

Review Article

Diversity of Mushrooms and Their Metabolites of Nutraceutical and Therapeutic Significance

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Mushrooms are well known for their nutritional as well as therapeutic values worldwide. Interest in mushrooms has peaked because immunity and cellular protection are important issues for health conscious consumers and for those individuals who are dealing with serious health issues. Mushrooms generally belong to Basidiomycetes which harbors numerous mushroom species with diversity of metabolites of nutraceutical and therapeutic significance. They have been reported to be the most valuable ones for humans. Investigations on the therapeutic and nutritional properties of mushrooms are underway throughout the world. Researchers are providing crucial data on the array of bioactive compounds found within these fascinating fungi. People are now accepting mushrooms more as food and food supplements. Various academic and research institutes are all involved actively in research on bioactive metabolites of mushrooms. The present paper aims at reviewing the diversity of mushrooms and the types of metabolites especially of nutraceutical and therapeutic importance present in these mushrooms and their role as bioactive agents.

1. Introduction

Man has lived in a hunter-gatherer society for most of the time since their origin and has depended entirely on biodiversity for their sustenance. It is obvious that, during gathering forays, fruiting bodies of larger fungi, or macromycetes, were also collected and early man must have sampled anything of bitable nature. These fruiting bodies have been referred to as mushrooms or toadstools for many centuries. The word “truffle” has also been used in literature for some fruiting bodies of edible fungi, but these are characterized as growing below ground and must have been discovered subsequently in these gathering forays. Theophrastus (300 BC) is the first writer to mention truffles and does so under several names. Since earliest times, mushrooms have been treated as a special kind of food. The Greeks believed that mushrooms provide strength for warriors in battle. The Pharaohs prized mushroom as delicacy, and the Romans regarded mushrooms as the “Food of the Gods,” and they even had mushrooms on the menu which was served only on festive occasions. The Chinese treasured mushrooms as a health food. Mushrooms have probably been eaten for as long as people have walked

the face of the Earth. These records concern wild mushrooms, but there are stories of mushrooms being cultivated in Asia as far back as the early middle ages. Mushrooms are the macrofungi with fleshy, subfleshy, or sometimes leathery, umbrella-like sporophores that bear their fertile surfaces either on lamellate or lining the tubes, opening out by means of pores. The lamellate members are commonly called “mushrooms” or “toadstool” depending upon whether they are edible or poisonous and the tube bearing or poroid members as “boletes” [1]. Diversity of mushrooms varies greatly ranging from the typical *Agaricus* mushrooms with a stalk and umbrella-shaped top to the polypores, Earth Stars (*Geastrum*), the Stink Horns (*phalloides*), and Puff Balls (*Lycoperdon*). Edible mushrooms are either collected from nature or more commonly cultivated and harvested under defined conditions with rigorous quality control on size, shape, tenderness, and palatability. Due to the high product yield and the low reproducibility costs from fungi, major interest has been shown in the respective markets for the metabolites derived from fungi. Both cellular components and secondary metabolites of large number of mushrooms have been shown to affect the immune system of host and

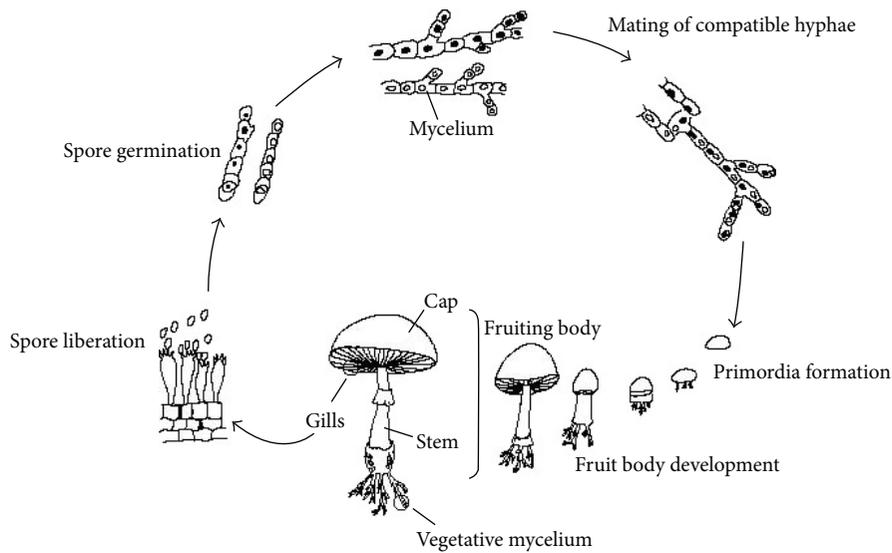


FIGURE 1: Life cycle of *Agaricus bisporus* [7].

therefore could be used to treat variety of diseases. Secondary metabolites are generally produced following active growth, and many have an unusual chemical structure. Interest in these compounds is considerable, as many natural products are of medical, industrial, and/or agricultural importance. Production of lipids, vitamins, and polysaccharides as well as intermediates in the synthesis of cell constituents such as amino acids and nucleotides are also of great economic importance in present-day industry [2–6].

Pure culture studies on mushrooms and related basidiomycetous fungi have laid the foundation for several biotechnological innovations including mass cultivation for diverse purposes. Strain improvement and selection among edible mushrooms like *Agaricus*, preparation of mushroom spawns and their application to composted natural substrates, and standardization of cultivation conditions to ensure proper mycelial colonization of the substrates to be followed by differentiation of the fruit bodies which are the commodities of commercial value are again well documented. Relatively less attention has been given to the nutrient value of edible mushroom mycelia cultivated in submerged culture. One of the pioneering efforts in this direction has been that of Humfeld and Sugihara in USA who patented mass cultivation of *Agaricus* mycelia in submerged cultures and explored their potential as protein feed supplements in animal and human nutrition. Whether the mycelium grown in submerged culture has the same flavor and nutritional aspects as that of the mushroom fruit bodies has been debated but because of the slow rate of growth of the mycelia in submerged culture and large volumes involved, the use of mushroom mycelia as feed supplements to enhance feed protein values in animal diets seems to be economically attractive. The basidiomycetes have some highly characteristic features, which separate them from other fungi. They are the most evolutionarily advanced fungi, and even their hyphae have a distinct “cellular” composition. Basidiomycetes produce basidiospores that are produced on a specialized

structure called basidium. Although haploid, basidiospores may be either uninucleate or binucleate at maturity. After these basidiospores are released from mature fruiting bodies, they germinate to form hyphae. Collectively, hyphae make up mycelium. Hyphae derived from the spores of two different mating types then fuse to form secondary mycelium which has two nuclei and is ultimately responsible for the formation of fruiting bodies (Figure 1).

2. Diversity of Mushrooms of Nutraceutical and Therapeutic Significance

It has become increasingly apparent in recent years that the organisms traditionally referred to as fungi are not all closely related. This prompted some authors to use term “fungi” in a very general sense and the term “Fungi” with a capital “F” specifically for the so-called true fungi that appear to be related to one another. The true fungi are placed in the kingdom Fungi. Modern systematics, based on morphological characters and analysis of rDNA sequences, divides the kingdom Fungi into four major phyla or divisions: Chytridiomycota, Zygomycota, Ascomycota, and Basidiomycota. The two fungal phyla that produce large, visible fruit bodies are the Ascomycota and Basidiomycota. The Ascomycota contains at least 40,000 different species worldwide, many of them rather inconspicuous, but including such familiar groups as the morels and truffles, the cup fungi, and most of the lichens, as well as many microscopic molds and yeasts. They all produce their spores within macroscopic cells called asci, which typically open under pressure when mature, shooting the spores out into the air currents [8]. The Basidiomycota contains at least 30,000 different species worldwide and includes many of our most familiar fungi, including all the agarics (mushrooms and toadstools), puffballs and stinkhorns, bracket fungi, chanterelles, and club and coral fungi, as well as the plant-parasitic rusts and smuts [8]. All of them produce their spores on the external surface of

microscopic cells called basidia and their fruit bodies have evolved in many ingenious ways in order to liberate these spores. The fungi comprising the phylum Basidiomycota commonly are known as basidiomycetes. Basidiomycota includes classes Hymenomycetes, Ustilaginomycetes, and Urediniomycetes. Hymenomycetes includes orders Agaricales, Aphyllphorales, Auriculariales, Dacrymycetales, Ceratobasidiales, and Tuslasnellales. Among Hymenomycetes, mainly the orders Agaricales, Aphyllphorales, and Auriculariales and class Gasteromycetes contain the mushrooms of pharmaceutical importance. The rest of the orders, that is, Dacrymycetales, Ceratobasidiales, and Tuslasnellales, contain parasitic and disease causing forms. Hymenomycetes also includes another subgroup (order) Tremellales. Ustilaginomycetes includes orders Ustilaginales and Exobasidiales which include smut causing forms, while Urediniomycetes include orders Uredinales, Septobasidiales, Sporidiales, and Eocronatirum that are responsible for causing rusts in various crop plants [9].

2.1. Order: Agaricales. The basidiomycetes include a large order Agaricales whose fruiting bodies are called mushrooms. Agaricales have been known to humans ever since we first became aware of our environment and are among the relatively few fungi that have common names in addition to scientific binomials: the death cup, *Amanita phalloides*; the shaggy mane, *Coprinus comatus*; the Jack-o'-lantern, *Omphalotus olearius*; and the honey mushroom, *Armillaria mellea* [9]. The fungi belonging to Agaricales probably have been studied to a great extent compared to members of any other order of Basidiomycota. As a group, agarics occur in a wide variety of habitats ranging from arctic to the tropics. While some species are known only from restricted areas, others exist in areas that are widely separated geographically. Even so, most species do seem to show preference for a certain type of natural habitat as well as for a particular substrate. They contain parasitic, saprobic, and mycorrhizal forms [9]. According to Chang [10], about 14 species of agarics are cultivated for food. Of these, only six are grown on industrial scale: enokitake or enoki mushroom, *Flammulina velutipes*; shiitake mushroom, *Lentinula edodes*; paddy straw mushroom, *Volvariella volvacea*; the oyster mushroom, *Pleurotus ostreatus*; and the meadow mushrooms, *Agaricus brunnescens* and *A. bitorquis*. Russulaceae is one of the most abundant and widely distributed ectomycorrhizal agaric families in the world [11, 12] containing three genera *Russula*, *Lactarius*, and *Russulina* (a synonym of *Russula*). Singer [11] reported 317 species of *Russula* and 122 species of *Lactarius* from all over the world. Two new tropical species each belonging to *Russula* and *Lactarius* have been reported from the forest region of Central India and were taxonomically described [13]. Table 1 describes the important mushroom species producing metabolites of nutraceutical and therapeutic relevance.

2.2. Order: Aphyllphorales. The order Aphyllphorales is another important group of Basidiomycota of about 1200 species. The order can be grouped as those Hymenomycetes that possess holobasidia but usually lack gills. The hymenia are borne on definite gymnocarpous basidiocarps; that is, the

hymenium is exposed while the spores are still immature. The major importance of the species of Aphyllphorales as a whole is their saprobic activities as decomposers, particularly in degradation of cellulose and lignin. Although most species are saprobic in soil, litter, bark, and dead wood, some species may be truly parasitic or pathogenic on forest trees and nonwoody crops. The group also contains mycorrhizal forms associated with forest trees. A large number of species of Aphyllphorales have been used medicinally and many of them have been used in Indian folk medicines like *Ganoderma lucidum*, the fabled Ling Chi of Chinese herbal medicine [53]. Also known as Reishi, *Ganoderma lucidum* products often are advertised in natural food publications. They cure venereal disease and cancer and aid in purification of blood and lowering of cholesterol. About 12 species of *Phellinus* have been used in Indian folk medicine [54]. Antibiotics have been isolated from several of the Aphyllphorales, including a species of *Phlebia* [55]. A few species of aphyllphoralean fungi are edible, including the basidiocarps of the beef steak fungus (*Fistulina hepatica*); the bear's head fungus (*Hericium erinaceum*); and the sulphur fungus (*Laetiporus sulphureus*). Sclerotia of other species including *Polyporus tuberaster* also have been used as food [56]. The order Aphyllphorales is very large and heterogenous one. Table 2 describes the important genera and corresponding nutraceutical and therapeutic metabolite producing potential by the members of Aphyllphorales.

2.3. Order: Auriculariales. All species within the Auriculariales are thought to be saprotrophs; most of them are wood rotters. They are typically found on dead attached or fallen wood, though a few (*Guepinia* and *Tremellodendropsis* species) are normally found on the ground. As a group, their distribution is cosmopolitan. Many genera of order Auriculariales possess important nutritive and therapeutic values as shown in Table 3.

2.4. Gasteromycetes. Gasteromycetes, the "stomach fungi," a polyphyletic assemblage of basidiomycetous fungi, are characterized by the fact that their basidiospores mature inside the basidiocarps and are not discharged forcibly from the basidia. They include puffballs, earthstars, stinkhorns, and bird's nest fungi. Although their basidiocarps vary in appearance, they all possess a distinct outer covering or wall termed the peridium. This covering may vary from almost paper thin in some taxa to thick and rubbery or even hard in others and may open naturally in various ways after the spores are mature or remain closed permanently, with the spores liberated only after the disintegration of the peridium through the action of external agents. Depending upon the species, the gleba tissue, that is, the fertile portion of the basidiocarp enclosed by peridium, may be monomitic, consisting of only thin walled, generative hyphae, or dimitic, consisting of both generative and skeletal hyphae. Most Gasteromycetes are either saprobes or mycorrhizal fungi. Although most are terrestrial forms, species of the genus *Nia* are wood rotters in marine habitats [69]. Table 4 summarizes the important genera producing metabolites of nutraceutical and therapeutic importance.

TABLE 1: Diversity of nutraceutical and therapeutic metabolite producing mushrooms found in order Agaricales (nomenclature source: Mycobank).

Family	Important genera	Therapeutic/nutritional value	References
Hygrophoraceae	<i>Hygrophorus</i>	Fatty acids with bactericidal and fungicidal activity prepared from <i>Hygrophorus eburneus</i> . Hygrophamides are important constituents of cell membranes and assumed to play important roles as antigens and their receptors.	[9, 14]
Tricholomataceae	<i>Clitocybe</i> , <i>Tricholoma</i>	<i>Tricholoma magnivelare</i> , the pine mushroom, or the white matsutake, is another edible mushroom known to enhance fertility and virility, strengthen the immune system, have anticancer activity, and even work as an aphrodisiac.	[9]
Amanitaceae	<i>Amanita</i>	<i>A. phalloides</i> , also known as “death cup,” is a well-known poisonous mushroom of this genus and is also reported to be used in tumor therapy.	[9, 15]
Agaricaceae	<i>Agaricus</i>	<i>A. campestris</i> and <i>A. rodmani</i> are edible. <i>A. brunnescens</i> (<i>bisporus</i>) is grown commercially.	[9]
Strophariaceae	<i>Stropharia</i> , <i>Naematoloma</i> , <i>Psilocybe</i>	The well-known edible members of the genus <i>Stropharia</i> include <i>Stropharia rugosoannulata</i> and <i>Stropharia aeruginosa</i> . These mushrooms are a low calorie and fat-free food choice, known to assist in weight loss. <i>Psilocybe cubensis</i> 's principal active compounds are psilocybin and psilocin which have mind-altering effects like euphoria and visual and mental hallucinations.	[9, 11]
Coprinaceae	<i>Coprinus Panaeolus</i>	<i>Coprinus atramentarius</i> is edible unless consumed with alcohol. <i>Coprinus comatus</i> has antioxidant properties.	[9]
Pluteaceae	<i>Pluteus Volvariella</i>	<i>P. cervinus</i> , <i>P. atromarginatus</i> , and <i>V. volvacea</i> all are edible.	[9]
Cortinariaceae	<i>Cortinarius</i> <i>Galerina</i>	<i>Cortinarius</i> sp. is inedible and some are poisonous too.	[16]
Psathyrellaceae	<i>Psathyrella</i>	<i>Psathyrella atroumbonata</i> Pegler is one of the most valuable edible mushrooms in Nigeria as it is very rich in protein and fibres.	[17]
Inocybaceae	<i>Inocybe</i>	<i>Inocybe aeruginascens</i> contains the formerly known alkaloids psilocybin, psilocin, baeocystin, and aeruginascin.	[16]
Strophariaceae	<i>Pholiota</i>	Polysaccharide isolated from <i>Pholiota nameko</i> (PNPS-1) led to significant decreases in very low-density lipoprotein/low-density lipoprotein cholesterol and an increase in high-density lipoprotein cholesterol. A novel lectin from <i>Pholiota adiposa</i> showed antiproliferative activity.	[18, 19]
Marasmiaceae	<i>Marasmius</i> , <i>Omphalotus</i>	<i>Marasmius oreades</i> , the fairy ring mushroom, is a good edible species containing Cu, Fe, Zn, folic acid, protein, and all the essential amino acids required by man.	[9]
Omphalotaceae	<i>Lentinula</i>	<i>Lentinula edodes</i> is low in sodium and glucose, rich source of fibre, and ideal for diabetics. In Japan, it is used as a natural treatment of cancer because of its complex carbohydrate, lentinan. It is also a source of selenium, an antioxidant that is said to prevent cancer.	[9]
Lyophyllaceae	<i>Termitomyces</i>	Methanolic extract of <i>Termitomyces albuminosus</i> mycelia showed high antioxidant properties. Polysaccharide-rich fraction of <i>Termitomyces eurhizus</i> accelerates healing of indomethacin induced gastric ulcer. Analgesic and anti-inflammatory effects of the dry matter of culture broth of <i>Termitomyces albuminosus</i> and its extracts.	[20–22]
Pleurotaceae	<i>Pleurotus</i>	Ribonucleases (RNases: mol. wt. 10.7 kDa) have been isolated and characterized from <i>P. ostreatus</i> that has the potentiality to neutralize HIV through degradation of viral genetic material.	[23]
Hydnangiaceae	<i>Laccaria</i>	<i>Laccaria edulis</i> , <i>Laccaria laccata</i> , and <i>Laccaria proxima</i> are all edible species.	[24]
Physalacriaceae	<i>Flammulina</i> <i>Armillaria</i>	<i>Flammulina velutipes</i> is rich in peroxidase, superoxide dismutase, and others and can prevent some severe diseases like cancer and coronary heart disease.	[25]

TABLE 2: Diversity of nutraceutical and therapeutic metabolite producing mushrooms found in order Aphyllophorales.

Family	Important genera	Therapeutic properties	Bioactive components	Mode of action	References
Hymenochaetaeae	<i>Inonotus</i> <i>Phellinus</i>	<i>I. obliquus</i> (chaga mushroom) is used for cancer, gastritis, ulcer and tuberculosis of bones, treatment of breast, liver, uterine, and gastric cancer, hypertension, and diabetes.	Phenolic compounds, melanin and lanostane-type terpenoids, and betulinic acid (pentacyclic triterpenoids)	Stimulates body to produce natural killer cells to battle infection and tumor growth	M. Blackwell, "unpublished data," 1994
		<i>I. dryadeus</i> possess antibacterial activity.	Nonlinear, complex (1-3) and (1-6) β -D-glucans, a type of polysaccharide		
Ganodermataceae	<i>Ganoderma</i>	<i>Ganoderma lucidum</i> (also known as Reishi) shows antitumor, immune-modulating activities for treatment of hypoglycemia, hepatoprotection, and the effect on blood vessel system. This mushroom has been used in traditional Chinese and Japanese medicines. Reishi is commonly prescribed for a host of conditions such as anxiety, high blood pressure, bronchitis, insomnia, and asthma but is particularly renowned for its use in hepatitis and other diseases of liver. It also prevents "fatty-liver" and cirrhosis due to alcohol abuse.	Mucopolysaccharides and polysaccharide-protein complexes	Activates the immune response of the host and leads to the induction of cell differentiation and metabolizing enzymes, the inhibition of angiogenesis, and the expression of the urokinase-type plasminogen activator (uPA) and the uPA receptor in cancer cells	[26]
		<i>Ganoderma applanatum</i> have been reported to show immunostimulating properties, fight cancer, stop pain, eliminate indigestion, and reduce phlegm, antibiotic and antiviral.	β -D-glucans and their protein complexes, for example, xyloglucans and acidic β -D-glucan containing uronic acid, dietary fibres, lectins, and terpenoids		
Cantharellaceae	<i>Cantharellus</i>	The edible species <i>C. cibarius</i> , commonly known as chanterelles, have antimicrobial activity against some Gram positive and Gram negative bacteria, yeasts, filamentous fungi, and actinomycetes. They are also known for their antitumor, antioxidant activity and antigenotoxic potential.	Ethyl alcohol, chloroform, and ethanol		[27, 28]

TABLE 2: Continued.

Family	Important genera	Therapeutic properties	Bioactive components	Mode of action	References
Schizophyllaceae	<i>Schizophyllum</i>	Pharmacologically, <i>S. commune</i> is very important because it produces polysaccharide which shows anticancer activity in xenography and clinical practice.	Schizophyllan (β -D-glucan)	Immunomodulation	[29]
Sparassidaceae	<i>Sparassis</i>	<i>Sparassis crispa</i> (cauliflower fungus), its fruiting bodies have antitumor properties and also contain chemicals which may stimulate immune system and inhibit growth of superbug MRSA (methicillin-resistant <i>Staphylococcus aureus</i>).	Bioactive β -D-glucan, phenyl derivatives, chalcones, and sesquiterpenoids	Exhibits various biological activities, including enhancement of the hematopoietic response and induction of cytokine production	[30, 31]
Polyporaceae	<i>Polyporus</i>	<i>Polyporus umbellatus</i> have anticancer and diuretic properties. From <i>Polyporus alveolaris</i> , a polypeptide with antifungal properties has been isolated from the fresh fruit bodies of this species named alveolarin.	Nucleotides, nucleosides, proteins, amino acids, vitamins, polysaccharides, and triterpenoids	Their diuretic property has been used to get rid of the toxins that are responsible for causing infections in the urinary tract and is also found to be very effective against urethral blockages	[32]

TABLE 3: Diversity of nutraceutical and therapeutic metabolite producing mushrooms found in order Auriculariales.

Family	Important genera	Therapeutic/nutritional value	Bioactive component	References
Auriculariaceae	<i>Auricularia</i> <i>Exidia</i> <i>Exidiopsis</i> <i>Eichleriella</i> <i>Fibulosebacea</i> <i>Heterochaete</i> <i>Pseudostypella</i>	<i>Auricularia auricula-judae</i> and <i>A. cornea</i> are cultivated on a commercial scale, particularly in China and south East Asia.	The acidic heteroglycans isolated from <i>Auricularia auricula-judae</i> exhibit antitumor activity	[33, 34]
Hyaloriaceae	<i>Helicomysa</i> <i>Hyaloria</i> <i>Myxarium</i>	—	—	[9]

3. Nutraceutical Metabolites of Mushrooms

It is understood that human beings have constantly been in search of new substances that can improve biological functions and make people fitter and healthier. Recently, the society has turned towards plants, herbs, and food as sources of these enhancers. These products have been called variously vitamins, dietary supplements, functional foods, nutraceuticals, nutraceuticals, and so forth [70–72]. Mushrooms, in this regard, are now beginning to receive much deserved attention for their very real health giving qualities. It is their flavor and texture for which they have long been devoured by the mankind. Scientific appreciation of their nutritional and medicinal attributes is a recent phenomenon. Mushrooms are perhaps the only fungi deliberately and knowingly consumed by human beings and they complement and supplement the human diet with various ingredients not encountered or

deficient in food items of plants and animal origin. Besides, unique chemical composition makes them suitable for specific groups suffering with certain physiological disorders or ailments. This makes the mushrooms an ultimate health food.

The term “nutraceutical” was coined in 1979 by Stephen Deflice, founder and chairman of the foundation for Innovation in Medicine located at Cranford, New Jersey. The word “nutra” derived from nutrition and “ceutical” from pharmaceutical refers to substances that may be considered a food or part of a food and may provide health benefits. It was defined as a food or part of food that provides medical or health benefits, including the prevention and treatment of diseases [73]. Nutraceuticals may range from isolated nutrients, herbal products, dietary supplements, nutraceuticals, and diets to genetically engineered designer foods and processed products such as cereals, soups, and beverages. Doubtlessly, many of these products possess pertinent

TABLE 4: Diversity of nutraceutical and therapeutic metabolite producing mushrooms found in class Gasteromycetes.

Order	Family	Important genera	Therapeutic/nutritional value	References
Lycoperdales	Lycoperdaceae Geastraceae	<i>Calvatia</i> <i>Lycoperdon</i> <i>Radiigera</i> <i>Geastrum</i>	<i>Calvatia gigantea</i> and <i>Calvatia caelata</i> are used in burnt cases due to their anesthetic nature. <i>Calvatia</i> spp. are also used to stop bleeding from wounds. Calvacin isolated from <i>Calvatia gigantea</i> having antitumor activity. <i>Lycoperdon pusillum</i> is used to cure sores, abrasion or bruises, deep cut, hemorrhages, and urinary infections.	[35–37]
Tulostomatales	Calostomataceae Tulostomataceae	<i>Calostoma</i> <i>Tulostoma</i> <i>Battarrea</i>	<i>Calostoma cinnabarina</i> has been recorded to be an edible mushroom. Antibacterial activity has been reported in <i>Tulostoma obesum</i> .	[38, 39]
Sclerodermatales		<i>Scleroderma</i> <i>Astraeus</i> <i>Pisolithus</i>	Polysaccharide from <i>Astraeus hygrometricus</i> has been reported for macrophage stimulation.	[40]
Phallales	Phallaceae Clathraceae	<i>Mutinus</i> <i>Pseudocolus</i> <i>Linderia</i>	—	[9]
Nidulariales	Nidulariaceae Sphaerobolaceae	<i>Nidularia</i> <i>Sphaerobolus</i>	—	[9]

physiological functions and valuable biological activities [74]. A regular intake may enhance the immune response of the human body thereby increasing resistance to disease and in some cases causes regression of a disease state. The Dietary Supplement Health and Education Act of 1994 expanded the definition of nutraceuticals to include vitamins, minerals, herbs, botanicals, amino acids, and any dietary substances used by humans to fortify the diet by increasing total dietary intake [75, 76]. The term “mushroom nutraceuticals” has been coined by Chang and Buswell [77] to describe those compounds that have considerable potential as dietary supplements, used for the enhancement of health and prevention of various human diseases. The important edible mushrooms with remarkable nutraceutical properties include the species of *Lentinus* (*Lentinula*), *Auricularia*, *Hericium*, *Grifola*, *Flammulina*, *Pleurotus*, *Lactarius*, *Pisolithus*, *Tremella*, *Russula*, *Agaricus*, *Cordyceps*, and so forth. A mushroom nutraceutical is refined/partially defined extractives from either mycelium or fruiting bodies, which is consumed in form of capsule or tablet as dietary supplement (not as regular food).

The mushrooms are now recognized as a source of nutraceuticals in nutrient balancing, strengthening human immune system, enhancing natural body resistance, and lowering proneness to disease [1]. Since most nutraceuticals are extracted from edible mushroom species, there is a little scope of toxicity and overdose. The nutritional value of mushrooms is greater than one may think. More than just a condiment for salads, they are actually one of the healthier foods that one can eat. Mushrooms besides being culinary delicacies are also known for their nutritional and medicinal values, a fact which has also been supported by

many recent studies. Thus, mushrooms have started getting much deserved attention for their very real nutraceutical values. Mushrooms are consumed for their palatability and/or nutritional value. Palatability can be judged by color, texture, flavor, and taste, but the determination of nutritional value requires scientific work. It involves the analysis of proximate composition and a study of spectrum of amino acids, fatty acids, vitamins, minerals, nucleic acid, and so forth. It should be noted that the composition of a given species is affected by the diversity of its genetic make-up that leads to strain differences and by environmental conditions, including the nature of substratum. Mushrooms have good flavor, texture, and also all essential amino acids for humans, including lysine and methionine which are commonly deficient in plants [78]. The nutritional value of edible mushrooms nearly equals that of milk and meat. They contain high amount of essential amino acids (lysine, valine, and leucine), proteins, carbohydrates, vitamins, unsaturated fatty acids, fibers, and minerals. Mushrooms are very low in calorie, fat, and sodium. Mushrooms are also cholesterol-free.

Most mushrooms have high protein content, usually around 20–30% by dry weight. This can be useful for vegetarians or anyone looking to increase the protein content in their diet. Fiber helps to lower cholesterol and is important for the digestive system. Niacin and other important B vitamins are found in many edible mushrooms. As certain B vitamins are found in animal tissue but not plants, this can be another good supplement for vegetarians. Vitamin D is also present which is essential for the absorption of calcium. Fruiting bodies, in general, on dry weight basis, contain about 55% carbohydrate, 32% protein, and 2% fat, and the rest is ash

TABLE 5: Proximate composition of cultivated species of edible mushrooms.

Species	Moisture	Crude protein	Crude fat	Carbohydrates	Crude fiber	Ash	Energy	References
<i>Agaricus bisporus</i>	78.3–90.5	23.9–34.8	1.7–8.0	51.3–62.5	8.0–10.4	7.7–12.0	328–368	[41]
<i>Agaricus campestris</i>	89.7	33.2	1.9	56.9	8.1	8.0	354	[41]
<i>Boletus edulis</i>	87.3	29.7	3.1	59.7	8.0	7.5	362	[41]
<i>Flammulina velutipes</i>	89.2	17.6	1.9	73.1	3.7	7.4	378	[41]
<i>Lentinus edodes</i>	90–91.8	13.4–17.5	4.9–8.0	67.5–78.0	7.3–8.0	3.7–7.0	387–392	[41]
<i>Pleurotus ostreatus</i>	73.7–90.8	10.5–30.4	1.6–2.2	57.6–81.8	7.5–8.7	6.1–9.8	345–367	[41]
<i>Pleurotus sajor-caju</i>	90.1	26.6	2.0	50.7	13.3	6.5	300	[42]
<i>Volvariella volvacea</i>	89.1	25.9	2.4	—	9.3	8.8	276	[43]
<i>Russula vesca</i>	—	22.8	0.1	71	—	—	—	[44]
<i>Lactarius trivialis</i>	37	—	0.1	64	—	—	—	[44]
<i>Lentinus tigrinus</i>	6	—	0.1	62	—	—	—	[44]
<i>Agaricus arvensis</i>	94.9	2.87	0.14	1.91	—	0.18	20.38	[45]
<i>Lactarius deliciosus</i>	90	2.96	0.22	6.26	—	0.51	38.86	[45]
<i>Leucopaxillus giganteus</i>	92.43	3.4	0.41	3.11	—	0.65	29.73	[45]
<i>Stegastes imbricatus</i>	93.89	2.35	0.09	3.38	—	0.29	23.73	[45]
<i>Tricholoma portentosum</i>	93.05	2.12	0.38	3.64	—	0.81	26.46	[45]
<i>Cantharellus cibarius</i>	—	26.25	9.14	18	13.64	25.78	—	[46]
<i>Clitocybe odora</i>	—	41.13	14.29	11.50	12.72	17.44	—	[46]
<i>Laccaria laccata</i>	—	14.03	8.48	8.17	10.96	33.60	—	[46]
<i>Auricularia polytricha</i>	95.6	8.5	5.2	5.9	3.5	5.2	—	[47]
<i>Lentinus subnudus</i>	90.3	5.1	4.5	8.9	6.5	7.1	—	[47]
<i>Morchella esculenta</i>	94.5	25.4	10.8	8.9	8.3	10.8	—	[47]
<i>Pleurotus ostreatus</i>	4.46	20.82	0.56	68.35	45.5	5.81	—	[47]
<i>Pleurotus sajor-caju</i>	5.32	21.30	0.29	65.14	42.5	7.95	—	[47]

Note: all data are presented as percentage of dry weight except moisture (percentage of fresh weight) and energy value (Kcal per 100 g dry weight).

constituting the minerals [41]. Therefore, the commercial cultivation of these mushrooms is steadily increasing to exploit their metabolic products for human health. Mushrooms are also blessed with a variety of hydrolyzing and oxidizing enzymes [79]. Table 5 summarizes the general proximate composition of different nutrients found in various edible species of mushrooms.

3.1. Proteins. The protein content of four popular edible mushrooms, *Agaricus bisporus*, *Lentinus edodes*, *Pleurotus* spp., and *Volvariella volvacea*, which are cultivated in various countries, ranges from 1.75 to 3.63% of their fresh weight [80]. The value can be as high as 5.9%; however, an average value of 3.5 to 4% would appear to be representative. This shows that the protein content of edible mushrooms, in general, is about twice that of asparagus and cabbage and 4 times and 12 times those of oranges and apples, respectively. On dry weight basis, mushrooms normally contain 19 to 35% protein, as compared to 7.3% in rice, 13.2% in wheat, 39.1% in soybean, and 25.2% in milk. Therefore, in amount of crude protein, mushrooms rank below most animal meats but well above most other foods, including milk [81]. This can be useful for vegetarians or anyone looking to increase the protein content in their diet. *Pleurotus sajor-caju* (1.60 g/100 g), *Morchella esculenta*

(1.62 g/100 g), *Pleurotus ostreatus* (1.68 g/100 g), *Agaricus bisporus* (1.80 g/100 g), and *Boletus edulis* (2.20 g/100 g) are also a good source of protein [82].

3.2. Essential Amino Acids. Since proteins are made up from 20 amino acids in varying amounts, they are quantitatively different. There are nine amino acids that are not synthesized within the body. These are called essential amino acids (lysine, methionine, tryptophan, threonine, valine, leucine, isoleucine, histidine, and phenylalanine). The proteins of commonly cultivated mushrooms contain all nine amino acids essential for man. The most abundant essential amino acid turns out to be lysine and the lowest levels among the essential amino acids are tryptophan and methionine as mentioned in Table 6.

3.3. Fat. The fat content in different species of mushrooms ranges from 1.1 to 8.3% on dry weight basis. Thus, an average value of 4% would appear to be representative (Table 7). In general, the crude fat of mushrooms represents all classes of lipid compounds including free fatty acids, monoglycerides, diglycerides, triglycerides, sterols, sterol esters, and phospholipids. At least, 72% of the total fatty acids were found to be unsaturated in each one of these mushrooms, thus making

TABLE 6: Essential amino acid (EAA) composition of some important edible mushrooms.

Mushroom species	Valine	Leucine	Isoleucine	Threonine	Methionine	Lysine	Phenylalanine	Tryptophan	References
<i>Agaricus bisporus</i>	2.5	7.5	4.5	5.5	0.9	9.1	4.2	2.0	[48]
<i>Lentinus edodes</i>	3.7	7.9	4.9	5.9	1.9	3.9	5.9	Nd	[48]
<i>Pleurotus florida</i>	6.9	7.5	5.2	6.1	3.0	9.9	3.5	1.1	[48]
<i>Volvariella diplasia</i>	9.7	5.0	7.8	6.0	1.2	6.1	7.0	1.5	[48]
<i>Volvariella volvacea</i>	5.4	4.5	3.4	3.5	1.1	7.1	2.6	1.5	[48]
<i>Cantharellus cibarius</i>	3.5	16.3	3.3	4.2	1.0	4.3	3.2	1.7	[49]
<i>Tricholoma portentosum</i>	7.8	9.4	3.7	9.5	3.0	8.6	4.4	1.0	[50]
<i>Tricholoma terreum</i>	8.9	8.2	3.6	9.1	3.5	7.6	6.6	1.1	[50]
<i>Pleurotus ostreatus</i>	0.91	1.13	0.62	1.10	0.28	0.71	0.73	0.15	[51]
<i>Pleurotus sajor-caju</i>	0.98	1.3	0.75	0.98	0.34	0.78	0.86	0.09	[51]
* <i>Lactarius quieticolor</i>	41.9	4611	71.7	80.2	67.2	24.6	0.1	—	[52]
* <i>Gomphus floccosus</i>	10.5	22.7	5.0	17.7	57.2	14.3	0.2	—	[52]
* <i>Ramaria brevispora</i>	16.3	22.3	0.2	24.6	16.2	39.8	5.4	—	[52]
* <i>Coprinopsis cinerea</i>	0.5	248	0	21	0.6	1.4	0	—	[52]

Note: data presented as grams of amino acid per 100 grams of sample.

* Values are expressed on dry weight basis ($\mu\text{g}/100$ grams of sample).

Nd = not determined.

TABLE 7: The total lipids in some important edible mushrooms [57].

Mushroom	Percent of lipids in dry weight
<i>Volvariella volvacea</i>	3.0
<i>Lentinus edodes</i>	2.1
<i>Agaricus bisporus</i>	3.1
<i>Pleurotus sajor-caju</i>	1.6
<i>Auricularia auricular</i>	1.3
<i>Tremella fuciformis</i>	0.6
<i>Morchella esculenta</i>	1.96 (g/100 mg)
<i>Pleurotus ostreatus</i>	2.2 (g/100 mg)
<i>Boletus edulis</i>	3.6 (g/100 mg)

mushrooms a health food as they are essential in our diet, whereas saturated fatty acids may be harmful to our health [83].

3.4. Vitamins. Mushrooms have been reported to be good source for several vitamins. The B-group vitamins are abundant [77, 84–88] mainly thiamine (vitamin B1), riboflavin (vitamin B2), niacin, biotin, and other vitamins like ascorbic acid (vitamin C) [41]. The thiamine content ranges from 0.35 mg in *Volvariella volvacea* to 1.14 mg in *Agaricus bisporus*, to 1.16 and to 4.80 mg in *Pleurotus* spp., and to 7.8 mg in *L. edodes* (mg per 100 g dry weight of mushroom). The niacin content varies from 54.9 mg in *L. edodes* to 55.7 mg in *A. bisporus*, to 64.88 mg in *V. volvacea*, and to 46.0 and to 108.7 mg in *Pleurotus* spp. The riboflavin content is higher in *A. bisporus* (5.0 mg) and *L. edodes* (4.9 mg) than in *V. volvacea* (1.63 to 2.98 mg). Vitamin C content has been reported to be highest in *L. edodes* (9.4 mg/100 g dry sample) followed by *P. sajor-caju*, *A. bisporus*, and *V. volvacea* with 7.4 mg, 1.8 mg, and 1.4 mg [81].

3.5. Carbohydrate. According to [41], pentoses, methylpen-
toses, hexoses, disaccharides, amino sugars, sugar alcohols,

and sugar acids are constituents of mushroom carbohydrates. *Pleurotus* species contain carbohydrates ranging from 46.6 to 81.8% as compared to 60% in *A. bisporus* on dry weight basis. The fiber content ranges from 7.4 to 27.6% in *Pleurotus* species as compared to 10.4% in *A. bisporus* and 4 to 20% in *V. volvacea*.

3.6. Fiber. Fiber is considered to be an important ingredient in a balanced diet. Feeding diabetic patients with high fiber diets reduces their daily insulin requirement and stabilizes their blood glucose profile, possibly by decreasing the rate of glucose absorption [89]. High molecular weight materials excreted without digestion and absorption by humans are called dietary fiber [90]. Most of the active polysaccharides, water soluble or insoluble, isolated from mushrooms can be classified as dietary fibers. Mushrooms contain 10–50% dietary fibers in dried matter.

3.7. Minerals. Mushrooms are a good source of minerals. It is calculated that the concentrations of K, P, Na, Ca, and Mg constitute about 56 to 70% of the total ash content [63]. Potassium is particularly abundant and accounts for nearly 45% of the total ash content. It is an extremely important mineral that regulates blood pressure and keeps cells functioning properly. A large portobello mushroom is said to have more potassium than a banana. Sodium and calcium are present in approximately equal concentrations in all the mushrooms except for *Lentinus edodes* in which calcium is present in excessively large amount. The copper is higher in all species of *Pleurotus* and varies from 12.2 to 21.9 ppm. Cu aids in helping the body to absorb the oxygen and create red blood cells. Calcium and lead contents vary from 0.3 to 0.5 ppm and from 1.5 to 3.2, respectively, in all species of *Pleurotus*. Of all the heavy metals, the zinc content is generally highest in all species of *Pleurotus*. Copper aids in helping the body to absorb oxygen and participate in formation of red blood cells. Selenium is an antioxidant

TABLE 8: Levels of the trace metals ($\mu\text{g/g}$, dry weight basis) in the analyzed mushroom samples.

	Mg	Cr	Mn	Fe	Co	Ni	Cu	Zn	Pb	Cd	References
<i>Cantharellus cibarius</i>	866.3	1.57	22.09	118.2	0.05	1.07	32.49	54.29	n.d.	0.38	[58]
<i>Boletus aureus</i>	755.1	0.86	18.3	112.8	0.18	1.61	41.4	89.4	0.09	0.23	[58]
<i>Lentinula edodes</i>	40.7	—	1.00	14.8	—	0.15	1.48	9.44	BDL	BDL	[59]
<i>Lentinus cladopus</i>	21.1	—	0.54	35.3	—	0.09	0.97	1.58	BDL	BDL	[59]
<i>Pleurotus florida</i>	35.9	—	0.62	6.27	—	0.07	1.06	5.06	0.092	BDL	[59]
<i>Pleurotus djamor</i>	31.6	—	1.12	14.8	—	0.15	1.45	9.21	0.12	BDL	[59]
<i>Pleurotus ostreatus</i>	37.39	—	0.27	1.76	—	—	0.18	1.10	—	—	[60]
<i>Pleurotus sajor-caju</i>	30.06	—	1.19	0.94	—	—	0.37	0.68	—	—	[60]
<i>Calocybe indica</i>	51.21	—	0.53	1.81	—	—	0.91	0.78	—	—	[60]

BDL: below detectable level.

that helps to neutralize free radicals, thus preventing cell damage and reducing the risk of cancer and other diseases. Mushrooms contain more selenium than any other form of produce. Potassium is an extremely important mineral that regulates blood pressure and keeps cells functioning properly. Other important minerals such as phosphorus, zinc, and magnesium are also found in mushrooms. Table 8 depicts levels of different metals in important edible mushrooms.

3.8. Nucleic Acids and Nucleotide Derivatives. Nucleotides are organic molecules that serve as the monomers, or subunits, of nucleic acids like DNA and RNA. Nucleotides serve to carry packets of energy within the cell (ATP). In the form of the nucleoside triphosphates (ATP, GTP, CTP, and UTP), nucleotides play central roles in metabolism. Nucleoside compounds produced by basidiomycetous fungi have also been investigated in detail and some of them have exhibited interesting bioactive potential. For example, shiitake mushrooms *Lentinus edodes* whose fruit bodies are cultivated on fallen logs in Japan for their value as edible delicacies are also a source of lentinacin, a nucleoside compound with hypoglycemic (cholesterol lessening) activity. *Clitocybe inversa* has been described as producing an insecticidal metabolite termed clitocine. Microorganisms are characterized by a high nucleic acid content. Viikari and Linko [62] have reported that the nucleic acid content of microorganisms is in the range of 8 to 25% (dry weight), while those of algae and fungi are known to be 3 to 8% and 3.2 to 4.7% (dry weight), respectively [61]. The nucleic acid content of mushrooms in comparison with other sources is given in Table 9. The practical safe limit of nucleic acid intake of most adult populations is a daily maximum of 4 g as suggested by the Protein Advisory Group of the United Nations System [91]. This is because man lacks the urate oxidase enzyme for the oxidation of uric acid, which is the sparingly soluble metabolic product of

TABLE 9: Nucleic acid content of some edible mushrooms and other food.

Samples	Nucleic acid content	Source
Yeast	6.0–12.0% dry weight	[61]
Bacteria	8.0–16.0% dry weight	[61]
Algae	3.0–8.0% dry weight	[61]
Cereals	1.1–4.0 g/100 g protein	[61]
Meat and fish	2.2–5.7 g/100 g protein	[61]
Microorganisms	8.0–25.0 g/100 g protein	[62]
Mushrooms	2.7–4.1% dry weight	[63]

TABLE 10: Nucleic acid content of four edible mushrooms [63].

Mushrooms	Percent nucleic acid content (dry weight basis)
<i>Agaricus bisporus</i>	2.66
<i>Pleurotus cystidiosus</i>	2.93
<i>Pleurotus sajor-caju</i>	4.06
<i>Volvariella volvacea</i>	3.88

purine bases guanine and adenine [92]. As given in Table 10, *Pleurotus sajor-caju* contains the highest amount of nucleic acids among the four edible mushrooms that were studied, 4.06% on a dry weight basis. Accordingly, it is safe to consume as much as 392.5 g of fresh *P. sajor-caju* daily. The limit could be higher for mushrooms with lower nucleic acid content.

4. Therapeutic Metabolites of Mushrooms

Fungi are nature's most accomplished chemists. The compounds they synthesize range from simple ubiquitous molecules such as gluconic and citric acid, often referred to

as primary metabolites, to complex unusual molecules such as aflatoxin and ergot alkaloids, which are called secondary metabolites. Hundreds of medicinal mushrooms have been identified and their bioactive metabolites have been successfully used for the treatment of various diseases. These mushrooms are well known for their industrial and medicinal applications and a lot of work has been reported on these aspects by various workers. The climatic conditions prevailing in India have made it a natural habitat of large number of diverse mushroom flora and their metabolites. The use of mushrooms as medicine was mentioned by Berkeley [35]. He also reported the use of *Calvatia gigantea* (giant puffball) and *C. caelata* in burnt cases due to their anaesthetic activity. They are also used to stop bleeding from wounds. Notable medicinal mushrooms with a well-documented history of use include *Agaricus subrufescens*, *Ganoderma lucidum*, and *Ophiocordyceps sinensis*. Research has identified compounds produced by these fungi have inhibitory biological effects against viruses and cancer cells. Specific metabolites, such as polysaccharide-K, ergotamine, and β -lactam antibiotics, are routinely used in clinical medicine. The shiitake mushroom is a source of lentinan, a clinical drug approved for use in cancer treatments in several countries. In Europe and Japan, polysaccharide-K (brand name, Krestin), a chemical derived from *Trametes versicolor*, is an approved adjuvant for cancer therapy. The wood rotting fungus *Ganoderma lucidum* is an example that is cultivated today for its reputed medicinal benefits. Metabolites like nucleotides, nucleosides, proteins, amino acids, vitamins, polysaccharides, and triterpenoids have been reported to show activities like antitumor, anti-allergic, antiviral, anti-inflammatory activities, antiageing effect, hepatoprotective effect, hypoglycemic activity, and cardiovascular effect. They are used for the treatment of chronic hepatitis. They are useful for enhancing vital energy, increasing thinking ability, and preventing forgetfulness. Extracts and powders derived from *G. lucidum* are being marketed in the form of capsules or sugar-coated tablets as a cure of many diseases. Polysaccharides, proteins, lipids, enzymes, vitamins, and minerals from *Lentinus edodes* are reported to treat dizziness and headache and used as a health tonic. Lentinan isolated from *Lentinus edodes* has antitumor activity. Active principles are said to be immune stimulating polysaccharides strengthening health and immunity [65]. *Agaricus bisporus* has been reported for its 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) radical scavenging and total antioxidant capacity [93]. *Pleurotus ostreatus* has also been reported for its hypocholesterolemic, hypoglycemic, and hypolipidemic properties. Mushrooms have significant pharmacological effects or physiological properties, such as bioregulation (immunological enhancement), maintenance of homeostasis, regulation of biorhythm, cure of various diseases, prevention and improvement of life threatening diseases such as cancer, cerebral stroke, heart diseases, and immune deficiency diseases (including AIDS), or generation of immunosuppression during treatment [94]. A vast chemodiversity of the compounds has been reported in various mushrooms and important among them have been discussed below.

4.1. Polysaccharides. Polysaccharides are the best known metabolite present in mushrooms with antitumor and immunomodulating properties. β -D-glucans are a type of polysaccharide found in mushrooms that give them some medicinal properties. β -D-glucans bind to certain receptors on the surface of macrophages and other white blood cells. β -D-glucans have been shown to stimulate the production of some cytokines. They also help in prevention of asthma. Biologically active polysaccharides are widespread among higher basidiomycetous mushrooms, and most of them have unique structures in different species. These polysaccharides have different compositions, most belonging to the group of β -D-glucans; these have β -(1-3) linkages in the main chain of glucan and additional β -(1-6) branch points. High molecular weight glucans appear to be more effective than those of low molecular weight. Moreover, different strains can produce polysaccharides with different properties. For example, the proteoglycan Krestin was developed in Japan from the strain *Trametes (Coriolus) versicolor* CM-101, whereas polysaccharide-peptide (PSP) in China was developed in submerged culture from the strain Cov-1 of the same species. Table II shows the bioactivity of polysaccharides of some important mushrooms.

4.2. Terpenoids. Terpenes are known as an important variety of naturally occurring bioactive metabolites produced by many higher fungi. Diterpenoids, triterpenoids, and sesquiterpenoid are the typical representatives of terpenes with interesting biological activities. Terpenoids are known to show anti-infectious and anti-inflammatory activities. Triterpenoids are mainly common among fungal metabolites. Terpenoid compounds, particularly sesquiterpenoids of unique structure, characterize many basidiomycetes and while they are not found in other microbes, some of them have homologies with plant terpenoid compounds. Triterpenoids isolated from *Ganoderma lucidum* are a class of naturally occurring compounds and structurally highly oxidized lanostanes. Accumulated data show that triterpenoids exhibit a broad spectrum of anticancer properties, including antiproliferative, antimetastatic, and antiangiogenic activities [95]. About 80 terpenoids including ganoderic acid derivatives have been isolated from the fruit bodies and the mycelia of *G. lucidum* [96-105]. Some of them have shown cytotoxicity against hepatoma cells *in vitro* (ganoderic acids U, V, W, X, and Y), antihistamine releasing activity in rat mast cells (ganoderic acids C and D), inhibitory activity against angiotensin converting enzyme (ganoderic acid F), hepatoprotective activity (ganoderic acid A), and an inhibitory effect on farnesyl protein transferase (ganoderic acid A and methyl ganoderate A) [105]. *Merulius tremellosus* produced a sesquiterpene dialdehyde named Merulidial 1 having high antifungal activity. Likewise, *Marasmius alliaceus* has been the source of unsaturated sesquiterpene showing high toxic properties and inhibiting nucleic acid synthesis in carcinoma cells. Lentinelic acid obtained from *Lentinellus omphalodes* exhibited strong antibacterial activity towards Gram positive as well as negative bacteria such as *Bacillus subtilis* and *Aerobacter aerogenes* and also inhibited to a significant extent DNA, RNA, and protein synthesis in Ehrlich

TABLE II: Source, type, and bioactivity of some mushroom polysaccharides.

Mushroom name	Polysaccharide source	Type of polysaccharide	Bioactivity	References
<i>Pleurotus tuber-regium</i>	Sclerotium, mycelium	β -D-glucan	Hepatoprotective, antibreast cancer	[64]
<i>Ganoderma lucidum</i>	Fruiting body, culture broth	Heteroglycan, mannoglucan, glycopeptide	Hyperglycemia, immunomodulating, antitumor, antioxidative, antidecrepitude	[64]
<i>Auricularia auricular</i>	Fruiting body	Glucan	Hyperglycemia, immunomodulating, antitumor, anti-inflammatory, antiradiative	[64]
<i>Schizophyllum commune</i>	Mycelium	Glucan, schizophyllan	Antitumor	[64]
<i>Hericium erinaceus</i>	Fruiting body, mycelium	Heteroglycan, heteroglycan peptide	Hyperglycemia, immunomodulating, antitumor	[64]
<i>Lentinus edodes</i>	Culture broth, fruiting body	Mannoglucan, polysaccharide-protein complex, glucan, lentinan	Immunomodulating, antitumor, antiviral	[64]
<i>Sclerotinia sclerotiorum</i>	Sclerotium	Glucan, scleroglucan (SSG)	Antitumor	[64]
<i>Polystictus versicolor</i>	Fruiting body, culture broth, mycelium	Heteroglycan, glycopeptide, Krestin (PSK)	Immunomodulating, antitumor, antiradiative, hyperglycemia, anti-inflammatory	[64]
<i>Grifola frondosa</i>	Fruiting body	Proteoglycan, glucan, galatomannan, heteroglycan, and grifolan	Immunomodulating, antitumor, antiviral, hepatoprotective	[64]
<i>Inonotus obliquus</i>	Fruiting body, mycelium	Glucan	Antitumor, immunomodulating	[64]
<i>Agaricus blazei</i>	Fruiting body, mycelium	Glucan, heteroglycan, glucan protein, Glucomannan-protein complex	Antitumor	[64]
<i>Flammulina velutipes</i>	Fruiting body, mycelium	Glucan-protein complex, glycoprotein	Antitumor, anti-inflammatory, antiviral, immunomodulating	[64]
<i>Ganoderma applanatum</i>	Fruiting body	Glucan	Antitumor	[64]
<i>Polyporus umbellatus</i>	Mycelium	Glucan	Antitumor, immunomodulating	[64]
<i>Clitopilus caespitosus</i>	Fruiting body	Glucan	Antitumor	[64]
<i>Pleurotus citrinopileatus</i>	Fruiting body	Galactomannan	Antitumor	[64]
<i>Trametes robiniophila</i>	Mycelium	Proteoglycan	Immunomodulating, hepatoprotective, anticancer	[64]
<i>Tremella fuciformis</i>	Fruiting body, mycelium, culture broth	Heteroglycan	Hyperlipidemia, hyperglycemia, immunomodulating, antitumor, antidecrepitude, antithrombus	[64]
<i>Tremella aurantialba</i>	Fruiting body, mycelium	Heteroglycan	Immunomodulating, hyperglycemia	[64]
<i>Pleurotus ostreatus</i>	Fruiting body	Glycoprotein	Antitumor, hyperglycemia, antioxidant	[64]
<i>Morchella esculenta</i>	Fruiting body	Heteroglycan	Hyperglycemia, antitumor	[64]
<i>Omphalia lapidescens</i>	Fruiting body	Glucan	Anti-inflammatory, immunomodulating	[64]
<i>Phellinus linteus</i>	Fruiting body	Glucan	Antitumor	[64]
<i>Armillariella tabescens</i>	Mycelium	Heteroglycan	Antitumor	[64]
<i>Dictyophora indusiata</i>	Fruiting body	Heteroglycan, mannan, glucan	Antitumor, hyperlipidemia	[64]
<i>Tricholoma mongolium</i>	Fruiting body	Glucan	Antitumor	[64]

TABLE 11: Continued.

Mushroom name	Polysaccharide source	Type of polysaccharide	Bioactivity	References
<i>Cordyceps</i> sp.	Fruiting body, mycelium, culture broth	Glucan, heteroglycan	Antitumor, immunomodulating, antitumor, hyperglycemia	[64]
<i>Coriolus versicolor</i>	Fruiting body, mycelium	Polysaccharides PSK and PSP	Antiviral effect on HIV and cytomegalovirus <i>in vitro</i> and anticancer	[65]
<i>Marasmius androsaceus</i>	Fruiting body, mycelium	Polysaccharide	Analgesic/sedative effect	[66]
<i>Volvariella</i> sp.	Fruiting body, mycelium	Polysaccharide	Cardiac tonic	[66]
<i>Coprinellus disseminatus</i>	Fruiting body, mycelium	Polysaccharide	Antitumor	[67]
<i>Trametes coriolus</i>	Fruiting body, mycelium	Polysaccharide PSP-a glycopeptides	Antitumor and immunostimulant	[67]
<i>Tricholomopsis rutilans</i>	Fruiting body, mycelium	Polysaccharides extract	Anticarcinogenic activity Antioxidative and anti-inflammatory	[65]
<i>Tremella fuciformis</i>	Fruiting body, mycelium	Polysaccharide	Hypocholesteric and hypolipidemic	[67]
<i>Schizophyllum commune</i>	Fruiting body, mycelium	Polysaccharide schizophyllan	Antitumor effect	[67]

ascetic carcinoma cells. The terpenoids, namely, Illudin-M and Illudin-S, extracted from *Clitocybe illudens* are very effective against *Plasmodium gallinaceum* [106].

4.3. Steroids. Steroids are a type of organic compound that contains a characteristic arrangement of four cycloalkane rings that are joined to each other. Examples of steroids include the dietary fat cholesterol, the sex hormones estradiol and testosterone, and the anti-inflammatory drug dexamethasone. Recently, two known sterols with new cyclooxygenase (COX) inhibitory and antioxidant activities were isolated from the fruiting bodies of *Agrocybe aegerita* which is an edible mushroom [107]. Additionally, Wu et al. [108] reported that two novel secoergosterols, tylopiol A (106) and tylopiol B (107), were isolated from the fresh fruiting bodies of *Tylopilus plumbeoviolaceus*.

4.4. Glycoproteins. Glycoproteins are proteins that contain oligosaccharide chains (glycans) covalently attached to polypeptide side-chains by process known as glycosylation. Phallolysin is a glycoprotein obtained from *Amanita phalloides* which causes cytolysis of many mammalian cells [109]. Two distinct lectins, TML-1 and TML-2, with hemagglutinating and antiproliferative activity have been isolated from the cultured mycelium of the edible mushroom *Tricholoma mongolicum* [110].

4.5. Polyketides. Higher fungi have been recognized as profile producers of polyketides in the past as well as in the present. Polyketides are a class of secondary metabolites produced by almost all living organisms. These are structurally complex organic compounds that are often highly active biologically. Many pharmaceuticals are derived from or inspired by polyketides. Polyketides are structurally a very diverse family of natural products with diverse biological activities and pharmacological properties. Polyketides are the

most abundant medicinal sources that have been shown to display a wide range of potentially useful therapeutic values like antibiotic, anticancer, antifungal, hypolipidemic, and immunosuppressive properties [111].

4.6. Others. Higher basidiomycetes especially mushrooms possess unlimited and useful therapeutic metabolites including alkaloids, flavonoids, saponins, tannins, anthraquinones, and steroids. Their presence makes these mushrooms popular to consume as good food sources and also valuable in drug development (Table 12).

Saponins are known to inhibit Na^+ efflux by blockage of the influx of concentration in the cells, activating $\text{Na}^+-\text{Ca}^{2+}$ antiporter in cardiac muscles. The increase in Ca^{2+} influx through this antiporter strengthens the contraction of heart muscles [112].

Alkaloids have been reported in curing many deadly human diseases like AIDS, cancer, and lung diseases [113]. Alkaloids regulate Na^+ ions and channels and microbial activity, have stimulating properties, and induce immunogenic cell death. Alkaloids are also known to have inhibitory effects on angiogenesis and therefore are useful in inhibiting the growth of cancerous cells [114].

High flavonoids level may help to provide protection against oxidative stress induced diseases by contributing along with other antioxidant vitamins and enzymes to the total antioxidative defense system of the human body. Many studies have attributed that antioxidant properties are due to the presence of flavonoids [115]. Hence, this may be a reason for the high lipid peroxidation inhibition found in certain species of the studied mushrooms.

Anthraquinone has been shown in certain studies to help in digestion as a laxative, to reduce inflammation in arthritis patients, and to inhibit the growth of cancer cells.

Triterpene glycoside affects the activity of the gastrointestinal tract; cyanogenic glycosides interfere with iodine

TABLE 12: Miscellaneous therapeutic metabolites of mushrooms and their bioactivity.

Mushroom name	Active principle	Activity	Reference
<i>Ganoderma lucidum</i> Common name: Reishi	Triterpenes, Ganoderiol F Ganoderic acid B Ganodermanontriol. Ganodermediol Polysaccharide (ganopoly) Triterpenes Polysaccharides Ganoderon A, Ganoderon B, Ganoderon C β -D-glucan Glycoprotein	Active against HIV-1 Cytotoxic to hepatoma cells Active against herpes simplex virus-1 Causing palliative effect on cancer related symptoms and hepatitis B treatment Protection against atherosclerosis Hypoglycemic effect during treatment of type 2 diabetics Immunostimulative antitumor activity Antitumor activity	[65, 67]
<i>Ganoderma applanatum</i>	Steroids Applanoxidic acid G Applanoxidic acid G	Antagonist to both Gram positive and Gram negative bacteria Active against influenza virus type A Active against mouse skin tumor promoters Useful in treatments of pain	[65]
<i>Lentinula edodes</i> Common name: shiitake	Oxalic acid present on caps Polysaccharide lentinan Emitanin Soluble lignin Eritadenine (a nucleotide derivative)	Antibacterial activity Inhibits Sarcoma 180 and HIV induced cytopathic effect Used in tumor/chemo/radiotherapy/surgery Anti-HIV activities Antilipidemic activity and reduces risk of atherosclerosis	[65]
<i>Flammulina velutipes</i>	Sesquiterpenes, proteins, and polysaccharides Enokipodins Velutin protein Alcoholic and hot water extracts of its sporophores	Antitumor Antifungal and antibacterial Inactivating ribosome and inhibiting HIV-1 reverse transcriptase Cytostatic effects against tumor cells Antiallergic and anticomplementary effects	[65]
<i>Auricularia- auricula judae</i>	Acidic heteroglycans	Antitumor	[65]
<i>Auricularia polytricha</i>	Antiplatelet compound Adenosine	Artherosclerotic activity	[65]
<i>Pleurotus ostreatus</i>	Lovastatin	Artherosclerotic activity	[65]
<i>Grifola frondosa</i>	Polysaccharide β -D-glucan Maitake D-fraction Proteins with β -D-glucan (Grifolan) Xyloglucan, fucomannoglucan Heteroglucans proteins Mannogalactofucan Heteroxylan Galactomannoglycan	Antiviral activity and immunostimulatory effect HIV-antitumor activity Antitumor activity	[67]
<i>Laetiporus sulphureus</i>	Dehydrotrametenolicacid	Hypoglycemic activity Insulin sensitizer and reducing hyperglycemia	[67]
<i>Lenzites betulina</i>	Betulinam A	Radical scavenger	[67]
<i>Cordyceps militaris</i>	Polysaccharides (Cordycepic acid and β -D-glucans) Triterpenoids Nucleosides (cordycepin, 3-deoxyadenosine) Proteins, amino acids Vitamins (B-complex and ascorbic acid) Minerals (trace elements)	Cancer Fatigue Respiratory and pulmonary diseases Liver and renal disorders Male and female sexual dysfunctions Cardiovascular diseases	[65]
<i>Cordyceps sinensis</i>	Adenosine, cordycepin, and ergosterol	Antioxidative property	[68]

TABLE 12: Continued.

Mushroom name	Active principle	Activity	Reference
<i>Morchella esculenta</i>	Polysaccharides, proteins, enzymes, vitamins, minerals, and amino acids No cholesterol	Cures pneumonia, fever, cough, cold, and stomachache Cures diseases for pregnant and lactating minerals For respiratory ailments	[65]
<i>Pleurotus sajor-caju</i>	Proteins having polysaccharide xyloglucan, xyloproteins	Antitumor	[67]
<i>Agaricus campestris</i>	Glycoproteins	Antitumor	[67]
<i>Boletus edulis</i>		Antitumor	[67]
<i>Calvatia gigantea</i>	Calvacin	Antitumor	[67]
<i>Cyathus stercoreus</i>	Polyketide Cyathusals A, B, and C Pulvinatal antioxidant effect	Antitumor	[67]
<i>Tricholomopsis rutilans</i>	Polysaccharides Phenol foscimin B Sterols	Antitumor, anti-inflammatory, and antioxidant	[67]
<i>Oudemansiella radicata</i>	E-b methoxy acrylate	Antibiotic effect	[66]
<i>Collybia velutipes</i>	Eritadenine	Decreasing cholesterol	[66]

organification and thus can cause or promote goiter and hypothyroidism. An array of glycosidic compounds is currently used in medicine. It involves glycosides of vitamins, polyphenolic glycosides (flavonoids), alkaloid glycosides, glycosides in the group of antibiotics, glycopeptides, cardiac glycosides, steroid and terpenoid glycosides, and so forth.

Many tannin molecules have also been shown to reduce the mutagenic activity of a number of mutagens. Many carcinogens and/or mutagens produce oxygen-free radicals for interaction with cellular macromolecules. The anticarcinogenic and antimutagenic potentials of tannins may be related to their antioxidative property, which is important in protecting cellular oxidative damage, including lipid peroxidation [116].

5. Conclusion

The need to maintain or rebuild a healthy defense mechanism has led researchers in search of natural health supporting properties from fungi including mushrooms. Human beings have constantly searched for new substances that can steadily and efficiently improve biological functions. Nutraceuticals are destined to play important role in future therapeutic developments. There are evidences that beneficial treatment of some diseases can also be obtained by consumption of functional foods or through the use of extracted biologically active compounds in the form of nutraceuticals/dietary supplements. The mushroom family in particular shows promise for its ability to enhance immune function. Mushrooms grow wild in many parts of the world and are also commercially cultivated. Nutritionally, mushrooms are a valuable health food and have been used medicinally for centuries in various parts of the world. Although the nutritional facts and culinary uses of mushrooms are well adapted, the fungi's medicinal qualities have yet to make the mainstream.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

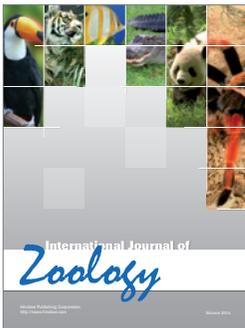
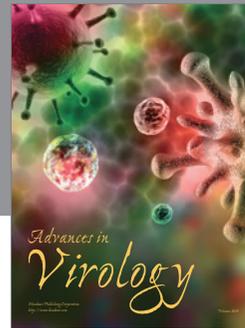
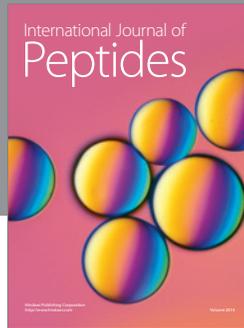
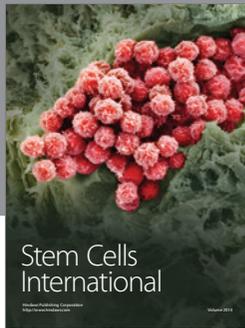
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