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Medicinal Mushrooms as Therapeutic Agents: A Narrative Review

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ABSTRACT

Medicinal mushrooms have been used for centuries in traditional medicine systems and are increasingly recognized in modern biomedical research for their diverse therapeutic potential. Their bioactive constituents, particularly polysaccharides, triterpenoids, and phenolic compounds, exert significant pharmacological effects, including immunomodulatory, antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. Species such as Ganoderma lucidum (Reishi), Lentinula edodes (Shiitake), Grifola frondosa (Maitake), and Cordyceps sinensis have demonstrated notable efficacy in preclinical and clinical studies, acting through mechanisms that regulate immune responses, inhibit tumor proliferation, modulate oxidative stress, and support metabolic health. The growing body of evidence positions medicinal mushrooms as promising complementary agents in the prevention and management of chronic diseases such as cancer, diabetes, cardiovascular disorders, and neurodegenerative conditions. However, despite their therapeutic promise, limitations such as variability in bioactive compound content, lack of standardized formulations, and insufficient large-scale clinical trials hinder their integration into mainstream medical practice. This review highlights the pharmacological mechanisms, therapeutic applications, and future prospects of medicinal mushrooms, emphasizing the need for rigorous scientific validation and regulatory oversight to ensure their safe and effective clinical use.

Keywords: Polysaccharides**,** Triterpenoids**,** Phenolic compounds**,** Immunomodulation, and Anticancer.

INTRODUCTION

Mushrooms and their extracts have been used for human consumption and the treatment of diseases for thousands of years. Immunomodulating properties, antioxidant activity, and antimicrobial effects of many medicinal mushrooms have been described. Polysaccharides, such as β-glucans and α-glucans, triterpenoids, such as ganoderic acid and lucidenic acid, together with many phenolic compounds, exhibit the strongest biological activities. These three classes of chemical compounds have been reported to play an important role in human health, mainly in immunomodulating, antioxidant, anti-inflammatory, and antimicrobial activities. The global demand for the utilization of mushrooms is constantly increasing, particularly in the search for new sources of medicine, which can be used in modern therapies and treatments of many diseases. Based on analysis of the available literature, the current paper reviews the main medicinal mushrooms, their chemistry, and mechanism of action, demonstrating the therapeutic use of mushrooms as alternative natural agents in the treatment of cancer, cardiovascular diseases, diabetes, and respiratory tract disorders. Development of a marked tolerance of many pathogenic microorganisms to antibiotics associated with a considerable incidence of side effects caused by synthetic drugs has created an urgent need to search for new bioactive natural compounds. Numerous studies indicate a diversity of compositions of biologically active substances with antibacterial, antiviral, antifungal, antioxidant, and anticancer properties in the kingdom of fungi. The possibility of infection and cross-contamination resulting from the use of synthetic antibiotics can also be eliminated. Research on the biological activity of fungi and their extracts has therefore become extremely popular. Of particular interest are medicinal mushrooms, that is, species whose extracts can be used in the prevention and treatment of various diseases. Their composition of biologically active substances capable of influencing the activity of the body's immune cells has been recognized and appreciated throughout the centuries in the traditional medicine of China, Japan, and Korea. Preparations with proven antiallergic, anticancer, antidiabetic, anti-inflammatory, antioxidant, and antimicrobial

properties and effects on blood pressure have also become common. Their use as alternatives in the treatment of cancer is especially emphasized.

Historical Use of Mushrooms in Medicine

Mushrooms have been consumed and utilized for medical purposes for thousands of years. Several mushroom species are widely known for their bioactive properties and use in human health, and this has led to their growing application in the form of whole plants, in powder form, and extracts in the search for new drugs [1]. Since ancient times, medicinal mushrooms have become an integral part of traditional medicine systems, used to prevent illnesses, treat tumor disorders, and develop immunity. Most ancient cultures believed that these organisms were the direct descendants of plants and therefore classified them among herbs [1, 2]. This assumption has later been proved incorrect, and mushrooms are now classified under the kingdom Fungi. Nevertheless, they remain important for the pharmaceutical and nutraceutical industries due to their effective pharmacological activities. Medicinal mushrooms contain a wide range of vital compounds such as polysaccharides, vitamins, minerals, proteins, phenolics, flavonoids, and terpenoids; the different medical objectives are described on an activity basis in detail [2]. Although mushrooms have been used extensively in prescription medicines worldwide, particularly in the countries of the Far East, they still prove to be an underexploited source of nutraceuticals worldwide; research should therefore be directed towards the clinical studies and therapy-oriented chemical profiling of various genera.

Chemical Composition of Medicinal Mushrooms

Medicinal mushrooms contain diverse bioactive molecules, most commonly polysaccharides but also triterpenoids and phenolic compounds, which may contribute to the prevention and treatment of chronic disorders [3]. Polysaccharides primarily from the fungal cell wall of the fruit bodies or mycelia are the most abundant, although isolated mycelial preparations may lack significant polysaccharide content. Fruit bodies also contain large amounts of triterpenoids and smaller quantities of phenolic compounds [3]. Extracts from non-medicinal mushrooms, such as the edible Agaricus bisporus, may also contain bioactive polysaccharides with health-promoting effects. Polysaccharides, especially homoglycans with α- or β-d-glucose units linked 1→3, 1→4 or 1→6, show diverse pharmacological activities, including immune-modulatory, antioxidant and antimicrobial effects 2. Triterpenoids, including lanostane derivatives, exhibit anticancer, anti-inflammatory, and antiviral activities. Phenolic compounds from mushrooms also display antimicrobial and antioxidant properties [3].

Polysaccharides

Fungal polysaccharides, including α- or β-glucans isolated from fruiting bodies, cultured mycelium, or broth, exhibit potential anticancer, immunomodulating, and antioxidant activities [4]. Polysaccharides from Morchella esculenta are medicinally important because they are not only immunomodulators but also function as antioxidants [5]. β-Glucans act as biological response modifiers that mediate host immune responses through direct interaction with host immune cells [1]. In vivo activity reflects the immunomodulating properties of mannogalactoglucan-type polysaccharides from the cultured fruiting body of Lentinus edodes.

Triterpenoids

Wood-rotting mushrooms contain more than 140 triterpenes and related compounds, of which Ganoderma lucidum is the most studied. Various bioactivities of triterpenes have been discovered, such as cholesterol synthesis regulation and anti-inflammatory, antibacterial, antiviral, antitumor, and analgesic activities. About 150 types of ganoderic acids have been identified, of which ganoderic acid A, ganoderic acid B, and ganoderic acid C1 are the most common. G [3, 4]. Lucidum triterpenoids possess anti-inflammatory, hepatoprotective, hypocholesterolemic, hemolytic, and anti-HIV properties. Ganoderic acid is an active ingredient of G. lucidum and has several biological activities [3]. The triterpenoids in G. lucidum also produce characteristic bitterness. Ling Zhi-8 (LZ-8), the immunomodulatory protein of G. lucidum, exhibits immunoregulatory and anticancer activity. G. lucidum extracts suppress HIV-1 protease activity. The laccase gene from G. lucidum has been used to develop the biosensor application. The polysaccharides of G. lucidum consist of only glucose, whereas the triterpenoids consist of carbon, hydrogen, and oxygen in a 30-carbon skeleton, which are responsible for the mentioned biological activities [4].

Phenolic Compounds

Three-quarters of the world's most widely used medicines for gastrointestinal, respiratory, cardiovascular, and integumentary illnesses are produced from natural sources. The fingerprint of phenolic products in herbs and medicinal plants is becoming a common factor. Numerous reports on phenolic extractives have been published in the literature, and the screening of such agents for bioactivities has been summarized [2, 3]. Effective cancer chemoprevention agents include antioxidants that quench reactive oxygen species and free radicals and modulate cancer-related transformation marking and transformation signaling. Other cancer chemoprevention agents stop cells from escaping their natural path of programmed cell cycle death by apoptosis. A plethora of biological activities are related to polyphenols isolated from P. eryngii, such as antiproliferative activity of polyphenols on human hepatocellular carcinoma (HepG2) cells and inhibitory effects of bis (3′-indolyl) methane (BIM) on human liver tumorigenesis initiated by aflatoxin B1 (AFB1) [4]. Strain survival over opposed conditions of

environmental pressure, radiation, thermal alteration, low or high pH values, and concentration of cyto/enzymotoxic metals demands a vast intracellular signaling network and sensing mechanism. Subcellular or intracellular localization of these compounds builds the other side of the acuteness of the defense mechanism. Phenolic compounds closely localized to the cell membrane act as stabilizers of membrane structure/fluidity. Sequestration of metallic/enzymatically active species can be made deliberate as per the intracellular conditions. This extraordinary localization property, in turn, protects the yeast strains from oxidative stress [2, 4].

Mechanisms of Action

A wide range of chemical substances found in medicinal mushrooms can be classified as primary and secondary metabolites. Primary metabolites, which include essential sugars, fats, and amino acids, begin to form during the lag phase of growth and peak at the beginning of the log phase. Secondary metabolites, such as antioxidants, triterpenes, lectins, sterols, and β- and α-glucans, are produced during the end of the log phase and contribute largely to the medicinal properties of mushrooms [1, 2]. While fruiting bodies and spores of mushrooms are used in traditional medicine, mushroom mycelium offers several advantages, including a shorter growth cycle, lower production costs, and ease of preservation and transportation, making it a cost-effective commercial product. The health benefits attributed to medicinal mushrooms arise mainly from their immunomodulatory, antioxidant, and antimicrobial properties, closely tied to their chemical profile [3]. Polysaccharides play an important role in immune modulation, whereas triterpenoids contribute to antioxidant activity, and phenolic compounds exhibit antioxidant, anti-inflammatory, antimicrobial, and antihyperglycemic activities. These therapeutic properties render medicinal mushrooms effective in treating diverse pathological conditions such as cancer, cardiovascular diseases, diabetes, and respiratory tract disorders [4].

Immune Modulation

Medicinal mushrooms have been used for centuries to promote health and treat disease [2, 4]. Polysaccharides, one of the main constituents of many mushroom species, can exhibit a number of beneficial effects in addition to immune modulation, including antioxidant and antimicrobial activities. Several species of medicinal mushroom, Agaricus bisporus, Agaricus blazei, Antrodia cinnamomea, Ganoderma lucidum, Grifola frondosa, Hericium erinaceus, Inonotus obliquus, Lentinus edodes, and Pleurotus ostreatus were selected for review, and their chemical compositions and clinical evidence are summarized [3].

Antioxidant Properties

Medicinal mushrooms, especially their polysaccharide fractions, exhibit noteworthy antioxidant effects. These include scavenging reactive oxygen species (ROS) and enhancing total antioxidant capacity in both living organisms and in vitro settings. Phenolic compounds, along with triterpenoids, are also recognized as significant antioxidants [3]. For example, Ganoderma species contain a range of antioxidant substances, such as phenols and polysaccharides, contributing to their beneficial properties. Similarly, Phellinus species are rich in antioxidant compounds, including phenolic acids, hispidin, hispolon, villosin, and inoscavin, which help prevent diseases related to the vascular and immune systems. Considerable antioxidant activities have been demonstrated for other medicinal mushrooms as well. Grifola frondosa polysaccharides decrease oxidative damage generated in mouse brain tissue, Helvella leucopus polysaccharides prevent lipid peroxidation induced by $FeCl_2$, and Pleurotus djamor polysaccharides effectively scavenge DPPH radicals [1, 2]. Lentinula edodes contains phenolic acids, in addition to polysaccharides, that contribute to its antioxidant activity. Coprinus comatus extract exhibits strong scavenging capacities toward the free DPPH radical.

Antimicrobial Effects

Several compounds isolated from mushrooms have exhibited antimicrobial potential. For instance, Extracted Polysaccharides of Agaricus bisporus (AB) showed antioxidant and antimicrobial properties in both in vitro and in vivo studies, including anti-inflammatory and immunostimulating activities in A. bisporus [2]. The antimicrobial activity of A. bisporus has been attributed to vitamin, amino acid, and mineral contents, polysaccharides, and phenolic acids. A derivative of A. bisporus, 2-Amino-3H-phenoxazin-3-one, produced by Achromobacter xylosoxidans HP01, demonstrated broad antimicrobial activity against plant pathogens, fungi, and bacteria; it was not toxic to quail eggs up to 100 mg/mL and did not induce phytotoxicity. Additional evidence supports the antimicrobial capacity of Agaricus species: methanolic extract of A. arvensis exhibited broad antibacterial activity; A. brasiliensis aqueous extract inhibited Helicobacter pylori; and A. bisporus and A. campestris demonstrated activity against Salmonella typhi. Ganoderma species have been reported to possess antimicrobial activity; extracts from Ganoderma lucidum, G. pfeifferi, G. resinaceum, and G. adspersum, using various solvents, showed such properties, with α-d-mannose identified as a key active compound. Aqueous extract of Ganoderma applanatum proved effective against Pseudomonas aeruginosa and Proteus mirabilis, while conlucidic acid, a triterpene acid from the same mushroom, reduced the growth of Helicobacter pylori [2].

Major Medicinal Mushrooms

Low medicinal mushroom intake is associated with a higher risk of advanced prostate cancer. Lentinan, a polysaccharide from Lentinula edodes, is used for cancer therapy in Asia. Polysaccharides from DT and Coriolus versicolor, especially β-(1,3)-glucans with β-(1,6) linked side chains, are important. Propolis contains ursolic acid with antiviral activity against HSV-1 and adenovirus; against HSV-1, activity depends on triterpene presence. Recognized mushrooms are Cordyceps sinensis and Ophiocordyceps sinensis; C. militaris contains more carotenoids [1]. Different cultivation methods affect bioactive compound content. A compound from the stromata of Cordyceps sobolifera has antiviral activity. Cordymin is an antifungal peptide from Cordyceps militaris. Aptamers selected against the active region of laccase from Ganoderma lucidum; laccase can degrade diverse toxins. Cordycepin from Cordyceps militaris has several pharmacological activities, including anticancer [1].

Reishi (Ganoderma lucidum)

The Reishi mushroom is a saprophytic fungus that grows on multiple hardwood species, particularly dense broadleaf trees such as elm, maple, chestnut, and oak. The active compounds in this mushroom include beta-glucan, triterpenoids, ganoderic acid, polysaccharides, and alcohols [1]. The presence of these compounds in reishi mushrooms provides various therapeutic benefits and pharmacological properties such as antioxidant, anti-inflammatory, antibacterial, antiviral, antifungal, anticancer, antidiabetic, and antiangiogenic effects. Daily intake of reishi mushroom promotes a healthy lifestyle, prevents chronic diseases associated with aging, and actively supports the immune system [3]. Originally used in Eastern medicine, the clinical properties of reishi have been reconsidered for Western therapeutic protocols. Researchers have found that the presence of bioactive compounds in this mushroom contributes to the prevention and treatment of cardiovascular diseases. Several studies have demonstrated that polysaccharides and triterpenoids act through various mechanisms to exert hypolipidemic and anti-atherosclerotic effects. Moreover, these compounds also provide neuroprotective activity by acting on neuronal cells; various studies have revealed the anticancer effect of polysaccharides isolated from the fruiting body against prostate cancer, breast cancer, colon cancer, lung cancer, ovarian cancer, melanoma, and colorectal cancer. Another investigation concluded that active triterpenoids possess pneumoprotective effects that alleviate cough symptoms [1, 3].

Shiitake (Lentinula edodes)

The shiitake mushroom, a brown-shelled and umbrella-shaped fungus, is cultivated in Asian countries and northwest America. The fruiting body contains various bioactive secondary metabolites, including sulfur-containing compounds such as lentinan and eritadenine, which have been reported to exhibit antibiotic, lipid-lowering, and anti-inflammatory effects [1, 5]. Polysaccharides extracted from shiitake are known for their antitumor, immunomodulating, and reprogramming effects on the gut microbiota. A clinical trial involving 52 healthy women treated with 100 g cooked shiitake daily over four weeks observed reduced levels of inflammation biomarkers. The anticancer potential of cultivated shiitake was also evaluated through intraperitoneal injection of cultivated mycelia in both normal and tumor-bearing mice. The administration improved immunity by increasing the activity of macrophages, T cells, and natural killer cells, promoted tumor destruction by inducing apoptosis, and enhanced liver function by exhibiting strong antioxidant activities [1, 5].

Cordyceps (Cordyceps sinensis)

Cordyceps has been prescribed in traditional Chinese medicine for the treatment of a diverse range of illnesses, including cancer, fatigue, kidney problems, and chronic respiratory conditions [6]. Both mycelium and fruiting bodies of Cordyceps sinensis and Cordyceps militaris exhibit significant anticancer activity via immune modulation and apoptosis induction [7]. Polysaccharides and the nucleoside analogue cordycepin represent the primary agents responsible for these bioactivities. Data from restorative assays demonstrate that Cordyceps extract promotes health recovery at doses around 8 mg/kg/day, whereas higher doses (e.g., 10 mg/g/kg) may diminish efficacy. Authentic sourcing and taxonomic standardization remain challenges; contamination with lead wire used illicitly to increase product weight constitutes an additional concern. Capsules usually contain 600–750 mg of Cordyceps material, which is also traditionally cooked with meats in medicinal preparations [6, 7].

Maitake (Grifola frondosa)

The maitake mushroom, or Grifola frondosa, is a medicinal mushroom belonging to the family Polyporaceae. Maitake is rich in polysaccharides, including the main compound β-glucans; among these, the α-D-glucan fraction has been found to be the most effective as an immunomodulator. Polysaccharides of Maitake also provide antioxidant, anticancer, immunomodulating, antiviral, antibacterial, blood sugar-lowering, hepatic, and cardiovascular (lipid reduction) properties and are considered important in the control of cell growth and the prevention of chronic diseases, such as cancer, obesity, diabetes, and hypertension [1]. The maitake mushroom has been studied for more than 25 years as a nutritional source and for use in herbal medicine. Investigations have been conducted on the intake of present-day diets combined with extracts of the mushroom and have shown that the disease onset related to malignant tumors is inhibited [1]. The halting of the growth of cancer cells and the

reduction of tumor masses are explained by the initiation of the release of cytokines from macrophages stimulated by the immunomodulating polysaccharides. Moreover, the administration of the water extract of Grifola frondosa may modulate blood glucose levels in streptozotocin-induced diabetic rats. The antihypertensive properties of the mushroom have also been examined. Both total ethanol and water extracts of Grifola frondosa exhibited hypotensive activity, and the active components were suggested to be peptides. A clinical study demonstrated that the fruiting body extract of Grifola frondosa produces effects on blood pressure and renal function, possibly by controlling blood lipid and blood sugar levels and maintaining renal function [1].

Turkey Tail (Trametes versicolor)

The turkey tail mushroom (Trametes versicolor) is a polypore bracket fungus reported worldwide. Its common Korean name, yun-gu or cloud whale, means "cloud" and resembles the shape of a whale's tail fin [4]. In addition to Korea, it is distributed in China, Japan, and Russia. Polysaccharide peptide (PSP) and polysaccharide-K (PSK) can be isolated from turkey tail mushrooms and serve as adjuncts for treating patients with breast, colorectal, and lung cancer [4]. PSP reportedly has immunological properties such as antioxidant and anti-inflammatory characteristics. The combination of PSP and chrysanthemum also relieves respiratory symptoms such as cough, wheezing, and sputum. In patients with advanced non-small-cell lung cancer, PSP pills have been used as adjuvants to chemotherapy. PSP and PSK induce mitosis and the activation of lymphocytes, including helper T cells, natural killer cells, and dendritic cells, leading to immunomodulatory effects. These immunomodulatory effects occur because of the stimulation of the adaptive and humoral immune responses through the upregulation of signaling receptors, including the Toll-like receptor [4], and through the activation of the complement system. In addition, PSK inhibits the growth of inflammatory cells by suppressing COX-2 activity and the production of prostaglandin E2.

Clinical Applications

Medicinal mushrooms have been employed to alleviate symptoms and support the treatment of various illnesses, including cancer, cardiovascular issues, diabetes, and respiratory problems. Cancer therapies aim to inhibit malignant cell proliferation, induce apoptosis, reduce chemotherapy and radiotherapy side effects, stimulate the immune response, and prevent metastasis [2]. Cardiovascular benefits involve lowering blood pressure, managing heart rate and arrhythmias, and reducing cholesterol through bioactive compounds such as beta-glucans [8]. Mushrooms are also utilized to control diabetes, apply anti-inflammatory effects, and promote digestive health. Furthermore, constituents extracted from certain species hold promise as potential treatments for respiratory diseases [2, 8].

Cancer Treatment

A variety of mushroom species produce diverse bioactive compounds, which have immunomodulating, antitumor, antioxidant, anti-inflammatory, and antimicrobial effects. Their role in cancer treatment is widely known and documented. Preclinical and clinical studies have shown that mushroom-derived polysaccharides, triterpenoids, and other constituents inhibit tumor cell growth in vitro and in vivo [9]. Mushroom-derived polysaccharides activate and/or regulate the immune system by affecting various immune cells, thereby inhibiting cancer cell growth and metastasis. Some mushrooms regulate several cancer-related signaling pathways such as PI3K/Akt, Wnt/β-catenin, and MAPK. Other compounds target components involved in drug resistance and immune checkpoints. Mushroom-derived components may act as therapeutic agents in reversing multidrug resistance and improving quality of life by enhancing prebiotic activity [10]. The majority of cancer studies on medicinal mushrooms remain preclinical, and the small number of published clinical studies report effects such as reduction of adverse events, antitumor activities, and immunomodulation. A small number of clinical and epidemiologic studies provide promising indications but fail to meet quality criteria; sample sizes are insufficient, and the test material cannot be characterised with confidence. The results strongly underline the need for well-designed, randomised, blinded, and controlled clinical studies, with a larger sample size and appropriate preparation methods. Long-term applications may provide additional benefits. The preventive potential of medicinal mushrooms in lowering cancer risk through diet and lifestyle should also be addressed [9, 10].

Cardiovascular Health

Medicinal mushrooms contain bioactive compounds and provide numerous health benefits. Their use in treating various disorders, such as cardiovascular illnesses, cancers, diabetes, and neurological diseases, has been documented extensively [2]. Many bioactive compounds with antimicrobial, anti-inflammatory, immunomodulatory, anticancer, antioxidant, antihyperlipidemic, antidiabetic, and prebiotic properties have been identified from both fruiting bodies and mycelium [2]. P. ostreatus mushrooms decrease triglycerides and blood cholesterol by inhibiting lipid absorption; hypertension, obesity, and thrombosis may also be treated with medicinal fungi. M. esculenta, I. obliquus, and G. frondosa have exhibited strong anti-hypercholesterolemic activity, while G. lucidum and P. linteus can lower blood pressure. Mushrooms such as G. lucidum, A. blazei, H. erinaceus, and Cordyceps spp. have beneficial properties against HIV and other viruses. G. lucidum, G. frondosa,

and P. linteus extracts strongly inhibit the formation of atherosclerotic plaques [2]. The cardiovascular benefits from Cordyceps and Pleurotus may be attributed to ergosterol, adenosine, and cordycepin (Cordyceps), lovastatin (Pleurotus), phenolic compounds, and β-glucans isolated from various mushroom species. Materials with these properties have been detected in many supplements sold online, although beta-glucan content in these products is often lower than that indicated on the label [11]. Additional concerns exist with contaminant levels that exceed legal standards in several commercial products, warranting greater market regulation and enhanced quality control. Regulation and standardisation of mushroom products remain major challenges for the field, while efforts continue to isolate bioactive compounds and characterise their mechanisms of action. Current research facilities should support the development of new materials that are able to cure illnesses with minimal side effects. In the meantime, the existing array of medicinal fungi offers significant therapeutic promise for the foreseeable future [11].

Diabetes Management

Medicinal mushrooms are popular natural products used as dietary supplements and folk medicines worldwide. Clinical and experimental studies have authenticated their antioxidant, anti-inflammatory, immunomodulatory, anticancer, and anticarcinogenic activities [12, 13]. Polysaccharides, triterpenoids, phenolic compounds, and their derivatives, extracted by novel methods, have been explored and found bioactive, with polysaccharides comprising over 40 % of bioactive components. Some species, such as Agaricus, Ganoderma, Coprinus, Lentinus, and Pleurotus, exhibit hypoglycemic properties that can be beneficial in managing diabetes [12]. Diabetes is an incurable condition leading to hyperglycemia and severe complications. In vivo studies have examined several medicinal and edible mushroom species for antidiabetic compounds, leading to the identification of polysaccharides as promising candidates [13]. Mechanisms of action include the prevention of oxidative stress-induced β-cell damage, stimulation of insulin signaling pathways, and modulation of glucose-metabolizing enzymes. These findings highlight the potential benefits of incorporating certain medicinal mushrooms into diabetes management strategies [12, 13].

Respiratory Disorders

Various species of medicinal mushrooms have a history of use in the treatment of respiratory tract disorders and both lower respiratory-tract and breast-related infections [2].

Safety and Toxicology

The beneficial effects of medicinal mushrooms, including Ganoderma lucidum, Lentinula edodes, and Grifola frondosa, are well documented [2]. Their bioactive components positively affect several pathological states, including cancer, cardiovascular disorders, diabetes, and respiratory ailments. Although these mushrooms are generally safe, adverse effects such as cramps, nausea, and skin allergies may arise during prolonged treatments. Additionally, strong interaction with conventional drugs has been reported [2].

Potential Side Effects

Generally safe and well-tolerated, medicinal mushrooms may occasionally cause digestive upset, diarrhea, skin irritation, or allergic reactions. Additional effects, less frequently reported, include headache, rashes, and mucous membrane dryness [2]. Observations from Japan and South Korea suggest that mushrooms with lightly toxic or indigestible components can accelerate peristaltic movements and exert laxative effects. Mushrooms characterized as “hot” or astringent in traditional Chinese medicine are known to potentially induce skin irritation, itching, or dermatological inflammation. Due to their immune stimulatory activity, medicinal mushrooms should be avoided in autoimmune diseases, especially when immunosuppressive drugs are used concurrently [10]. Such stimulation may also interfere with immunosuppressive therapies used in organ transplantation patients [1].

Interactions with Medications

Mushrooms have been used extensively in folk medicine. Studies on medicinal mushrooms revealed their important role in the pharmaceutical industry. Many natural medicines derived from fungi have had positive effects on the immune system, as well as antioxidant and anti-inflammatory effects [2]. Medicinal mushrooms represent a large source of biologically active compounds. Although many constituents of the mushroom have been identified, only a few compounds with biological activities have been isolated, characterized, and screened for biological activities. Bound and free phenolic content is also evaluated for different species that are responsible for many beneficial properties to humans [1]. Mushrooms contain numerous bioactive compounds that exhibit medical activities, such as polysaccharides, sterols, proteins, chitin, polyphenols, and triterpenoids. Mushrooms play a role in immune modulation as antimicrobial, antioxidant, anti-inflammatory, and anticancer agents. Mushrooms also give one of the best balances of many nutritional requirements, such as protein, carbohydrates, minerals, vitamins, and fiber. Only a few studies deal with the interactions between medicinal mushrooms and drugs, despite many reports on complementary and alternative medicine interactions with medicinal drugs. Some investigations in the literature reported interactions among the main bioactive compounds present in medicinal mushrooms and drugs [1, 2].

Current Research Trends

Current research on medicinal mushrooms is progressing dynamically [6]. For instance, the extraction of polysaccharide complexes from these fungi has proven highly effective, yielding a product exhibiting not only biological activity but also exceptional protective efficiency against oxidative stress. However, the natural presence of polysaccharide complexes alone does not guarantee safe use, highlighting the need for thoroughly established toxicological profiles, especially given the increasing prevalence of community fungal exposure [13]. Advances toward pharmaceutical application include introducing liquorice extract, rich in phenolic compounds, to elevate the polyphenol content in Ganoderma lucidum. Nevertheless, this addition exerts concentration-dependent effects. Clinical research targeting a range of conditions, from breast cancer to COVID-19, has identified shiitake and Agaricus species as particularly promising agents for ongoing trials [12, 13].

Novel Extraction Techniques

In recent decades, extensive scientific investigations into medicinal mushrooms have unveiled their immunomodulatory, anticancer, antidiabetic, cholesterol-lowering, antibiotic, and antiviral effects [5]. Therefore, extraction procedures that elevate the bioavailability of mushroom-derived bioactive compounds and metabotoxins have garnered considerable attention. Current extraction methods for bioactive substances vary widely, tailored to isolate specific constituents such as alkaloids, carotenoids, fibers, flavonoids, glycosides, inglen, phytosterols, polyphenols, tannins, terpenes, vitamins, betanins, chlorophylls, and essential oils. Emerging approaches have harnessed enzymes, ultrasound, microwave, supercritical fluid, pressurized liquid, pulsed-electric field, high-voltage electric discharge, and high hydrostatic pressure techniques [8]. These innovative procedures have been proven highly efficient, environmentally sustainable, and time-saving, facilitating the extraction of bioactives from diverse sources. Plant extracts rich in polysaccharides, flavonoids, and polyphenols demonstrate synergistic antioxidant activities, corroborating their traditional application in antiaging and cataract prevention. Several extraction methods focus on enhancing the yield of antioxidants in Black Truffle.

Bioavailability Studies

Medicinal mushrooms represent a group of fungi known for their ability to produce metabolites that influence the physiology, metabolism, and immune system of humans and animals. They typically grow on wood and can be either edible or non-edible. Despite the growing interest in the medicinal use of these fungi and the scientific validation of some claims, there remains a plethora of others, especially related to the treatment of severe diseases that are yet to be sufficiently corroborated by rigorous studies or clinical evidence [8]. A broad range of bioactivities, including anti-inflammatory, anticancer, immunomodulating, antimicrobial, antioxidant, hypoglycaemic, and hypolipidaemic effects, has been associated with mushroom consumption. Several mechanisms of action have been demonstrated, mainly for heteropolysaccharides and triterpenoids, which appear to regulate both adaptive and innate immunity. Compounds such as phenolic components with antioxidant capacities also contribute to cardiovascular benefit; other applications leveraged are the antitumor and bronchodilating effects, and the ability to reduce glucose and cholesterol levels. Furthermore, some species are recommended for the treatment of diabetes and various stress-related conditions [7, 8].

Clinical Trials

Numerous clinical studies have evaluated the therapeutic activities of medicinal mushrooms in various diseases, including cancer, cardiovascular diseases, diabetes, and respiratory disorders. Agaricus, Antrodia, Daedalea, Ganoderma, Grifola, Lentinus, Pleurotus, Schizophyllum, Tremella, and Trametes have been used against cancer and cardiovascular disorders. Ganoderma lucidum shows antidiabetic and anti-inflammatory activities, while Cordyceps has applications in respiratory problems [8, 9]. Trametes versicolor and its active polysaccharides are used in cancer therapy. Agaricus bisporus is a frequent source of edible mushroom consumption, containing many bioactive compounds, but only a few have been clinically tested. Agaricus blazei, a species native to Brazil, has shown promising therapeutic properties during in vitro and in vivo studies. Several clinical trials have assessed the biological effects of Agaricus blazei Murill in healthy, cancer, or chemotherapy-treated individuals, confirming the positive immunomodulatory effects of AbM [10].

Future Directions

The future of medicinal mushrooms rests largely on further chemical and pharmaceutical studies, which will undoubtedly continue to exploit the consequent application of the compounds in medicinal, industrial, and agricultural purposes [1, 8]. It is believed that the development of more novel approaches to control, cultivation, and metabolite extraction will allow more effective and significant delivery of mushroom active compounds, along with the creation of more potent derivatives of compounds capable of therapeutic use [1]. Given the range of fungal species largely unexploited to date, it is expected that the future will see medicinal mushroom research advance across many pharmacological models and therapeutic sectors. Nevertheless, these developments will require a combined interdisciplinary approach and widespread interactions across distinct fields of research, including botany, agriculture, chemistry, pharmacognosy, microbiology, biotechnology, and medicine [8].

Standardization of Products

Unwarranted variability involves a fundamental consequence of herbal prescriptions becoming mixtures of ill-recognized preparations [11]. Such a state is particularly conspicuous in the mushroom field, where the indiscriminate choice of products reduces the determination of the bioactivity budget of a prescribed assay. The delivery of the material is thus dubious, and the monitoring of the treatment becomes, therefore, a futile effort [11]. Medical verifications become misleading in such situations, since no direct link exists between the composed effect and the treatment. The wide availability of assorted mushroom products is sustained by a similarly ample diversity in the production process, which unequivocally influences the performance of the compounds. Marijuana, for instance, can differ considerably, depending on the mode of preparation. Several scientific groups have risen to the challenge of standardizing preparation protocols and marketing output in the area of medicaments from fungal sources [2, 11]. The Mushroom Standardized Formulations of Medicinal Grade come already as a mixture of extracts pre-dosed in known ratios, guaranteeing, on the basis of an NMR analytical approach, high stability under various pHs. The cocktail remains, furthermore, admissible to in vivo experiments on account of its dramatically low cytotoxicity [2].

Regulatory Challenges

Mushroom bioactive compounds, which exhibit a broad spectrum of pharmacological activities, constitute a growing multi-billion-dollar industry; they are present in traditional and novel formulations and sold as dietary supplements or functional foods [2, 11]. A very large percentage of the reports on the pharmacological properties of mushroom-based compounds and products are in vitro or in vivo studies, with a relatively low number of clinical trials. The reason behind this approach is that human studies require a clear definition of the compound considered and, due to the matrix complexity, the translation from the mushroom to the final derived product is not a simple process, making regulatory barriers very high [2]. These problems also emerge in the descriptions of the active ingredients' fate: pharmacokinetic studies have been focused on purified or enriched compounds released from the raw material. Their chemical-guided characterization is often not carried out by companies producing the raw materials or, even worse, those that use mushrooms as starting materials to produce supplements and formulations. Quality control during manufacturing by each company is mainly based on DNA barcoding analysis, which allows a precise identification of the matrices but cannot shed any light on the final composition. A systematic pipeline based on metabolomics applied to different species of mushrooms using the GC-MS and the NMR approaches to preferentially describe the secondary and the primary metabolites was reported [11]. A complete overview of the composition of the matrices for quality control can then be used to verify its purity and also followed during the manufacturing processes and storage [2, 11, 14–16].

CONCLUSION

Medicinal mushrooms represent a valuable source of bioactive compounds with wide-ranging therapeutic applications, particularly in immune regulation, cancer management, oxidative stress reduction, and metabolic health support. Evidence from traditional use, experimental research, and emerging clinical trials underscores their potential as complementary and integrative agents in modern medicine. Key species such as Ganoderma lucidum, Lentinula edodes, Grifola frondosa, and Cordyceps sinensis exemplify this potential through their rich profiles of polysaccharides, triterpenoids, and phenolics. Nonetheless, significant challenges remain, including inconsistent product quality, safety concerns related to contamination or overuse, and the lack of standardized dosing guidelines. To bridge the gap between traditional applications and evidence-based medicine, future research must prioritize well-designed clinical studies, quality assurance measures, and regulatory frameworks. By addressing these gaps, medicinal mushrooms could evolve from being regarded merely as traditional remedies to becoming validated therapeutic agents that contribute meaningfully to global health care.

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