*Review Article*

A Paradigm Shift in Agriculture: Using Mushroom Metabolites for Sustainable Plant Disease Control and Crop Health

ABSTRACT

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| Mushroom-derived metabolites have emerged as eco-friendly alternatives to chemical pesticides in managing plant diseases. These bioactive compounds not only enhance plant resistance but also reduce environmental degradation, thereby promoting sustainable agricultural practices. This review focuses on the potential applications of lentinan, schizophyllan, GL polysaccharides, and pleurotin (a *Pleurotus*-derived metabolite) in plant disease management. Lentinan, derived from *Lentinula edodes*, exhibits significant immunomodulatory properties, triggering systemic resistance in plants against various pathogens. It enhances the production of defense-related enzymes and secondary metabolites, thereby strengthening the plant’s innate immunity. Schizophyllan, extracted from *Schizophyllum commune*, demonstrates antifungal activity and functions as a biostimulant by reinforcing plant cell walls, which in turn disrupts fungal colonization.  Polysaccharides from *Ganoderma lucidum* have gathered attention for their dual role as biopesticides and growth promoters. These compounds induce systemic acquired resistance (SAR) in plants, enhancing their ability to withstand microbial attacks while simultaneously improving yield. Similarly, metabolites from *Pleurotus* species, including phenolic compounds and polysaccharides, exhibit broad-spectrum antimicrobial properties by inhibiting the growth of both bacterial and fungal pathogens. Moreover, these metabolites stimulate root development and nutrient absorption, further enhancing plant vigour. The use of mushroom metabolites represents a paradigm shift in plant disease management, offering a sustainable and cost-effective solution for global agriculture. Their ability to integrate seamlessly into existing pest management strategies while minimizing ecological impact underscores their potential as key components in the development of next-generation biofungicides. Future research should focus on optimizing extraction techniques, elucidating mechanisms of action, and assessing field-level efficacy to facilitate widespread adoption. This article highlights the potential of mushroom metabolites in fostering a sustainable agricultural future while addressing the challenges associated with chemical dependency in plant disease control. |

*Keywords:* Mushroom metabolite, Lentinan, Antifungal, Plant disease, Tramesan

1. INTRODUCTION

Mushrooms have been well known for their nutritional as well as therapeutic values worldwide. Mushrooms are macrofungi with a distinct fruiting body either hypogeous or epigeous, large enough to be seen with a naked eye and has to be picked by hand (Chang and Miles, 1992). Mushrooms, long revered for their culinary and medicinal properties, have emerged as a significant source of bioactive compounds with diverse applications, particularly in human and plant health. These compounds, collectively known as mushroom metabolites, encompass a wide array of molecules produced by fungi, including polysaccharides, terpenoids, phenols, and proteins. Many potential and unique property containing pharmaceutical substances have been recently extracted from mushrooms; particularly in modern medicine. Medicinal mushrooms have been found to contain an unlimited and comparatively less explored source of polysaccharides and polysaccharide–protein complexes with anti-cancerous and immunostimulant properties. The major advantage of medicinal mushroom usage are their bioactive components which are found to be safe for humans. Various compounds such as β-D-glucans, heteropolysaccharides, glycoproteins, lectins and terpenoids inhibit tumour cells and shows to have no negative effects on treated patients (Benkeblia, 2015).

Likewise, the agricultural sector faces significant challenges from plant diseases caused by a wide range of pathogens, including fungi, bacteria, and viruses. However, the use of synthetic compounds to manage the pathogen causing disease is limited due to many undesirable aspects, *viz*., carcinogenicity, teratogenicity, acute toxicity and prolonged degradation period leading to environmental pollution problems (Petrović *et al*., 2013). Due to these concerns, the green consumer profile demands a deletion for the synthetic chemicals from both food production and preservation. Eventually, this demand applies a pressure on the scientific community and agro-industrial and pharmaceutical companies and institutes to search for a compound that will satisfy the consumer need (Harvey, 2008). The present-day scenario has put on an interest in natural products derived from mushrooms due to their minimal side effects, lower toxicity, availability and better biodegradability. Mushroom metabolites offer a promising alternative as natural and sustainable disease control agents. Many mushroom metabolites exhibit direct antimicrobial activity against plant pathogens (Barseghyan *et al.,* 2016*)*. While some other metabolites can stimulate plant growth, enhancing nutrient uptake, and increasing overall plant vigour (Wu and Kawagishi, 2020). Mushroom metabolites can also be used in combination with other biocontrol agents, such as beneficial microorganisms, to enhance their efficacy (Park *et al.,* 2020; Sun *et al.,* 2022)*.*

**2. Compounds extracted from mushrooms and their underlying effects**

As previously mentioned, fungal compounds possessing bioactivity, which could be beneficial for averting and treating countless diseases, exhibit a wide array of characteristics. Among these, polysaccharides stand out as significant components of the fungal cell wall, renowned for their capacity to convey biological signals effectively. Specifically, they demonstrate properties such as anti-tumour effects, immune system regulation, antioxidant action, anti-inflammatory, antimicrobial activity, and anti-diabetic properties. However, the specific biological activities and their modulation are heavily affected by the structural and physical attributes of the molecule, including the degree of branching, linkage within the backbone, types of side-chain units, and the composition of constituent monosaccharides. Predominantly, α- and β-glucans are the most well-known and abundant biochemical compounds in this context. These compounds primarily exert immunomodulatory effects by binding to specific receptors on cell walls and triggering tailored immune response (Popovic *et al*., 2013; Zhao *et al*., 2020). Another vital group of compounds present in mushrooms, crucial for their biological effects, are terpenes. These compounds are defined by units of five-carbon isoprene atoms, and the addition of functional groups form terpenoids. They play an important role in immune system regulation by encouraging activation of genes responsible for the formation of proteins intricated in immune responses. Alongside this function, terpenoids also exhibit anti-inflammatory, antioxidant, and anti-tumour attributes. Mushrooms, particularly those belonging to the genus *Ganoderma*, are notable for their high concentrations of terpenoids.

***2.1 Ganoderma lucidum***

*Ganoderma* sp. (commonly known as Reishi Mushrooms) are well-known for their medicinal properties, even though some are significant plant pathogens, causing root and bud rot diseases in various trees. Triterpenes, steroids and polysaccharides are the major constituents in *Ganoderma* sp. (Boh *et al*., 2007). Triterpenoids (such as Ganoderic acid and Lucidenic acid) are the major constituents and they play a critical role in its biological effects (Seo *et al*., 2009). Proteins, peptides, amino acids, nucleosides, fatty acids, alkaloids and inorganic elements are also biologically significant constituents in Ganoderma sp. (Li *et al*., 2013).Ergosterol, which is primarily found in fungi is also present in *Ganoderma* sp., which indicates its potential role in inhibiting fungal growth. *Ganoderma* sp. is a potential elicitor of phytoalexins (t-resveratrol and t-piceatannol), which are the secondary metabolites generated upon biotic or abiotic stresses (Yang *et al*., 2010).

*G. lucidum* polysaccharides (GLP) is the main bioactive component in the water-soluble extracts of Reishi mushroom. The main structural feature of GLP is the β-1,3- D glucan linear structure (Wang *et al*., 2014a), which is consistent with many reported structures of fungal polysaccharides belonging to β-1,3-glucans. GLP had better control effect of the *Fusarium oxysporum f. sp vesicatoria* in cotton, when the mode of application was root irrigation, followed by seed dressing and then lastly spraying of GLP (Zhang *et al*., 2019). The peak increase in the concentration of PPO (polyphenol oxidase), SOD (superoxide dismutase) and POD (peroxide) at the fourth and fifth days after root irrigation confirms the potential inhibition of the pathogen. LOX and JAZ2, key structural genes of the jasmonic acid (JA) biosynthetic pathway, were largely induced under GLP treatment (Rahnamaie-Tajadod *et al*., 2017). The elevated expression levels of genes involved in the phenylalanine metabolic pathway, such as PAL, C4H1, and 4CL clearly demarcated an increase in defense genes on GLP application. In addition, after GLP treatment, expression of the basic chitinase gene and β-1,3-glucanase increased. Confirmatory tests conducted in greenhouse trials and field trials affirmed that *Ganoderma lucidum* polysaccharide (GLP) does not directly kill fungi but boosts plant immunity (by increasing the expression of resistance genes *NbPR1a* and *RS33*), leading to significant disease control (Yang *et al.,* 2022).

All the crude extracts of four Ganoderma species *viz*. *G. colossum, G. resinaceum, G. lucidum,* and *G. boninense*, prepared using n-hexane, diethyl ether, chloroform-acetone, and methanol had positive inhibition activity against the bacteria, *Pseudomonas syringae* and *Bacillus subtilis*. Among the extracts, the chloroform-acetone extracts of *G. colossum* exhibited the highest potency against both bacteria (Ofodile *et al*., 2005)

***2.2 Clitocybe* sp.**

The fruiting body and mycelia of *Clitocybe nuda* (wood blewit) have been reported to show antimicrobial activity against the human pathogens, *Staphylococcus aureus*, (Yamaç and Bilgili, 2006) and *Candida albicans* (Dulger *et al*., 2002). Apart from the health benefits, the culture filtrate of *C. nuda* inhibited plant pathogenic fungi and bacteria. For instance, reduced disease incidence of Phytophthora blight of pepper caused by *P. capsici* and leaf spot of pepper incited by [*Xanthomonas axonopodis*](https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/xanthomonas-axonopodis) pv. vesicatoria.

Secondary metabolites of *C. nuda* displayed antimicrobial activity against *P. capsici*. The culture filtrate of *C. nuda* was extracted with ethanol yielded three compounds namely, 2-methoxy-5-methyl-6-methoxymethyl-*p*-benzoquinone, 6-hydroxy-2*H*-pyran-3-carbaldehyde, and indole-3-carbaldehyde. Indole-3-carbaldehyde at a concentration of 500 ppm, showed complete inhibition of zoospore germination of *P. capsici*, while other compounds showed an inhibition rate of 97% and 86%, respectively. These compounds further serve as a potential candidature for new fungi-derived pesticides for the control of plant diseases (Chen *et al*., 2012). The inhibitory substance in the *C. nuda* culture filtrate was thermo stable and also stable at different pH. The inhibitory substance was dialyzable and confirms the filtrate to be a hydrophilic compound, but not a protein (Cheng and Huang, 2009).

Other species of *Clitocybe*, such as *Clitocybe odora* exhibited significant antifungal activity against both *Fusarium culmorum* and *F. moniliforme*. *In vitro* studies on different solvents extracts showed chloroform extract of *C. odora* was more effective than the acetone extract against both fungal pathogens. Comparably, the antifungal effects of *C. odora* extracts with commercial antibiotics (erythromycin and amoxycillin) highlighted the potential of *C. odora* as a natural antifungal agent (Türkoğlu *et al*., 2011).

Similarly, aqueous extracts of the forest-dwelling fungus, *C. nebularis* exhibited significant antifungal activity against various *Phytophthora* sp. with the highest inhibitory effect against *P. ramorum*. Additionally, the *C. nebularis* extracts showed substantial antagonism against *P. kernoviae* (14.7%), *P. lateralis* (34.7%), and *P. infestans* (86%) (Hearst *et al.,* 2013).

***2.3 Trametes versicolor***

*Trametes versicolor* (syn. *Coriolus versicolor*) commonly known as turkey tail mushroom is widely used in traditional Chinese medicine due to its high immunomodulatory effect (Ng, 1998). Polysaccharide Krestin (PSK) or polysaccharide peptide (PSP) are two natural products extracted from *T. versicolor*, and their main components are a highly heterogeneous mixture of β-glucan macromolecules that possess a molecular weight of approximately 100 kDa and contain various moieties, including peptides, bound to β-glucan backbones (Lu *et al*., 2011; Habtemariam, 2020). The inclusion of another polysaccharide, Tramesan (a 23 kDa α-heteropolysaccaride) (Scarpari *et al.,* 2017) critically possess elicitor role of durum wheat defenses for SLBC (Septoria Leaf Blotch Complex) caused by *Zymoseptoria tritici* and *Parastagonospora nodorum*. Tramesan-treated plants exhibited a lower severity of disease symptoms and the severity of *P. nodorum* was reduced by up to 25%, and *Z. tritici* by up to 30% under field conditions. Tramesan has demonstrated biological activity on plant as well as in animal cells (Scarpari *et al.,* 2017).

Recently, potato late blight caused by *Phytophthora infestans* was effectively controlled by the culture filtrate (CF) of *T. versicolor*. The culture filtrate rich in bioactive compounds with antimicrobial activities stimulates antioxidant system and promote plant defense. The culture filtrate can be potentially used as crude culture filtrate (CCF), or by separating the components (i.e., polysaccharides, proteins, lipids) for controlling the pathogen. CCF showed *in vitro* antimicrobial capacity, by inhibiting sporangial germination, mycelial growth and positive spike in the synthesis of the defense hormone (salicylic acid), implicating the possible application to stimulate resistance towards *P. infestans* (Fratini *et al.,* 2024).

Awakened need for new alternatives to control of powdery mildew on tomato (*Leveillula taurica*) eventually lead to test the effectiveness of hexanic extracts of *T. versicolor*. The hexanic extracts controlled *Leveillula taurica*, with average control of 47.41 and 57.82% and maximum of 58.16% and 65.09% on concentrations of 7.5% and 10%, respectively. Phytotoxicity symptoms were not detected on the tomato crop cv Cid after applications of hexanic extracts concentrations (Mendieta *et al.,* 2020).

Seed borne disease of tomato incited by *Clavibacter michiganensis* subsp. *michiganensis* (Cmm) and *Ralstonia solanacearum* were efficiently managed by *T. versicolor* extract. The antibacterial activity of the extract had a promising minimum inhibitory concentration 90% growth inhibition (MIC90) and the minimum bactericidal concentration (MBC). The *in vivo* germination test delineated no major reduction in seed germination when the extract was applied as seed treatment (Orzali *et al*., 2020). Irrespective of the bacteriostatic activity

Apart from antimicrobial activity, *T. versicolor* plays an indirect role in reducing T2 and HT-toxins in small grain cereals*,* produced by *Fusarium langsethiae*. Use of protein fractions (exo-proteome such as F90AS and F75AS), purified from the culture filtrate of the *T. versicolor*, proved to be highly efficient in inhibiting the growth of *F. langsethiae* and the biosynthesis of the T2 toxin. These results ensure a tight promise for its future use as a sustainable product to control *F. langsethiae* infection in cereals under field conditions (Parroni *et al.,* 2017).

***2.4 Pleurotus* spp.**

Oyster mushrooms are valued for their nutritional and medicinal properties, containing essential nutrients, bioactive molecules, and antioxidants (Khan and Tania, 2012). These fungi produce various metabolites with potential applications in plant disease management. Pleurotus being an important edible mushroom, its efficacy in directly controlling the various microbes is quite less researched. Most of the studies involving the oyster mushrooms revolve around the reuse of the spent mushroom substrate. The spent mushroom substrate (SMS) has a high organic matter content (22–40%), high nutrient levels, high cation exchange capacity and slow mineralization, making these substrates efficient for plant growth (Othman *et al.,* 2020). The methanolic extract of *Pleurotus ostreatus* was observed to be highly effective in controlling the mycelial growth of *Cladosporium* spp. by 88.6% (at 500µg/mL), suggesting its strong antifungal potency. The result also indicates a dose-dependent increase in inhibition of the pathogen, indicating a clear correlation between metabolite concentration and antifungal efficacy (Kantarcioglu, 2019).

Similarly, Pleurotin (a thioredoxin inhibitor) can disrupt the redox balance in fungal cells, potentially inhibiting their growth and pathogenicity (Berdicevsky et al., 2009). Pleurotin (extracted from *Pleurotus* spp.) significantly inhibited the mycelial growth of leaf spot disease caused by *Alternaria alternata* on broad bean, with increasing concentrations showing greater effectiveness. *In vivo* study under greenhouse conditions revealed a notable reduction in leaf spot symptoms compared to the untreated, inferring to the enhanced disease suppression and bio efficacy making it a potential alternative to synthetic fungicides (Awad and Hassan, 2023).

A complex cell wall extract (CCWE) from *Pleurotus ostreatus* known as Pleuran CCWE on field trials revealed a drastic reduction in disease incidence (50.5%) of downy mildew caused by *Plasmopara viticola*. Similarly, defense-related genes (PR1, PR2, PR4, PR5, PR8 and PR15) increased significantly, indicating activation of systemic defense pathways on prophylactic spraying with Pleuran CCWE against *Botrytis cinerea* (Faugeron-Girard *et al.,* 2020).

Spent substrate of *Pleurotus ostreatus* was used for managing the Fusarium wilt of banana and recognized an effective in the management under *in vivo* condition. The speculated metabolite that controlled pathogen was heat labile secondary metabolite. *In vitro* dual culture studies of *P. ostreatus*-*Foc* showed strong inhibition starting from 6th d.p.i (days post inoculation). Suppression of *Fusarium* was also observed on lower corm of the potted plants treated with *P. ostreatus,* in both pre-sterilized artificially inoculated soils and naturally infested unsterilized soils (Ocimati *et al*., 2021).

Autoclaved water extract from spent mushroom substrate (AWESMS) and autoclaved spent mushroom substrate (ASMS) from *Pleurotus eryngii* (king oyster mushroom) suppressed fungal and bacterial diseases in cucumber plants. The application of AWESMS of *P. eryngii* significantly reduced the sporulation of the powdery mildew fungus, *Podosphaera xanthii* on cucumber plants. The water-soluble and heat-stable mycelial components in SMS were responsible for inducing SAR (systemic acquired resistance) in cucumber plants. Moreover, disease protection in cucumber plants treated with AWESMS and ASMS of *P. eryngii* is caused by the activation of SAR (Parada *et al.,* 2012).

Pleurotin (complex polycyclic molecule) is a secondary metabolite produced by the fungus *Pleurotus griseus*, which is effective in controlling leaf spot disease caused by *Alternaria alternata* on broad bean. Pleurotin induced systemic resistance, by enhancing the production of both peroxidase and chitinase activitity. The treatment with Pleurotin also stimulated the plant growth and dry weight of all tested broad bean varieties symbolising the plant growth promoting effect of Pleurotin (Awad and Hassan, 2023).

Nematodes significantly affected plant health directly and induce various symptom such as root knots. The application of water suspension of *P. ostreatus* significantly reduced the population of *Meloidogyne* spp. in potted brinjal. Application ofwater suspension (*P. ostraetus*) significantly increased the mortality of the nematodes with time, reaching over 88% at 48 hr and 95% at 72 hr. The presence of metabolites in *P. ostreatus* not only reduced nematode populations, but also promoted the growth of brinjal (Nyangwire *et al*., 2024).

***2.5 Lentinus***

*Lentinus edodes* (shiitake mushroom), is a well-known mushroom, for nutritional. medicinal properties, antifungal activities and its role in combating phytopathogens. Its bioactive compounds have demonstrated potential in agricultural applications, particularly in managing fungal pathogens that affect plants.

Among several biological agents with disease control potential, *L. edodes* has exhibited anti-microbial properties. The culture filtrate of *L. edodes* shows potent antimicrobial activity against the plant pathogenic bacteria, *Ralstonia solanacearum*. The major component responsible for the antibacterial activity was oxalic acid effective against eight different phytopathogenic bacteria *viz*., *Xanthomonas campestris pv. campestris, R. solanacearum, Agrobacterium tumefaciens, Pectobacterium carotovorum subsp. carotovorum, X. oryzae pv. oryzae, X. axonopodis pv. citri, Pseudomonas tolaasii, X. axonopodis pv. glycines* and *X. axonopodis pv. vesicatoria* (Kwak *et al*., 2016).

Similarly, *in vitro* studies using culture-filtrate of *L. edodes* strains (ATCC 38164 and ATCC 28760) revealed the inhibition of *Erwinia amylovora* inciting fire blight of apple and *Xanthomonas campestris* pv*. vesicatoria* inciting bacterial spot of tomato. These *L. edodes* strains produced the least amount of oxalic acid, suggesting potential alternatives to the traditional control measures such as copper compounds and streptomycin for controlling bacterial spot of tomato and fire blight of apple (Kaur *et al.,* 2019).

Lentinan (a neutral polysaccharide) extracted from *L. edodes,* has been identified to enhance germination rate (51-54% for different wheat cultivars *viz*., Jimai 22, Shannong 23, and Luyuan 502) when applied after seed dressing (8g /100kg). The application enhanced the plant growth parameters and defense genes activity *viz*., phenylalanine ammonia-lyase, peroxidase, and superoxide dismutase significantly when compared to the control plot. Wheat sharp eyespot disease caused by *Rhizoctonia cerealis* was effectively controlled by the application of lentinan, which was due to the significant increase in transcription of the genes encoding alternative oxidase (AOX), β-1,3-glucanase (GLU), the salicylic acid signalling pathway-related gene NbPR1a. The transcription levels of alternative oxidase (AOX) are highly believed to be the target gene involving antifungal nature (Zhang *et al*., 2017).

In compliance with antifungal property, lentinan also depicts antiviral property. Although extracts from *L. edodes* have been shown to inhibit the tobacco mosaic virus (TMV) infection, investigation on the ability of LNT to control TMV was limited (Di Piero *et al*., 2006). The modified lentinan is composed of sulfated polysaccharide, with sulphated group in its hydroxyl part as bioactive moiety. The study revealed the inactivation effects of sulphated LNT (sLNT) and LNT against TMV to be 87.4% and 83.2% at 10.0 g/mL, respectively. LNT has shown to have affinity to TMV CP 4S and 20S protein, but not RNA. The proposed mode of action of lentinan in inactivation effect of TMV is because of its binding with TMV CP through dynamic quenching (Wang *et al*., 2013).

Lentinan is also regarded as potential biopesticide, as it can significantly reduce the dose of chemical pesticides (Gholami-Shabani *et al.,* 2019). The combination of lentinan and fluopimomide in the ratio 40:1 used for controlling *Rhizoctonia solani* (inciting cotton seedling damping-off) showed a synergistic effect in field trials with synergistic ratio of 1.228, respectively. The application of lentinan decreased malondialdehyde (MDA) content in cotton seeds and increased the activities of polyphenol oxidase (PPO), superoxide dismutase (SOD), and peroxidase (POD) in leaves (Sun *et al*., 2022).

Similarly, combination of Lentinan at 10 g/L and Ningnanmycin at 0.05 g/L is effective in controlling the Papaya Ringspot Virus (PRSV). The control efficacy was between 71.63-100% at seedling and fruiting stages, respectively. The interaction between Lentinan and Ningnanmycin is noted to have a more positive impact on disease control compared to their individual applications (Fan *et al.,* 2022).

Volatiles released from the spent mushroom substrate (SMS) of shiitake mushrooms (*Lentinula edodes*) were known to be effective for suppressing *Alternaria brassicicola*. inciting Alternaria sooty spot disease of cabbage. The compound identified was octan-3-one which inhibited spore germination of *A. brassicola* of cabbage (Muto *et al*., 2023). Previous studies also indicate the efficacy of aqueous extract of *L. edodes* in controlling late blight of potato and tomato (Godeanu-Matei *et al*., 2016).

***2.6 Schizophyllum commune***

*Schizophyllum commune* (white-rot fungus or split-gill mushroom), even though it is wood rotting fungi, it has engrossed great interest due to to its unique biological properties, ecological significance, and production of bioactive metabolites. It produces different metabolites such as schizophyllan and schizostatin. Among these two, schizostatin, a novel diterpenoid compound (possessing a β-1-3-linked backbone with single β-1-6-linked glucoside chains at approximately every third residue) has been identified as a potent squalene synthase inhibitor with an IC50 value of 0.84 μM (Tanimoto *et al*., 1996). Elucidating the structure of schizostatin (a trans-dicarboxylic acid moiety), it was synthesized through stereoselective coupling reactions (Kogen *et al*., 1996). Whereas, schizophyllan, a water-soluble homoglucan which possesses a β-(1-3)-linked backbone with single β-(1-6)-linked glucoside chains at approximately every third residue has numerous potential applications such as petroleum recovery, a thickener for cosmetic lotions, oxygen- impermeable films for food preservation, and high-value pharmaceutical applications (Zhang *et al*., 2001)

The antimicrobial activities of culture filtrate (CF) obtained from white-rot fungus proved its efficacy for controlling anthracnose and gray mold in pepper plants. The CF inhibited the mycelial growth of various fungal plant pathogens (*C. gloeosporioides*, *C. dematium* and *C. coccodes*), but was not effective against the bacterial pathogens (*Ralstonia solanacearum)*. Application of culture filtrate of *S. commune* (12.5%) reduced the incidence of anthracnose of black pepper (cv. Manita) in field conditions. The active compound responsible for the antifungal property was identified as schizostatin (Dutta *et al.,* 2019). Moreover, the compound, schizostatin could be used as a biochemical resource or precursor for development as a pesticide.

Recent research has revealed potential of schizostatin as an antifungal synergist (Gisi, 1996), particularly when combined with demethylation inhibitor (DMI) fungicides. In combination with tebuconazole, schizostatin demonstrated enhanced efficacy against *Botrytis cinerea,* the causative agent of gray mold disease (Park *et al.,* 2020). The transcript level of *erg11* (whose gene product is the target of DMIs) increased to 56.6-fold on treatment of schizostatin with tebuconazole, while the other genes (such as *erg7*, *erg24*, *erg27* and *erg9*) remained unchanged (Park *et al*., 2020).

*S. commune* is also a potential biocontrol agent that can be used to effectively control blueberry root rot caused by *Fusarium* in the field with inhibition rates of 70.30% and 22.86%, respectively (Li *et al*., 2024).

***2.7 Cordyceps* sp.**

Cordyceps is usually known as Chinese caterpillar fungus because it parasitizes and grows on a rare caterpillar (*Hepialis armoricanus*) (Paterson, 2008). Cordyceps has gained significant attention in pharmacological and biomedical research due to its diverse bioactive metabolites. These mushrooms, particularly species like *C. sinensis* and *C. militaris*, produce a range of compounds with therapeutic potential, having anticancer properties. It contains numerous polysaccharides, extracted from their fruiting bodies and mycelium (from submerged fermentation cultures and broth) contributing to 8% of its overall weight. Cordycepin (3′-deoxyadenosine), a primary bioactive compound in *C. militaris* mimics adenosine and disrupts RNA and DNA synthesis in cancer cells and inhibits cell proliferation and induces apoptosis (programmed cell death) (Sugar and McCaffrey, 1998; Ramesh *et al.,* 2012).

The mycelial extract of *Ophiocordyceps sobolifera* had the highest efficacy in managing anthracnose-infected chilli plants up to 28 days after inoculation (DAI) compared to culture filtrate. The metabolite cordytropolone, derived from *Ophiocordyceps sobolifera*, and adenosine, extracted from *C. sinensis*, exhibited moderate inhibition of the mycelial growth of *Colletotrichum capsici* and *C. gloeosporioides* (Jaihan *et al*., 2018). Adenosine, a nucleoside analogue and precursor to cordycepin, demonstrated antifungal activity against fluconazole-resistant strains of *Candida albicans* and *C. krusei* (Sugar and McCaffrey, 1998). Cordytropolone, a polyketide-derived tropolone compound with the chemical structure 2,4,6-cycloheptatrien-1-one, was effective against certain plant-pathogenic fungi, including *Colletotrichum* species (Morita *et al.,* 2003).

The antifungal properties of *Ophiocordyceps sinensis* against *Colletotrichum musae* was observed as mycelial inhibition in dual plate and agar well diffusion techniques at 10 DAI GC-MS analysis further, pointed out the significant role of widdrol hydroxyether (3.18%) in the antifungal activity of *O. sinensis* (Pravin *et al.,* 2020). Similarly, the antifungal activity of *O. sinensis* was remarkably found against *Fusarium spp.*, specifically *Fusarium oxysporum* f.sp. *lycopersici* and *Fusarium oxysporum* f.sp. *cubense.* Among the twelve different bioactive compounds identified, the methanolic fraction, including n-decanoic acid, glycerin, and 1,2,3-benzenetriol, were found to be responsible for the observed antifungal activity (Akshaya *et al.,* 2021).

Among the thirty-four metabolites, depsidone metabolites such as cordycepsidone A and cordycepsidone B extracted from *Cordyceps dipterigena* were identified as responsible factor for the antifungal activity against *Gibberella fujikuroi* (Varughese *et al.,* 2012).

***2.8 Hericium erinarius***

*Hericium erinaceus* (commonly known as lion's mane mushroom) and its bioactive metabolites were primarily studied for human health benefits, but recent attention has focused on the potential of fungal metabolites, including those from *H. erinaceus,* in plant disease management.

Water extract from spent mushroom substrate of *H. erinaceus* inhibited the mycelial growth of seven strain of tomato pathogenic fungi including *Phytophthora capsici* and the growth of *Ralstonia solanacearum*. treatment of 33.3% and 50% water extract from spent mushroom substrate of *H. erinaceus* controlled the wilt incidence by 58.3% and 83.3%, respectively (Lee *et al*., 2015). Water, n-butanol, and ethyl acetate extracts of spent mushroom substrate (SMS) of *H. erinaceus* exhibited high antibacterial activity against different phytopathogenic bacteria such as *Pectobacterium carotovorum subsp. carotovorum, Agrobacterium tumefaciens, R. solanacearum, Xanthomonas oryzae pv. oryzae, X. campestris pv. campestris, X. axonopodis pv. vesicatoria, X. axonopodis pv. citiri,* and *X. axonopodis pv. glycine*. Water extracts of SMS (WESMS) of *H. erinaceus* induced expressions of plant defense genes encoding β-1,3-glucanase (GluA) and pathogenesis-related protein-1a (PR-1a), associated with systemic acquired resistance (Kwak *et al*., 2015).

***2.9 Oudemansiella***

*Oudemansiella mucida* (commonly known as porcelain fungus) produces metabolites (extracted) which are of predominant interest due to their bioactive properties. The prevalent use of antifungal active substance strobilurin, extracted from *Strobilurus tenacellus* and *S. mucida*, is well versed ingredient in Strobilurin fungicide (such as Azoxystrobin, Pyraclostrobin and Trifloxystrobin). Other active compounds include mucidin and oudemansin (Clough, 1993). These compounds also have bacteriostatic effect, and provide a theoretical basis for the application of *O. mucida* in biopesticide.

The fermentation broth of *O. mucida* showed significant antibacterial activity against five common plant pathogens (*Alternaria longipes, A. brassicae, Gloesporum fructigenum, Fusarium graminearum* and *A. alternata*) (Deng *et al.,* 2020). The ethyl acetate had the strongest antimicrobial effects compared to other extracts. UHPLC-MS analysis revealed the involvement of six putative strobilurins, including strobilurin A and its stereoisomers, with antimicrobial activity. The antifungal activity of culture filtrate of strobilurin extracted from *O. canarii* in controlling white mold disease, caused by the phytopathogen *Sclerotinia sclerotiorum* clearly depicts the less explored potential (de Oliveira Vieira *et al.,* 2021).

**3. Indirect effects of mushroom metabolites in controlling phytopathogens**

The use of mushroom metabolites in controlling crop pests presents a promising alternative to conventional chemical pesticides, offering eco-friendly and sustainable pest management solutions. These metabolites, derived from both edible and entomopathogenic fungi, have shown significant insecticidal properties against various agricultural pests.

Levodopa or l-3,4-dihydroxyphenylalanine (L-DOPA) extracted from *Strobilomyces floccopus* and from *Hygrocybe conica* showed insecticidal activity against *Spodoptera eridania* (Southern armyworm), a major pest attacking a wide variety of crops such as cotton, vegetable crops and field crops (Mier *et al.,* 1996). Various extracts of oyster mushroom (*Pleurotus* *ostreatus*) such as hot water, methanol-chloroform, and petroleum ether extracts, exhibited significant toxicity against adult *Tribolium* *castaneum the major storage pest*.Themethanol-chloroform extract of *Pleurotus ostreatus* had the lowest LD50 value (0.206 mg/cm) implicating its potent efficacy against the pest (Rahman *et al.,* 2011).

The control of citrus psyllid (*Diaphorina citri)*, a vector of citrus greening was reported using the application of *Cordyceps javanica* mixed with oil and was as effective as insecticide, spinetoram in suppressing citrus psyllid populations (61-83%) up to 14 days after treatment. Application of *C. javanica* oil mix showed compatibility with beneficial insects such as lady beetles (Avery *et al.,* 2021). Edible mushroom metabolites, such as pentadecanoic acid (PNA), palmitic acid, and β-sitosterol (βT), extracted from *Pleurotus* sp*.* have demonstrated effectiveness against the soybean weevil, *Rhyssomatus nigerrimus*. Mixtures of these metabolites resulted in higher mortality rates, with combinations like PNA + βT achieving up to 54.44% mortality over 15 days (Castañeda-Ramírez *et al*., 2024).

**4. Zombie fungus (*Cordyceps* sp.) and their impact on pests affecting different crops**

*Cordyceps* parasitize mainly on insects and other arthropods (they are thus entomopathogenic fungi). Several species of the fungus *viz*. *C. wuyishanensis* and *C. maolanoides* were obtained from nymphs of cicada and dung beetle pupa, respectively; whereas, *C. maolanensis* infects Coleopteran larvae. Not only popular for the medicinal benefits such as improving liver function, reducing cholesterol, adjusting protein metabolism, inhibiting lung carcinoma, but also pose a major threat to pest world. For instance, coconut root grub (*Leucopholis coneophora*), a serious pest of coconut found in sandy loam tracts of Kerala and Karnataka is polyphagous pest that damages the roots of coconut palms and other crops. Root grub though is a soil inhabiting pest; chemical control is not advisable and hence search for a promising bio-control agent is a thrust in this field. Natural incidence of *Cordyceps* (DMRO-526) has been found on coconut root grub, thus inhibiting the spread of the disease. Further studies on artificial inoculation of the fungus will help to develop potential entomopathogenic fungi for controlling coconut root grub and also, we can use the grub for growing these medicinal fungi (Kumar and Aparna, 2014).

Similarly, *Ectropis grisescens*, a notorious pest in tea plantations which solely relied on synesthetic pesticides for management, had high resurgence was found to be biologically controlled using *Cordyceps* sp. WZFW1. The virulence test of *Cordyceps* sp. WZFW1 against *E. grisescens* revealed that the spray at 5.74 × 106 spore/mL concentration had a lethal time of 2.98 days and 7.47 days at 107 spore/mL, indicating *Cordyceps* sp. WZFW1 to be effective in controlling *E. grisescens* (Yang *et al.,* 2024).

A notable leap in controlling whiteflies (*Bemisia tabaci)* was reported in *C. javanica* which demonstrated that efficacy of both conidial and culture filtrate of *C. javanica* isolates which significantly affects the mortality of second instar of *B. tabaci* nymphs and a significant increase in mortality (61.3 %) of *B. tabaci* nymphs was noticed after 48 hours of treatment (Shah *et al.,* 2020).

The strains of *C. cateniannulata* (CPIsp1201 and IPIsp1201) exhibited high virulence against *Stenoma impressella* larvae (pests of oil palm plantations) achieving mortality rates of 81.7% and 82.9%, respectively in two bioassays *viz*., under shaded conditions and in open field using natural populations, indicating their potential as biological control agents in oil palm plantations (Montes‐Bazurto *et al.,* 2020)

Infection and sporulation of *C. javanica* and *C. fumosorosea* (isolated from *Bemisia tabaci*) on red gum lerp psyllid nymphs (*Glycaspis brimblecombei*, an important pest in *Eucalyptus* plantations) caused the mortality of *G. brimblecombei* nymphs, up to seven days after the application of *Cordyceps* sp. isolates. The mortality was recorded up to 88.6% and 81% in all the isolates of *C. fumosorosea* and *C. javanica,* respectively for third instar of *B. tabaci* nymphs, which in turn depicts the potential of the fungus to control the pest. The bioactive compounds, such as trichodermin, 5-methylmellein, brevianamide F, enniatin and beauvericin produced by *C. fumosorosea* and the secondary metabolites, emericellin and fumosorinone produced by *C. javanica* contributed towards their insecticide properties (Domingues *et al.,* 2022).

Conclusion

Mushroom metabolites represent a rich and diverse source of bioactive compounds with significant potential for human and plant health. Their immunomodulatory effects and their ability to control plant diseases offer promising avenues for developing novel therapeutic strategies and sustainable agricultural practices. Continued research into the chemistry, biology, and applications of mushroom metabolites is crucial to fully unlock their potential and contribute to a healthier and more sustainable future. Moreover, integrating these natural bioactive compounds into mainstream agricultural and pharmaceutical systems could reduce dependency on synthetic chemicals, thereby minimizing environmental hazards and resistance development. Advances in biotechnology and molecular biology may further aid in optimizing the extraction, characterization, and functional evaluation of these metabolites.

**Future prospects**

Continued research to identify and characterize novel antimicrobial compounds from a wider range of mushroom species. Developing effective and stable formulations for the delivery and application of mushroom metabolites in agricultural settings. Integrating mushroom-based products into sustainable IPM strategies for optimal disease control. Exploring the potential of genetic engineering to enhance the production of desired metabolites in mushrooms. Further emphasis is to be given in terms of research to isolate and characterize the specific and active compounds having anti-phyto pathological effect from less explored mushrooms such as bird’s nest fungi (*Cyathus* sp.), Jew’s ear mushroom (*Auricularia* sp.) and so on. Collaborative efforts across different disciplines, including mycology, plant pathology, pharmacology, and environmental science, to harness the full spectrum of benefits offered by mushroom-derived bioactives.

**Challenges and Considerations**

Consistent production and quality control of mushroom-based products and metabolites are crucial for reliable and effective disease management. Extensive field trials are needed to evaluate the efficacy of mushroom metabolites under different environmental conditions and against various pathogens. Large-scale production and commercialization of mushroom-based products need to be economically viable for widespread adoption. Obtaining regulatory approvals for the use of mushroom metabolites as biocontrol agents can be a complex and time-consuming process. There happens to be an array of less or least explored mushrooms, which have antagonistic action towards plant pathogens.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models

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