Chapter

Wild Medicinal Mushrooms: Potential Applications in Phytomedicine and Functional Foods

Clement Olusola Ogidi, Victor Olusegun Oyetayo and Bamidele Juliet Akinyele

Abstract

The accumulated secondary metabolites in medicinal mushrooms have been widely accepted as sources of safe and effective nutraceuticals, cosmeceuticals, and pharmaceuticals. Medicinal and edible mushrooms are foods appreciated for their exquisite flavor and medicinal properties. The nutritional values and biologically active compounds in mushrooms have immense potentials for producing new drugs of great health benefits to mankind. In recent times, medicinal mushrooms are being exploited for new and natural compounds that could modulate immune cell's response, and possess antimicrobial, antioxidants, and anticancer properties. In Nigeria, where there is vegetation that supports the luxuriant growth of varieties of naturally occurring macrofungi, some of the wild macrofungi have not been properly identified, adequately studied, and fully harnessed for their potentials as food and medicine. It is therefore pertinent to bring to limelight the nutraceutical potentials of some of these wild macrofungi that are currently underutilized.

Keywords: Nutraceuticals, medicinal mushrooms, mycochemicals, basidiomycetes

1. Introduction

Medicinal and edible mushrooms are mostly found in the higher basidiomycetes, and they usually have a saprophytic and aerobic growth habit, which allows them to grow on different lignocellulosic materials [1]. Fungi as a kingdom have very diverse group of living organisms found across all ecosystems [2]. Fungi are eukaryotes; they have microscopic organelles within their cells called nuclei which contain genetic materials in the form of threadlike chromosomes and enable hereditary characters to be passed on to subsequent generations [3]. The Basidiomycetes make up a colossal variety of fungi. Their taxonomic determination has been controversial and sometime challenging due to limited distinguishing characters and disagreement in features characteristics to be adopted for separating the different species [4]. The use of fruit body morphological characteristics such as appearance, color, dimension, spores and form of the fungus on pure culture, physiological factors, and environmental growth preferences can often mislead the identification of macrofungi without the use of microscopic examination coupled with molecular tools [5]. Therefore, the advancement and upsurge in the use of Deoxyribonucleic Acid (DNA) technology has proven to be a powerful tool for traditional taxonomic methods by solving the challenges of taxonomic chaos [6]. The rapid development with the use of versatile molecular techniques has provided easy approach, which is already being used to identify unknown basidiomycete isolates by comparing their DNA profiles with those fruit bodies that have been authenticated in GenBank. DNA techniques for the identification of fungi have been widely used in human and veterinary medicine; it is rapid and displays the accurate identity of pathogenic fungi in order to select appropriate treatment. They have also been applied to food quality control for the detection of contaminants [7]. The body or thallus of the basidiomycete fungus (the mycelium) is normally hidden within the substrate, and it is generally only the fruit body or basidiocarp that is visible at the surface. For this reason, the fruit body tends to show the greatest morphological variation. Conventional mycologists rely on a number of macroscopic and microscopic features of the fruit body to distinguish between macrofungi species [5].

2. Mushrooms

Mushrooms are foods that are commonly consumed since earliest history; ancient Greeks believed that mushrooms are a source of strength for warriors in battle; the Romans regard mushrooms as the “Food of the Gods” served them only on festive occasions. For centuries, the Chinese culture has treasured mushroom as a health food, an “elixir of life” [8]. Mushrooms are originally defined as macrofungi with a distinctive fruiting body, which is large enough to be seen with the naked eye and picked by hand [1]. They do not have the green pigment called chlorophyll that enables the plant to utilize energy from sunlight to change chemical into substances necessary for growth, a process commonly known as photosynthesis instead mushroom produces a wide range of extracellular enzymes [9]. This enables them to degrade complex organic matter into soluble substances, which can be absorbed for nutrition and stored as secondary metabolites [2]. The growth and fruiting of an individual mushroom species on particular substrate will depend upon their ability to produce enzymes that degrade the major component of the substrate such as cellulose, hemicelluloses, and ligin [10].

Macrofungi produce valuable enzymes and bioactive molecules with different therapeutic effects. Therefore, they are considered as flourishing organisms to develop different healthcare and biotechnological products [11]. Mushrooms have been a part of the human culture for thousands of years with considerable interest in civilization history because of their sensory characteristics and medicinal properties; they have been recognized for attractive culinary with low calories, carbohydrates, fat, and sodium with no amount of cholesterol [12, 13]. It has been estimated that there are about 140,000 species of mushrooms present on earth and only 5% are explored for uses, while 7000 were undiscovered species that could be of medicinal value to mankind [14]. With recent advances in medical and nutrition sciences, natural products from both edible and nonedible mushrooms have received extensive attention from individuals and health professionals due to the presence of biologically active compounds with denoted health benefits [15].

Owing to the increasing demand of natural bioactive compounds as an option to replace some synthetic drugs or additives in the pharmaceutical and food industries, the interest in fungi (medicinal mushrooms) has risen in recent years. The potential uses of the mushrooms have appeared as a nutraceutical, nutritional therapy, phytonutrients, phytotherapy, and pharmaceutical due to the accumulated number of secondary metabolites [16]. Several biologically active compounds such as polysaccharides (beta 1-3, 1-4, 1-6 glucans, hetero-beta glucans, proteo-glucans), krestin, lentinan, coriolan, schyzophillan, sesquiterpenes, quinones, hydrophobins, galectins, sterols, ergothionin, tri-teripenes, sterols, germanium, nucleotide, drosophilin, armillasin, amphalone, eloporoside, and volatile (skatole) were reported in medicinal mushrooms [17]. Mushrooms are the producers of extracellular proteolytic enzymes with fibrinolytic and thrombolytic activities [18]. Thus, the available information about bioactive molecules and enzymes in medicinal mushrooms suggests that they are promising candidate of choice microorganisms to develop health-enhancing biotechnological products. The presence of wide biomolecules in medicinal mushrooms has been attributed to different therapeutic effects such as antibacterial, antifungal, cytotoxic, antiinflammatory, insecticidal, nematocidal, and antioxidant [19].

2.1 Lifecycle of higher fungi (macrofungi)

The lifecycle of basidiomycetes includes special stages such as the alternation of generations [3]. Spores from basidium are generally produced for sexual reproduction, rather than asexual reproduction [20]. The club-shaped basidium carries spores called basidiospores. In the basidium, nuclei of two different mating strains (− and +) fuse (karyogamy), giving rise to a diploid zygote that then undergoes meiosis as shown in **Figure 1**. The haploid nuclei migrate into basidiospores, which germinate and generate monokaryotic hyphae. The mycelium that results is called a primary mycelium. Mycelia of different mating strains can combine and produce a secondary mycelium that contains haploid nuclei of two different mating strains. This is the dikaryotic stage of the basidiomycetes lifecycle, which also referred to as dominant stage. Eventually, the secondary mycelium generates a basidiocarp,

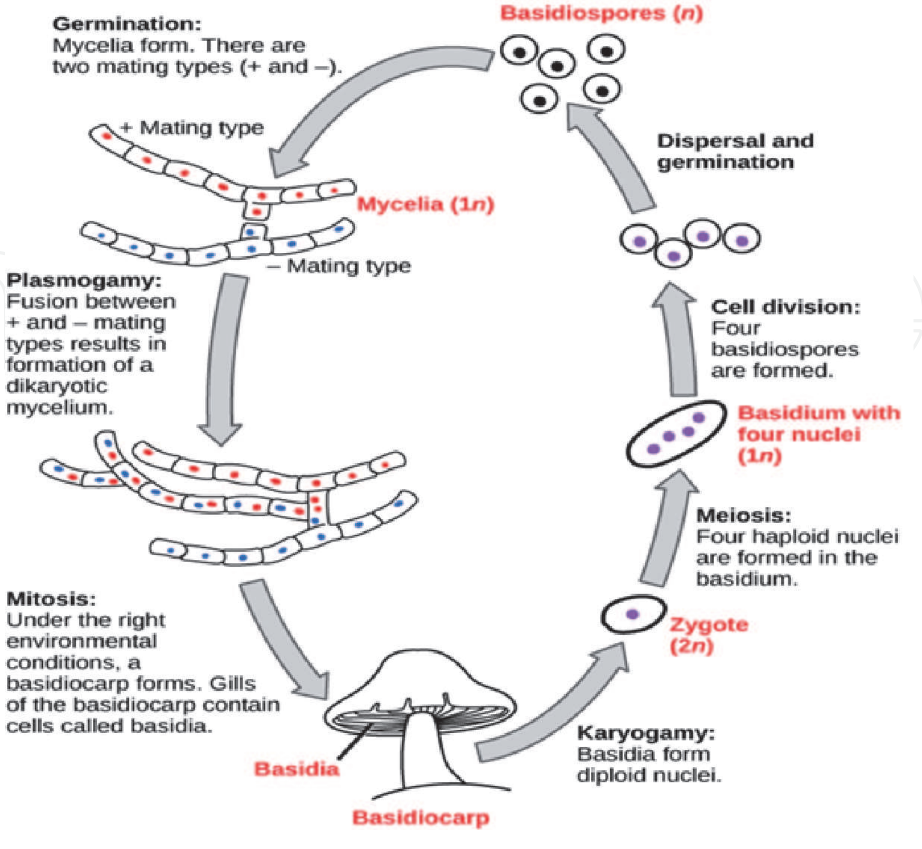

Figure 1.
Reproductive stages of Basidiomycetes: macrofungi [5].

a fruiting body that protrudes either above the soil (epigeous macrofungi) as the basidiocarp bears the developing basidia on the gills under its cap at depths of 10–20 cm or below the soil surface as hypogeous macrofungi or truffles. In the phylum Basidiomycota, sexual reproduction is often dictated by two independent sets of mating-type specific genes, which control the stages of the sexual cycle. The genes encode premating lipopeptide pheromones and their cognate receptors mediate the recognition of mating partners, cell fusion, and homeodomain transcription factors, which form heterodimers to regulate postmating behavior. Sexual reproduction in many fungal species has a central role in pathogenic development, promoting genetic variation, adaptation to fluctuating environments, and a long-term survival [21].

3. Examples of some wild and medicinal mushrooms

3.1 *Ganoderma* species

It is a polypore mushroom, which grows on wood. *Ganoderma* can be differentiated from other polypores because they have a double-walled basidiospore. The name *Ganoderma* is derived from the Greek *ganos* "brightness-sheen" or "shining" and *derma* "skin" [22]. *Ganoderma* is characterized by basidiocarps that are large, perennial, and woody brackets, also called "conks." They are lignicolous, leathery either with or without a stem. The fruit bodies typically grow in a fanlike or hooflike form on the trunks of living or dead trees. They have double-walled, truncate spores with yellow to brown ornamented inner layers. The genus was named by Karsten in 1881. Members of the family Ganodermataceae were traditionally considered difficult to classify because of the lack of reliable morphological characteristics, the genus was divided into two sections: *Ganoderma* with a shiny cap surface as *G. lucidum* and Elfvingia with a dull cap surface as *G. aapplanatum* [23]. Phylogenetic analysis using DNA sequence information derived from mitochondrial Small Subunit (SSU) rDNA has helped to clarify our understanding of the relationships among *Ganoderma* species. The genus may now be divided into some monophyletic group, namely *G. colossus*, *G. applanatum*, *G. tsugae*, Asian *G. lucidum* group, *G. meredithiae*, and *G. resinaceum* [24].

3.2 *Rigidoporus* species

The fungi form many white, somewhat flattened mycelia strand of 1–2 mm thick that grow on and adhere strongly to the surface of the root bark. *Rigidoporus microporus* is a broad fruit body (20 cm wide), leathery, faintly velvety, broadly attached shelf, and often imbricate with the substrate. Their color ranged from orange to red or brown and later faded [25]. These rhizomorphs grow rapidly and may extend several meters through the soil in the absence of any woody substrate. Thus, healthy rubber trees can be infected by free rhizomorphs growing from stumps or infected woody debris buried in the ground as well as by roots contacting those of a diseased neighboring tree [26].

3.3 *Tremella* species

Tremella spp. belong to the family Tremellaceae. *Tremella* spp. are parasites of other fungi and most produce anamorphic yeast states when Basidiocarps (fruit bodies) are produced; they are gelatinous and colloquially classed among the "jelly fungi." Over 100 species of *Tremella* are currently recognized worldwide. Two species namely: *T. fuciformis* and *T. aurantialba* are commercially cultivated for food [27]. The name comes from the Latin *tremere* means "to tremble." Linnaeus placed *Tremella* in the algae including seaweeds, cyanobacteria, and myxomycetes as well as fungi, but Persoon revised *Tremella* in 1794 and 1801. He repositioned and considered *Tremella* as a genus (*Tremella* Pers.) from the originally created by Linnaeus (*Tremella* L.). *Tremella* Pers. has now been conserved under the International Code of Botanical Nomenclature with *Tremella mesenterica* as a species [28]. *Tremella* species produce hyphae that are typically (but not always) clamped and have haustorial cells, which penetrate the hyphae of the host. The basidia are "tremelloid," occur in globose to ellipsoid with vertically or diagonally septate. Conidiophores are often present and similar to yeast cells [28]. *Tremella mesenterica* occurs widely in broadleaf and mixed forests. It is widely distributed in temperate and tropical regions, which include Africa, Asia, Australia, Europe, and North and South America. Although considered bland and flavorless, the fungus is edible. *Tremella mesenterica* produce bioactive compounds that are attracting research interest because of their various biological activities [29].

3.4 *Agaricus* species

It is an important genus of mushroom containing both edible and poisonous species with over 300 members worldwide. The genus includes the common (button) mushroom (*Agaricus bisporus*) and field mushroom (*Agaricus campestris*). Members of *Agaricus* are characterized by having a fleshy cap (pileus) from the underside gills that produced the naked spores [30]. Members of *Agaricus* also have a stem (stipe), which elevates the pileus above the substrate and a partial veil and protects the developing gills and later forms a ring on the stalk [31]. *Agaricus* spp. are known as the most common mushroom with different names: button mushroom, white mushroom, table mushroom, champignon mushroom, crimini mushroom, Swiss brown mushrooms, Roman brown mushrooms, and Italian mushroom.

3.5 *Grifola frondosa*

It is a polypore mushroom that grows in clusters at the base of trees, particularly oaks. The fruiting body of *G. frondosa* occurs as large as 60 cm; it has a cluster consisting of multiple grayish-brown caps that are often curled or spoon-shaped with wavy margins of 2–7 cm broad. The undersurface of each cap bears approximately 1–3 pores per millimeter with the tubes rarely deeper than 3 mm. The milky-white stipe (stalk) has a branchy structure and becomes tough as the mushroom matures. *G. frondosa* is a perennial fungus that often grows in the same place for a number of years in succession. It is prized in traditional Chinese and Japanese herbology as a medicinal mushroom due to the ability to balance out altered body systems into a normal level. Most Japanese find it tasty and the texture is enormously appealing, though the mushroom has been alleged to cause allergic reactions in rare cases and becomes inedible such as all polypores when they are older because it is too tough to eat [33].

3.6 *Lentinus* species

It is a genus of fungi in the family Polyporaceae and widely spread in subtropical regions [34]. *Lentinus* spp. possess extracellular enzymes and thus act as wood-decaying basidiomycetes, gregarious on fallen wood of a wide variety of deciduous trees such as shii, oak, chestnut, beech, maple, sweetgum, cotton, alder, hornbeam, ironwood, chinquapin, and mulberry in a warm or moist climate [35]. The geographic distribution of *L. edodes* (Shiitake) in nature is widely extended through the various continents such as Asia, Europe, Australia, Africa, and America, and often time it is utilized as a medicinal food [34]. The genus name, *Lentinus*, is derived from the Latin *lent*, meaning "pliable," and *inus*, meaning "resembling." Pegler [36] correlated morphological differences with geographic distribution to recognize three species of shiitake: *Lentinus lateritia* in Southeast Asia and Australasia and *Lentinus novaezelandieae* in New Zealand. Other species of *Lentinus* include: *L. crinitus* and *L. tigrinus* [35].

3.7 *Calocybe indica*

Calocybe indica, commonly known as the milky-white mushroom, is a species of edible mushroom native to India. The sturdy all-white mushrooms appear in summer after rainfall in fields (grassland), on road verges, and generally on substrate rich in organic material. It is being grown commercially in several Indian states and other tropical countries and traditionally eaten in West Bengal for medicinal purposes [37]. The robust mushroom is all-white in color and has a firm consistency. Its cap is 10–14 cms (4–5 $^{1}/_{2}$ in) across, convex initially before flattening out with age. The cuticle (skin) can be easily peeled off the cap. The crowded gills are white, and the cylindrical stem is 10 cms (4 in) high with no ring nor volva. It has a subbulbous base, being 1.8 cms ($^{3}/_{4}$ in) wide at the apex (top), 3.5 cms (1 $^{1}/_{2}$ in) in the middle, and 2.4 cms (1 in) wide at the base. The mushroom does not change color on cutting or bruising, though old dried specimens have a buff color. The flesh has a mild flavor that has been described as oily, and a faint smell reminiscent of radishes. The spore print is white, and the oval spores measure 5.9–6.8 μm long by 4.2–5.1 μm wide [37]. The mushrooms appear between May and August after spells of rainfall. The fungus is saprophytic, though it has been reported to form ectomycorrhizal relationships with the roots of the coconut tree (*Cocos nucifera*), palmyra palm (*Borassus flabellifer*), tamarind (*Tamarindus indicus*), and yellow poinciana (*Peltophorum pterocarpum*) [37].

3.8 *Pleurotus ostreatus*

Pleurotus ostreatus, the oyster mushroom, is a common edible mushroom. It was first cultivated in Germany as a subsistence measure during World War [38] and is now grown commercially around the world for food. It is related to the similarly cultivated king oyster mushroom. Oyster mushrooms can also be used industrially for mycoremediation purposes, it attacks and kills nematodes and bacteria with impunity. The oyster mushroom is one of the more commonly sought wild mushrooms, though it can also be cultivated on straw and other media. It has the bittersweet aroma of benzaldehyde [38]. *Pleurotus ostreatus* is easily recognized by the way it grows on wood in shelflike clusters; its relatively large size; its whitish gills that run down a stubby, nearly absent stem; and its whitish to lilac spore print. It appears between October and early April across North America and features a brown cap. A number of very similar species are closely related, including *P. pulmonarius* (which is often paler and appears between late April and September) and *P. populinus* (which is found in the wood of quaking aspen). The mushroom has a broad, fan, or oyster-shaped cap spanning of 5–25 cms; natural specimens range from white to gray or tan to dark-brown; the margin is enrolled when young, and is smooth and often somewhat lobed or wavy. The flesh is white, firm, and varies in thickness due to stipe arrangement. The gills of the mushroom are white to cream and descend on the stalk if present. If so, the stipe is off-center with a lateral attachment to wood. The spore print of the mushroom is white to lilac-gray and best viewed on dark background. The mushroom's stipe is often absent. When present, it is short and thick [39]. It is mainly saprophytic but can be a facultative parasite on a stressed host. Sporophytes can be found growing naturally on both living and dead trees of a wide array of broadleaf hardwoods and conifers. Many different subspecies, varieties, and strains can be found within this species, but there are two major ecotypes: brown forms from North America and blue/brown forms from Europe [40].

3.9 *Lenzites* species

Lenzites spp. are wood-decaying fungi in the class Agaricomycetes, order Polyporale, family Polyporaceae, and genus *Lenzites*. *Lenzites* spp. were circumscribed by Elias Magnus Fries in 1835 and reportedly found in parts of Europe, Asia, and Africa [41]. The species is a white-rot pathogen living on woods; it has corky fruiting bodies in the shape of semicircular plates formed on the trunks of several types of deciduous trees. The fruiting body has a lamellar fruit layer (gills) producing spores. The upper surface of the cap may be in various shades of brown and sometimes zonate. The pore surface is white to tan at initial stage but as the fruit body matures, some of the pore walls break down, forming slits with blunt partitions. This results in the characteristic of a mazelike (daedaloid or labyrinthinine/labyrinthiform) appearance. The tube walls are 10–30 mm long with thick walls. The basidiospores are within 6–8 μm, smooth and elliptical in shape [42]. *Lenzites* spp. are widely available and index fungorum has reported 26 species [43].

The three synonymous wood-rotting fungi, namely: *Lenzites* spp., *Daedalea* spp., and *Trametes* spp., have been screened as cellulose-degraders from 20 different genera of both brown and white-rotters of Polyporaceae on the basis of their potential to degrade carboxymethylcellulose. The utilization of different carbon sources in the growth medium was studied with these fungi for the identification of enzymes involved in saccharification. Carboxymethyl cellulose and beta-glucosidase were identified as the two major enzymes involved in this process. Extracellular carboxymethyl cellulose from *L. saepiaria* has been purified to homogeneity and the enzyme partially characterized [44]. *Lenzites* spp. have been investigated for bioremediation application, production of laccase—a lignin-degrading enzyme, which has been isolated and purified for the production of various dyes, pigments, and bio pulping to eliminate the pollution hazards associated with the use of chlorine pulping process [45]. They have been used as a natural comb for brushing down hair of horses, and fruit bodies were used for anesthetizing bees [46]. *Lenzites* spp. are also known to have some medicinal properties, including antioxidant, antimicrobial, antitumor, and immunosuppressive activities, but only few species such *as L. betulina* and *L. warnieri* have been examined and documented [47].

4. Health benefits of edible and medicinal mushrooms

4.1 Nutritional benefits

Mushrooms contain the amino acids, vitamins, macro, microelements, and a substantial amount of dietary fibers. Higher Basidiomycetes have much insoluble dietary fiber bound with chitin, hemicellulose, mannans, glucans, glycogen, and trehalose in their cell wall. Cheung [48] has reported the health benefits of dietary fiber, which include the following: relieves of constipation, prevention of colon disease and hemorrhoids as well maximize the viscosity of the food matrix, slow-down of digestion, lower blood glucose, and strengthens immune system with antitumor activity. Mushrooms are excellent sources of dietary fiber, which can be used for the enrichment of biopharmaceutical products [49]. Mushrooms are known to possess complexes of polysaccharides and protein, which enhance innate and cell-mediated immune responses and exhibit antitumor activities in animals and humans [50]. Edible and medicinal mushrooms contain considerable amount of essential and nonessential amino acids. Essential fatty acid (linoleic acid), a precursor of 1-octen-3-ol, has been the principal active compound that contributed to the aroma and flavor of mushrooms. The bioavailability of mineral in medicinal mushrooms, except sodium in low concentrations, has made edible mushrooms choice of food that regulate blood pressure, maintain cellular function, and promote the availability of metalloenzymes, biochemical processes, and metabolic growth [51, 52].

The nutrient contents of various edible mushrooms play a vital role in maintaining the normal function of human body [53]. The utilization of macrofungi as a nutritional source provides opportunity to fulfill the protein-energy demand and thus balance the problem of nutritional deficiency [12]. Hence, it has been well proven and documented in the world literature that mushrooms provide definite nutrition and health benefits for humans. Nowadays, people eat mushrooms as functional foods, food-flavoring material in soups or sauces due to their unique and subtle flavor with devoid of undesirable side effects. The reason behind the consumption of mushrooms since ancient times is due to their nutritional benefits, organoleptic values, and pharmacological applications [54]. Badalyan [55] reported a significant reduction of blood cholesterol levels when lovastatin from submerged mycelia of *Pleurotus ostreatus* and *P. eryngii* var. *ferulae* was used as a dietary supplement. It needs to be noted that edible and some medicinal macrofungi are used as food, medicine, and formulated feeds for animals [56, 57].

4.2 Immunomodulatory activity

The combination of vitamins A, B, C complex, fiber, minerals, and other bioactive compounds in mushroom is a basic healing requirement to improve the human immune system against bacteria, fungi, and virus infections. *Ganoderma lucidum* contains a high concentration of organic germanium, polysaccharides, and triterpenes; these active components have been proven to strength, regulate immune system, and eliminate allergic reactions such as asthma, rheumatoid, arthritis, and lupus [58]. Findings of Zhu et al. [59] revealed that the bioactive compounds in edible and medicinal mushroom improve blood circulation, increase the activities of immune cells such as macrophages, natural killer cells (NK), and T-cells, and therefore reduce the tumor formation by 86%. *Lentinus edodes* contains lentinan that stimulates the production of immune system such as interleukin and tumor necrosis factor (TNF) which help to prevent the spread of cancer [60].

G. lucidum stimulated the production of interleukin-II due to the presence of ganoderic acid, which is active against liver cancer [61]. Medicinal mushrooms help in fighting infection as they stimulate the maturation of macrophage cells that engulf and neutralize bacteria particularly secondary infection [62]. Most importantly, mushrooms contain a large selection of biologically active polysaccharides, which are known to function as biological response modifiers (BRM). Biological response modifiers are substances that stimulate the body's response to infections and diseases. They contain repetitive structural features that are the polymer of monosaccharides residues joined to each other by glycosidic linkage [63, 64]. This offers a high capacity for carrying biological information because of their structural variability, ability to interconnect at several points to create a wide array of linear and branched molecules that will carry different biological information [65].

4.3 Anticancer properties

Cancer is medically known as malignant neoplasm—a disease involving unregulated cell growth [66]. Cancer is a devastating disease that may spread to more distant parts of the body through the lymphatic system or bloodstream. It afflicts many people around the world because it is the second leading cause of death after heart disease [67]. Several studies from Asian countries show that edible and medicinal mushrooms played an important role in the prevention and treatment of cancer [68]. In Eastern Europe, fruiting bodies of *Inonotus obliquus* have been used as a medicine for the treatment of cancer due to the presence of triterpenes and ergosterol peroxide [17]. The antitumor effect of several extracts and isolated compounds from mushrooms have been carried out on tumor cells and in animal assay [30]. The clinical evidence for anticancer activity of medicinal mushroom comes from the extracted polysaccharides, lentinan, PSK (Krestin), or schizophyllan [50].

Mushrooms prevent breast and prostate cancer due to the presence of beta-glucans and conjugated linoleic acid [69]. Anticarcinogenic effects of linoleic acid had been attributed to the ability to suppress estrogen [70]. *Agaricus bisporus, Lentinus edodes*, and *Grifola frondosa* possess bioactive substances that inhibit the activity of aromatase—an enzyme involved in estrogen production, which is a prime reason for breast cancer in the woman after menopause [71]. Other wild mushrooms such as *Pleurotus* spp., *Agaricus blazei*, *Ganoderma lucidum*, *Clitocybe nebularis, Trametes* spp., *Piptoporus betulinus*, *Inocybe umbrinella*, *Coprinus comatus*, *Fomes fomentarius*, *Lactarius flavidulus*, *Albatrellus confluens, Cordyceps sinensis, Schizophyllum commune*, and *Inonotus obliquus* have **Figure 2** been credited with anticancer activity due to some bioactive compounds [72].

4.4 Antimicrobial properties

The development of new synthetic antimicrobial compounds has led to a drastic increase in bacterial resistance and the subsequent evolution of multidrug-resistance among microorganisms [73]. In the quest for effective and sustainable antimicrobial substances against pathogenic microorganisms, a new group of microorganisms has been increasingly studied, among which mushrooms have emerged as a viable source of new antimicrobials [74]. Mushrooms need antibacterial and antifungal compounds as a defensive tool to survive in their natural environment. It is therefore not surprising that antimicrobial compounds could be isolated from many mushrooms for human benefits [50]. Sesquiterpenoid and hydroquinones produced by the *Ganoderma pfeiffer* inhibited the growth of Methicillin-resistant *Staphylococcus aureus* [75]. The extracts obtained from *L. quercina* inhibited the growth of *S. epidermidis*, *S. saprohyticus*, and *S. aureus* isolated from stool, urine and wound infections [76]. Applanoxidic acid isolated from *G. annulare* (Fr) shows antifungal activity against *Trichophyton mentagrophytes*, while the ethanolic extract of *L. edodes* was reported to possess antiprotozoal activity against *Paramecium caudatum* [77]. Ganoderic acid, ganodermadiol, ganodermanotriol, lucidadiol, triterpenes, and applaanoxidic acid isolated from *Ganoderma* species have been reported to possess in vitro antiviral activity against human immunodeficiency virus type I (HIV-1) and influenza virus type A [78]. Water-soluble lignin isolated from *Inonstus obliqueis* inhibited HIV protease; the

Figure 2.
Examples of some medicinal mushrooms in Nigeria [32]. A: Macrolepiota sp. B: Agaricus arvensis. C: Ganoderma lucidum. D: Schizophyllum commune. E: Pycnoporus cinnabarinus. F: Auricularia auricula. G: Lenzites quercina. H: Termitomyces. I: Pleurotus tuber-regium. J: Pleurotus ostreatus. K: Lentinus squarrosulus. L: Daldinia concentrica. M: Trametes versicolor. N: Chloropyllum sp. O: Meripilus giganteus. P: Lycoperdon spadiceum. Q: Coprinus lagopides. R: Microstoma sp. S: Xylaria hypoxylon. T: Tremella fuciformis.

protein-bound polysaccharides from *Trametes versicolor* (L. fr) have antiviral effect against HIV and cytomegalovirus. Antiviral agents from different mushroom species such as *Piptoporus betulinus*, *Fomitopsis officinalis*, and *Coprinellus micaceus* have been tested against different viruses, namely: Papilloma, infleuza (H5N1), Hepatitis B, C, D, and E [17]. El-Fakharany et al. [79] reported that a laccase has been purified from *P. ostreatus* mushroom, which is capable to inhibit the hepatitis C virus entry into peripheral blood cells and hepatoma HepG2 cells and its replication, whereas the isolation of a novel ubiquitinlike protein from *P. ostreatus* mushrooms manifests an inhibitory activity toward HIV-1 reverse transcriptase [80].

Studies carried out by Karacsonyi and Kuniak [81] revealed that beta-D Glucan (pleuran) isolated from fruiting bodies of *P. ostreatus* promoted the survival of mice susceptible to bacterial infections. Phenolic and tannin constituents of *P. ostreatus* may also elicit antibacterial activity through various mechanisms of action characterized by cell membrane lysis, inhibition of protein synthesis, proteolytic enzymes, and microbial adhesins [82]. The oil of the macrofungus extracted with petroleum ether and acetone was observed to inhibit the Gram-positive and Gram-negative bacterial tested in vitro to suggest that *P. ostreatus* has a broad-spectrum antibacterial activity [82], whereas organic extracts (methanol and chloroform) of *P. ostreatus* have been manifested as effective against Gram-positive bacteria which showed to be a potential source of antibacterial agents [83]. Comparative studies were carried out on the antibacterial activity of *P. ostreatus* and biosynthesized silver nanoparticles using *P. ostreatus* against Gram-positive bacteria using standard zones of inhibition, in which synthesized silver nanoparticles using *P. ostreatus* showed maximum zone of inhibition [84].

4.5 Antioxidant properties

The interplay between free radicals, antioxidants, and cofactors is important in maintaining stable health and age-related diseases [85]. Free radicals induce oxidative stress, which is balanced by the body's endogenous antioxidant system with input from cofactors and by the ingestion of exogenous antioxidants [86]. When the generation of free radicals exceeds the protective effect of antioxidants and some cofactors, it can cause oxidative damage, which can result in aging and other diseases such as cardiovascular, cancer, and neurodegenerative disorders [87]. The progressive severe and chronic disorders caused by free radicals have led to alternative sources of antioxidants compounds from wild mushrooms, which could be a remedy to dietetic aliments [88]. Hence, there is an emerging interest in the use of naturally occurring antioxidants for the preservation of foods, in other to manage a number of pathophysiological conditions.

Epidemiological studies have consistently shown that a high dietary intake of mushrooms is strongly associated with the reduced risk of developing chronic diseases such as cancer and cardiovascular disease [89]. This suggests that changes in dietary intake and consumption of natural foods provide desirable health benefits beyond basic nutrition to reduce the risk of chronic diseases. Medicinal mushrooms such as the species of *Termitomycetes*, *Pleurotus*, *Lentinus*, and *Lenzites* have shown potent scavenging properties against free radicals [90]. Generally, mushrooms contain ergothioneine, a naturally occurring and powerful antioxidant that protects the body's cells from generated free radicals as well as boost up immunity [91, 92]. The antioxidant activity of macrofungi had been attributed to the presence of useful metabolites in medicinal mushrooms. Therefore, the bioactive compounds in wild medicinal mushrooms make them a good source of antioxidant compounds to prevent degenerative diseases such as cardiovascular illnesses, neurodegenerative disorders, rheumatoid arthritis, and cancer that had been attributed to generated free radicals in the body.

Mushroom is an ideal low energy diet for diabetics; it has no fats, no cholesterol, very low carbohydrates, moderate protein, vitamins, minerals, dietary fibers, and a lot of water [48]. Moreover, mushrooms contain natural insulin and enzyme that break down sugar or starch [93]. *Diabetes mellitus* is a metabolic disorder affecting a large number of people [94]. Therefore, more effective and safer treatment for diabetes patients needs to be investigated in order to overcome the peripheral of insulin resistance. A polysaccharide fraction of *Grifola frondosa* (SX fraction) has been reported to exhibit hypoglycemic action in patients with type 2 diabetes [60]. Coriolan, glucans, ganoderan A and B from *Ganoderma lucidum*, and glucuronoxylomannan from the fruit bodies of *Tremella mesenterica* exhibited hypoglycemic effects in several tests and ameliorated the symptoms of diabetes (**Figure 3**) [95].

4.6 Antidiabetes properties

Many medicinal mushrooms have been found to be suitable for diabetic and heart patients due to low starch and low cholesterol content. Several mushroom species have been reported to be effective for both the control of blood glucose levels and the modification of the course of diabetic complications. This is because they are known to contain bioactive components that help with the proper functioning of metabolic organs such as the liver, pancreas, and other endocrinal glands,

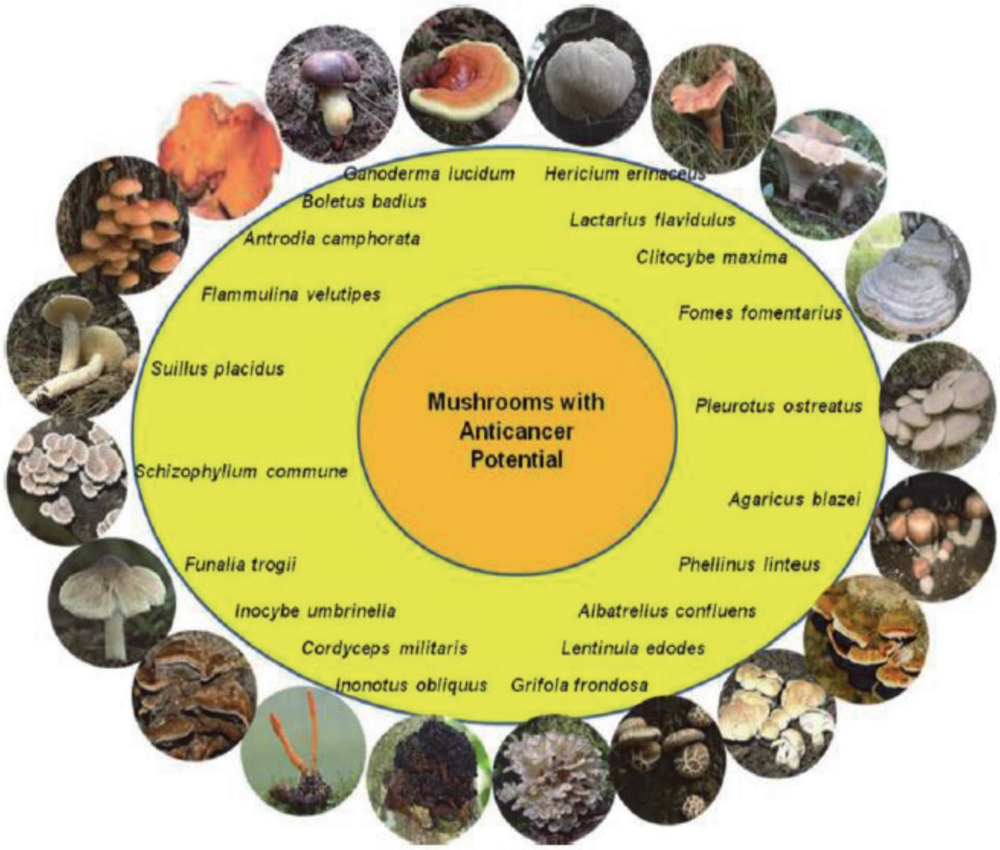

Figure 3.
Some medicinal mushrooms with nutraceutical potentials [72].

thereby promoting the formation of insulin and related hormones that ensure healthy metabolic functioning [50]. Mushrooms contain polysaccharides such as beta-glucans which can restore the function of pancreatic tissues eventually triggering increased insulin output by beta-cells, thus leading to decrease blood glucose levels. Beta-glucans have been shown to improve the sensitivity of peripheral tissues to insulin [96].

5. Underutilization of medicinal mushrooms in Nigeria

Most of the wild macrofungi found in Nigeria **Figure 2** are similar to mushrooms reported to possess anticancer properties [72]. One of the wild mushrooms from Nigeria—*Lenzites quercina* displayed anticancer activity against Hela and RD cell lines (**Figures 4** and **5**) in our latest findings [97, 98]. In recent studies, researchers had focused on the maximum utilization of natural bioactive compounds from edible and medicinal mushrooms **Figure 6**. Few species of medicinal mushrooms have been examined for anticancer activities in Nigeria. This may due to the lack of information on the identity and anticancer activities of available wild species of mushrooms.

Despite the millennial existence and empirical documentation of mushrooms, the ethnological knowledge of macrofungi, historical uses of mushrooms as food, medicine, source of income, and sociological impacts are apparently dawdling the ethnomycology research drive in Nigeria [99]. The poor identification and documentation of medicinal and edible mushrooms have created some degrees of inconsistencies in their usages relatively to the medicinal practice, food, and mythological beliefs [100]. The random utilization of mushrooms, the limited scope of taxonomic

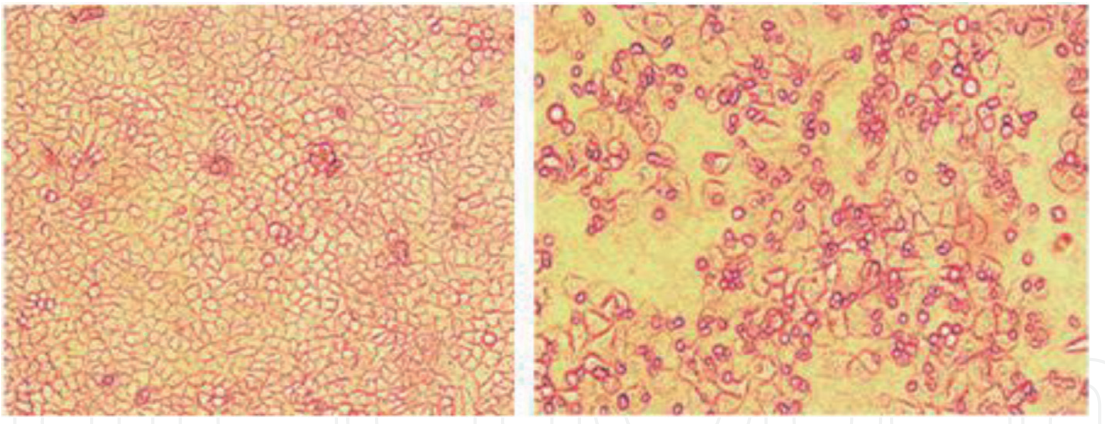

Figure 4.
Anticancer activity of Lenzites quercina extract against HeLa (a) cell line (HeLa) without extract and (b) cell line (HeLa) with extract at 100 μg.

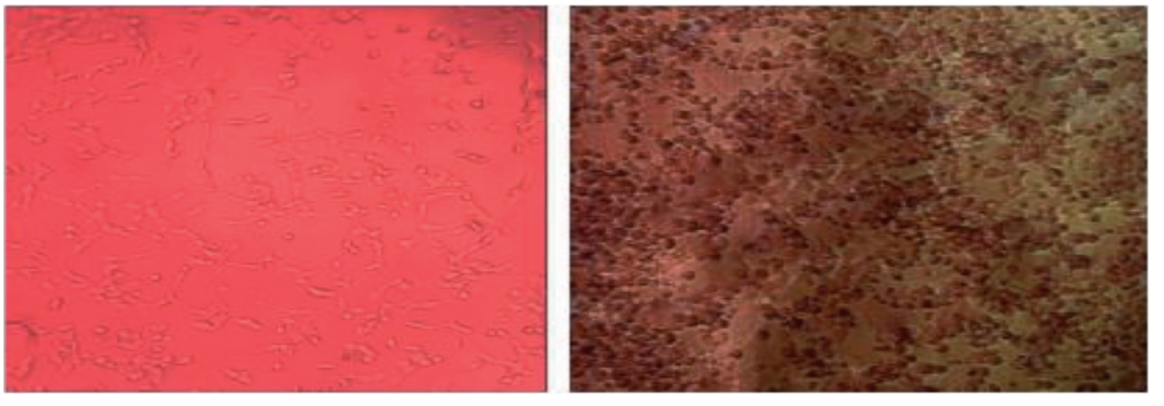

Figure 5.
Anticancer activity of Lenzites quercina extract against RD (a) cell line (RD) without extract and (b) cell line (RD) with extract at 100 μg.

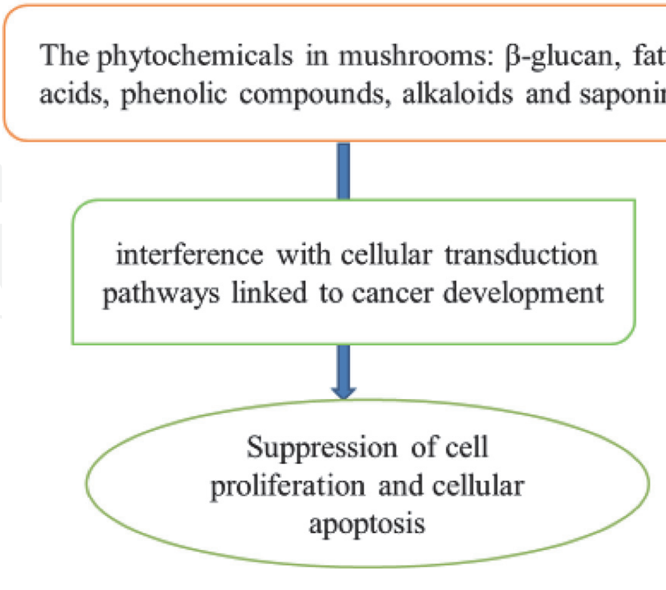

Figure 6.
Effect of bioactive compounds in medicinal mushroom on cancer cell lines.

consistencies of the existing mushroom, anthropogenic, ethnographic, ethnoecological, and religion have hindered the correct estimate of macrofungi for proper utilization and exploration in Nigeria and Africa.

6. Conclusion

The relevance of medicinal mushrooms in modern-day pharmaceuticals and nutraceuticals is an innovative conception in medical fields and food industries. The positive transformation of mushrooms into edible foods or products requires government support by sponsoring programs to assist agricultural development in mushroom isolation, identification, cultivation, and utilization. This could be a means to diversifying into food production to solve the food insecurity and as well deconcentrate the economic reliance on crude oil.

Author details

Clement Olusola Ogidi[1]*, Victor Olusegun Oyetayo[2] and Bamidele Juliet Akinyele[2]

1 Biotechnology Unit, Department of Biological Sciences, Kings University, Odeomu, Nigeria

2 Department of Microbiology, The Federal University of Technology, Akure, Nigeria

*Address all correspondence to: clementogidi@yahoo.com

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