryngii* as an active ingredient. The extract has been shown to inhibit the binding of serotonin receptors with selective serotonin reuptake inhibitors in animal models, thereby activating signaling mediated by serotonin receptors to prevent depression [101, 102]. Pharmaceutical compositions comprising extracts of *Poria cocos* or dried *Agaricus* fruit bodies are also claimed for anti-depression activity [103, 104]. A composition comprising the bioactive compounds coralloicins A, B, and C isolated from the mushrooms *Hericium coralloides* or *H. erinaceus* for treating depression is claimed by Rembiotics [105]. Antidepressant compositions comprising serotonergic psychedelics from mushroom species including *G. lucidum*, *H. erinaceus*, *C. sinensis*, *C. militaris*, *Cordyceps liangshanensis*, *Cordyceps gunnii*, or *Cordyceps cicadicola* in combination with cannabinoids extracted from *Cannabis sativa* have been claimed for the treatment of psychosis and psychotic disorders [106]. Sichuan Edible Fungi Research Institute has claimed a method for preparing an enzyme-removed water extract of *Flammulina velutipes* mushroom containing γ-aminobutyric acid content of 0.15–1%, and its use in the preparation of an antidepressant product [107].

Anti-aging activity

Oxidative stress from reactive oxygen species can disturb the body's natural mechanisms to fight harmful free radicals, causing accelerated aging and other medical complications such as ND and a decline in physiological function. Recent research has shown that the medicinal and edible mushroom species, namely *G. lucidum*, *H. erinaceus*, *P. ostreatus*, and *A. bisporus* containing bioactive ingredients such as carbohydrates, proteins, lipids, and phenolic compounds, possess the potential to combat the adverse impacts of skin aging while fortifying cellular health [108–110]. Nippon Menard Cosmetic Co. Ltd. has identified a highly safe supercritical, water and/or organic solvent extract of *G. lucidum* spores that has an excellent proliferation-promoting effect on stem cells, and hence can make a significant contribution in the field of anti-aging [111]. In another three patents, the assignee has demonstrated the neurogenesis, dermal, and hematopoietic stem cell differentiation action of the supercritical extract of *G. lucidum* spores which improves memory and learning associated with aging [112–114]. A Chinese patent jointly filed by Tongling Jieya Biologic Technology Co. Ltd. and Anhui University has claimed the preparation of *Tremella aurantialba* polysaccharide (TAP-W) and its use as a skin care substance that increases the content of skin collagen, and shows excellent tyrosinase inhibitory activity in ultraviolet-induced pigmentation in mouse skin [115]. A composition containing combined extracts of *P. linteus* and *Tremella fuciformis* in a mass ratio of (1–4):1 is claimed by Guangzhou EMG Biotech Co. Ltd. for the preparation of skin care products [116].

Musculoskeletal diseases

Pharmaceutical composition containing *I. obliquus* extract as an active ingredient for treating muscle diseases has been claimed by the assignee Phytomed. The mushroom ingredient increases the activity of mammalian target of rapamycin (mTOR), involved in muscle protein synthesis, and has an excellent effect

in suppressing the mRNA expression of muscle-specific RING finger protein 1 (MuRF1) and atrogin-1, involved in muscle protein degradation. Additionally, being a natural pharmaceutical product, it can be safely used without side effects [117]. Grape King Bio. Ltd. has claimed that an extract of a fermented product of *P. linteus* and/or its derivative can improve sarcopenia and maintain the amount of muscular endurance [118]. Several medicinal mushroom genera have been shown to improve bone stability by influencing ossification, mineralization, and resorption [119]. Pharmaceutical compositions containing mushroom active ingredients such as *P. linteus* extract, *T. fuciformis* product fermented with lactic acid bacteria, or aqueous *Auricularia auricula* extract are claimed for preventing osteoporosis [120–122]. The *A. auricular* extract is shown to exhibit an anti-osteoporosis effect by simultaneously regulating differentiation of osteoclasts and osteoblasts involved in osteoporosis. Another pharmaceutical composition comprising *L. edodes* mushroom extract derived vitamin D2 as an active ingredient is claimed for promoting bone formation [123]. Jilin Agricultural University has claimed the method of extracting bioactive galactomannan from *P. ostreatus* useful for protecting myoblasts from oxidative damage and preparing protective muscle cells [124].

Anti-thrombotic activity

Anti-thrombotic attributes of different types of mushrooms have been reviewed, and it is shown that *Ganoderma lucidium*, *Pleurotus giganteus*, and *A. auricula-judae* possess encouraging anti-thrombotic activities [125]. Ten patents have claimed a pharmaceutical composition comprising extracts of different mushrooms, including *T. fuciformis*, *Lentinus strigosus*, *Ganoderma gibbosum*, *G. lucidum*, *L. edodes*, and *P. linteus* as active ingredients for preventing or treating various thrombotic diseases. In two patents filed jointly by Kyungpook National University Ind Academic Coop Foundation and Industrial Cooperation Foundation Jeonbuk National University, the inventors demonstrated that the alcoholic extract of *T. fuciformis* mushroom, and 6-hydroxy-2,2-dimethyl-3-chromen isolated from *Panus rudis* can effectively treat various thrombotic diseases by inhibiting platelet aggregation and thrombus formation, inhibiting calcium ion mobilization, platelet granule secretion, while releasing adenosine triphosphate (ATP) following collagen stimulation [126, 127]. In another four patents, the inventors have claimed pharmaceutical compositions comprising extracts of mushrooms like *G. gibbosum*, *G. lucidum*, *L. edodes*, and *P. linteus*, which exhibit strong antithrombotic and anticoagulant activity by inhibiting thrombosis-related enzymes, thus improving blood circulation [128–131]. Subcritical water GLE has also been claimed for promoting the differentiation of a hematopoietic stem cell into a blood cell, thus providing immunity among the elderly, and preventing hematopoietic diseases such as anemia, neutropenia, and thrombocytopenia [132]. *A. bisporus* polysaccharide extract composed of galactose (6-galactose, 2,6-galactose, T-galactose, and 3,6-galactose), T-fucose, 6-mannose, and glucose has been claimed to have an ameliorating effect on atherosclerosis by reducing the blood fat levels and improving inflammatory response and oxidative stress as demonstrated in mice [133]. Fujian University of Traditional Chinese Medicine has claimed a polyherbal pharmaceutical composition comprising 8–14 parts each of *Antrodia camphorata*, Dilong, and *Angelica dahurica*, and 4–8 parts licorice for promoting angiogenesis and treating cerebral apoplexy and ischemic cerebral stroke [134]. An Indian application filed by Shoolini University of Biotechnology and Management Sciences has studied the haemostatic properties of wild *Irpex lacteus* mushroom methanolic extract showing positive pro-coagulation time and vasoconstriction properties in vitro testing [135].

Lifestyle diseases

Lifestyle-related diseases, primarily hypertension and diabetes has increased remarkably in recent years. Furthermore, obesity is reported to cause these lifestyle-related diseases to develop and progress secondarily, and synergistically increase the risk of developing arteriosclerosis. The onset and progression of these lifestyle-related diseases and metabolic syndrome are closely related to dyslipidemia. Studies show that polysaccharides derived from the mushrooms *P. ostreatus*, *Schizophyllum commune*, *Grifola rondosea*, *Sclerotium rolfsii*, *G. lucidum*, *L. edodes*, and *Hericium erunaceus* have a therapeutic effect against metabolic syndrome, characterized by obesity, hypertension, and elevated blood sugar levels [136, 137].

Pharmaceutical composition containing a dry extract of *I. obliquus* with humic substances (4:1), such as humic and fulvic acids in a 73:27 weight ratio, is claimed for treating metabolic syndrome [138]. An additional three patents have also disclosed compositions comprising active mushroom ingredients such as mycelial culture of *I. lacteus* [139], *P. cornucopia* [140], and *Ceriporia lacerate* [141] for the treatment of metabolic diseases such as diabetes, improving lipid metabolism, and treating obesity. Inventors have demonstrated that the presence of 35.21% β-glucan, and 44.34% extracellular polysaccharides, based on the dry weight in mycelial extract of *I. lacteus* (KACC83046BP) reduces blood glucose levels, thus showing high industrial potential for the development of a natural material-based antidiabetic agent free of adverse effects. A solid or liquid pharmaceutical formulation comprising mycelia of *L. edodes* cultured for 5–10 days in a medium of barley and rice bran mixture is claimed for treating obesity. The inventors have further demonstrated that the mushroom extract suppressed the increase in liver weight by inhibiting fat accumulation in liver tissue in obese mouse model [142]. A composition containing an extract of the *A. polytricha* strain (KACC93319P) has been claimed to inhibit the differentiation of preadipocytes into adipocytes, and show excellent anti-obesity activity by inhibiting weight increase due to high fat diet, visceral fat accumulation, blood glucose level, low-density lipoprotein (LDL) cholesterol, and triglyceride accumulation [143]. Another PCT application has claimed a composition comprising an aqueous or ethanolic extract of one or more edible or medicinal mushrooms, along with one or more cannabinoids derived from ethanolic extract of *C. sativa* for treating obesity by promoting weight loss [144]. Beijing University of Chinese Medicine has claimed a traditional medicinal composition comprising chicory root, *P. cocos*, and rhizoma smilacis glabrae useful for treating diseases related to lipid metabolism disorders such as hyperlipidaemia, hypertriglyceridemia and/or low-density lipidaemia, and gastrointestinal dysfunction such as gastrointestinal absorption disorders, intestinal peristalsis disorders, constipation or diarrhea [145].

Anti-hepatitis activity

Scientists have examined the liver-protective effects of mushroom compounds to elucidate their role in hepatitis treatment [146]. Research suggests that tetramic acid-type compound (MCA17-1) from engineered *Calcarisporium arbuscula* can act as a potential liver fibrosis inhibitor [147]. More recently, AHCC, a standardized extract of cultured *L. edodes* mycelia has been shown to suppress hepatic fibrosis by inhibition of hepatic stellate cell activation [148]. Six patents claiming the treatment of liver fibrosis using mushroom material are discussed in this section. Two patents assigned to Cojet Biotech disclose the liver fibrosis treatment efficacy of the compound 5-methylbenzo[*d*][1,3]dioxole-4,7-diol (MBDD) derived from *Antrodia cinnamomea* extract by decreasing the activity of hepatic stellate cells [148–150]. The Academy of Military Medical Sciences has disclosed a hepatoprotective traditional Chinese medicine comprising GLE along with other herbal components that can be used as a vaccine adjuvant or an immunomodulator for treating liver injury, hepatitis, hepatic fibrosis, hepatic cirrhosis, or liver cancer [151]. Another Chinese patent has also claimed the use of GLE, spore oil, and polysaccharides in a complex injection formulation for protecting the liver [152]. A method for treating fatty liver disease caused by the intake of a high-fat diet is claimed by Novacell Technology Inc. by administering a pharmaceutical composition containing an effective amount of a powder or a mycelium of the hybrid mushroom *Pleurotus* spp. (GBN2WP0970) [153]. The active ingredient shows an excellent triglyceride absorption inhibitory effect without any adverse side effects. Fujian Agriculture & Forestry University has claimed a simple, economical, large-scale preparation method of a polypeptide from *Volvariella volvacea* showing antioxidant activity, hepatoprotective effect, and good inhibitory effect on alcoholic liver injury concluded through animal experiments [154].

Anti-addictive

Psychedelic-assisted therapy has shown promising results in the treatment for substance use disorders (SUDs) [155]. A total of three patents are included in this section, which indicate a beneficial effect of psilocybin-assisted therapy on drug addiction and opioid withdrawal through combined administration of *Psilocybe* and *Cannabis*-derived agents. A topical hydrogel analgesic comprising cannabinoids, menthol, and an effective amount of the active component psilocybin and/or psilocin extracted from the mushroom

Psilocybe is claimed for treating drug addiction, particularly opioid addiction [156]. Another patent also claimed a composition comprising a combination of cannabinoids, terpenoids, herbs, and psychedelic compounds from a mushroom, such that the combined effect produces a superior therapeutic effect for alleviating opioid medicinal withdrawal symptoms [157]. A pharmaceutical herbal mixture comprising *P. cocos*, along with other herbs for treating alcohol hangover and associated conditions, is also claimed [158].

Pain management

Chronic pain is a major public health concern, primarily managed by conventional therapeutic agents, including opioid and non-opioid analgesics, which suffer from adverse side effects. Many psychedelic drugs extracted from mushrooms are being evaluated for their potential pain management activity through direct serotonin receptor agonism, anti-inflammatory effects, or synaptic changes [159]. Three patents are identified under this section that disclose the use of mushroom content in controlling different types of pain. A controlled release delivery system comprising polymeric spheres having the psychedelic compounds psilocybin and psilocin from the mushroom *Psilocybe*, encapsulated in a polymeric fibrous membrane, is claimed for treating fibromyalgia, chronic musculoskeletal pain, and other neuropathic pain [160]. The controlled release delivery system utilizing psychedelics is not only safe, but precise in the dosage and operates in a sustained and controlled dose manner. Another patent has claimed the use of *Agaricus* extract in a pharmaceutical composition for treating intestinal pain when administered at a dose of 60 mg–2.5 g daily via oral route [161]. Inventors have also claimed the use of *Wolfiporia* extract in developing a traditional Chinese medicinal composition for treating primary and secondary dysmenorrhea in women [162].

Spleen strength enhancer

Mushrooms containing bioactive ingredients have been claimed to modulate and increase spleen strength. Two Chinese patents have disclosed the use of *Wolfiporia* and *P. cocos* extract for regulating spleen deficiency [163, 164].

Respiratory disorders

Scientific studies have demonstrated the positive effects of *G. lucidum* spore and fruiting body on tobacco smoke carcinogen-induced lung toxicity and carcinogenesis [165]. In this section, two patents are highlighted for the same effect. In one patent, a method of treating chronic obstructive pulmonary disease (COPD) caused by emphysema or chronic bronchitis using a pharmaceutical composition comprising dried *P. cocos* in 20–80 wt% is claimed [166]. Another Chinese patent has claimed a composition comprising GLE including 8–20% triterpenes, and *G. lucidum* spore powder for inhibiting pulmonary fibrosis caused by radiation lung injury [167].

Miscellaneous patents

A single patent claiming a product comprising extracts or active compounds from one or more mushroom types or a method for the treatment of any specific condition or multiple conditions is grouped under this category. Nine patents [168–176] identified in this category were analyzed in Table 3 on the basis of the mushroom genus, extract or bioactive involved, and biological role per type of disorder as disclosed in the retrieved patents.

Table 3. Miscellaneous patents.

Reference	Name of mushroom	Bioactive/Extract	Disease name(s)	Biological role	Formulation type
[168]	*Psilocybe* spp.	Psilocybin, psilocin, 4-hydroxytryptamine, [3-(2-dimethylaminoethyl)-1*H*-indol-4-yl] dihydrogen phosphate, 4-hydroxy-*N*,*N*-dimethyl-tryptamine, 4-hydroxy-*N*,*N*,*N*-	Traumatic events: post-traumatic stress disorder (PTSD)	Pathological conversion of short-term memory (STM) to long-term memory (LTM) by promoting disengagement of pathological LTM by a chemical agonist/antagonist	Controlled release fixed-dose combination with a cannabis-derived agent as a capsule/multi-layer

Table 3. Miscellaneous patents. (*continued*)

Reference	Name of mushroom	Bioactive/Extract	Disease name(s)	Biological role	Formulation type
		trimethyltryptamine, [3-(2-methylaminoethyl)-1*H*-indol-4-yl] dihydrogen phosphate, [3-(2-trimethylaminoethyl)-1*H*-indol-4-yl] dihydrogen phosphate	Nicotine or alcohol addiction, anorexia, depression	shock	tablet
[169]	Multiple species[1]	Extract	Burns	Promotes cell regeneration by increasing the amount of collagen production, exhibits stronger antibacterial activity	Ointment, dressing agent, patch
[170]	*Sparassis crispa*	Extract	Dry eye syndrome	Promotes hyaluronic acid production and/or secretion in ocular keratocytes	Administered by oral route or as an eye drop
[171]	Multiple species[2]	Extract	Bladder disease	Uropathic, analgesic, anti-inflammatory	Administered by oral, nasal, intravenous, intra-arterial, intramuscular, intraperitoneal, ocular, buccal, vaginal, rectal, subcutaneous, transdermal routes
[172]	*Poria cocos*	Extract	Chronic renal failure	Reduction of blood creatinine and urea nitrogen reduces the expression of Bax and Caspase-3 and up-regulates the expression of bcl-2, inhibiting apoptosis and delaying the progression of CRF	Granule, capsule, tablet, pill, or oral liquid
[173]	*Agaricus blazei*	Extract	Benign prostatic hyperplasia (BPH)	Inhibits 5-α-reductase, catalase, superoxide dismutase, interleukin-1 beta, cyclooxygenase-2	Administered by oral, parenteral, inhalation, transplantation, and transdermal routes
[174]	Multiple species[3]	Extract	Keloid scar	Inhibit the proliferation of keloid fibroblasts to eliminate or reduce the symptoms of keloids or eliminate scar tissue	Liposome structure with lipid layer and composite core layer
[175]	Multiple species[4]	Extract	Post-acute sequelae severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PASC)	Moderating a hyper immune response, destroying and removing the SARS-CoV-2 spike protein from the gut and body, detoxifying the body and the brain, replenishing key nutrients, mitigating depression and anxiety, and a regimen of physical and mental exercise	Oral administration
[176]	*Wolfiporia extensa*	Extract	Insomnia	Promotes sleep, improves sleep quality, and prolongs sleep time	Granule, ointment, oral liquid, capsule, tablet, or pill

1: *C. sinensis*, *H. erinaceus*; 2: *Agaricus* spp., *Agrocybe* spp., *Albatrellus* spp., *Amanita* spp., *Antrodia* spp., *Auricularia* spp., *Boletus* spp., *Calvatia* spp., *Cantharellus* spp., *Caripia* spp., *Clitocybe* spp., *Cordyceps* spp., *Cyathus* spp., *Daldinia* spp., *Dictyophora* spp., *Elaphomyces* spp., *Flammulina* spp., *Pomes* spp., *Fomitopsis* spp., *Funalia* spp., *Ganoderma* spp., *Geastrum* spp., *Grifola* spp., *Hericium* spp., *Inocybe* spp., *Inonotus* spp., *Lactarius* spp., *Lentinus* spp., *Lentinula* spp., *Leucopaxillus* spp., *Lyophyllum* spp., *Phellinus* spp., *Pholiota* spp., and *Pleurotus* spp.; 3: *F. velutipes*, *T. fuciformis*; 4: *I. obliquus*, *T. versicolor*, *H. erinaceus*.

Conclusion & opinion

In recent years, edible and medicinal mushrooms have been extensively researched for pharmaceutical effectiveness due to the presence of multiple bioactive content. Advanced biotechnology and medicinal

chemistry have played a significant role in providing techniques for the isolation of the active components from mushroom extracts and exploring them in drug development. However, such efforts are heavily dependent on improved methods of cultivation for the smooth and continuous availability of the raw materials. The outcomes of the researchers can be protected by intellectual property rights. An increasing trend in the number of patents has been observed related to the use of mushroom components for treating different medical conditions. Reviewing such patents can provide great value and an increased return to companies on the investment made in developing new medicines. In India, while general methods of agriculture and horticulture, including mushroom cultivation, are not typically patentable under Section 3(h) of the Patents Act, 1970, patents can be obtained for specific inventions relating to mushrooms, such as compounds extracted from wild mushrooms or processes for developing formulations comprising mushrooms. The present study highlights the research findings on the therapeutic use and pharmacological activities of medicinal mushrooms and their bioactive compounds as disclosed in a selected set of one hundred and thirty-three patent art. Global trends in patent filing activity reveals that the research is presently focused in the South Asian countries like Korea, China, and Japan; however, a growing research interest is also observed in the USA.

The study aims to provide future research directions to the many important unsolved problems related to identifying mushroom bioactive ingredients and metabolites responsible for the prevention of diseases, exploring their chemical characterization, mechanism of action for leveraging synergistic combinations with reduced side effects, developing novel formulations, and integrating them into personalized medicine approaches. Extensive work has been carried out in the fields of cancer, infectious diseases, neurodegenerative disorders, inflammation, and the management of lifestyle diseases using various mushroom species. Our study shows that the *Ganoderma* and *Phellinus* genera have been most commonly claimed for diverse medicinal applications, wherein both the extract and isolated bioactive compounds have been used. Besides experimenting with the promising anticancer activity of mushroom isolated chemical substances, inventors have also claimed combination therapies by adding mushroom extracts with other actives such as *Cannabis* derived compounds in synergism to achieve superior benefits against cancer, infection, and other conditions. Some inventors have also evaluated the stacking of extracts or powders of multiple mushroom species to treat various conditions with an increase in activity alongside reduced side effects. Modified analogs of the mushroom-derived chemical constituents are also claimed to improve bioavailability and lower dosage. More recently, recombinant proteins derived from the *Ganoderma* genus have been claimed for the treatment of cancer and alleviating psoriasis. Compositions comprising serotonergic psychedelics such as psilocybin and psilocin from the *Psilocybe* genus with or without cannabinoids have been particularly claimed for the treatment of psychotic disorders, depression, drug addiction, and pain management. Our study has also identified many promising patent applicants researching in the field of medicinal mushrooms for broad-spectrum pharmacological activities for future licensing and collaborative partnerships.

In summary, more than twenty-five different genera of mushrooms are reviewed herein for targeting a range of specific health concerns within the body. As herbal and personalized medicines are becoming the desired option among patients to address their distress from conventional regimes, we believe that the insights from this review will help to address these future trends in the field of medicinal mushrooms. Major challenges may arise in the continuous production of mushroom ingredients in the entire supply chain, from cultivation to the extraction and preparation of the commercial formulation, as the raw material is seasonal in nature. Further research and clinical studies, precise monitoring, and regulation of the effects of mushrooms are needed to confirm their constituent compounds and understand their mechanistic role before considering them as alternatives to conventional drugs. Investigating the potential role of mushroom bioactives, both individually and as modified derivatives, either single or in combination with other actives in a united effect, is believed to provide practical solutions for researchers around the globe to develop effective medications in the near future, ensuring a high level of safety and bioavailability.

Abbreviations

5-FU: 5-fluorouracil

5-HT2A: 5-hydroxytryptamine serotonin 2A

AD: atopic dermatitis

ATP: adenosine triphosphate

CCL2: C-C motif chemokine ligand 2

COX-2: cyclooxygenase-2

CXCL2: C-X-C motif chemokine ligand 2

EC_{50}: half maximal effective concentration

GLE: *Ganoderma lucidum* extract

IBC: inflammatory breast cancer

IBD: inflammatory bowel disease

IBS: irritable bowel syndrome

IC_{50}: half-maximal inhibitory concentration

IgE: immunoglobulin E

IL-1β: interleukin-1 beta

iNOS: inducible nitric oxide synthase

LDL: low-density lipoprotein

LPS: lipopolysaccharide

MP: microbial polysaccharide

mTOR: mammalian target of rapamycin

MuRF1: muscle-specific RING finger protein 1

ND: neurodegenerative diseases

NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells

PCT: Patent Cooperation Treaty

PGE2: prostaglandin E2

RA: rheumatoid arthritis

SF: sorafenib

THC: tetrahydrocannabinol

TNBC: triple negative breast cancer

TNF-α: tumor necrosis factor alpha

VEGF: vascular endothelial growth factor

Declarations

Author contributions

PB: Conceptualization, Investigation, Data curation, Methodology, Supervision, Writing—original draft, Writing—review & editing. AM: Conceptualization, Investigation, Data curation, Supervision, Writing—original draft, Writing—review & editing. SW: Formal analysis, Validation, Visualization. All authors read and approved the submitted version.

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The authors declare that there are no conflicts of interest.

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