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Review Article

Immune-stimulants and Adaptogenic Properties of Selected Wild Edible Mushrooms Collected from the Western Ghats, India

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ABSTRACT

Virus outbreaks such as the COVID-19 virus demand nutrition interventions among people all over the world. Consumption of foods with immune-modulating and nutraceutical characteristics is an effective strategy to avoid or lessen the severity of viral attacks and side effects. Immune stimulants function by enhancing macrophage activity and killing pathogens and diseased cells, while adaptogens work by supporting and regulating the endocrine system. This paper foreshadows the use of mushrooms as a functional food for the prevention and treatment of COVID - 19 by citing peer-reviewed papers from Google Scholar, PubMed, the WHO database, Science direct, and the author's own research. *Pleurotus ostreatus*, *Termitomyces heimii*, *T. microcarpus*, *T. clypiatus*, *Auricularia auricula*, *Phlebopus portentos*, *Ganoderma lucidum*, *Coprinus micaceus*, *Cantharellus cibarius*, *C. minor*, and *Lentinus bambusinus* were among the ethnomedicinal mushrooms studied. Immuno-modulating effects were found in polysaccharides, fungal immune-modulatory proteins (FIPs), terpenes, and terpenoids from wild mushrooms, as well as activation of immune effector cells such as lymphocytes, macrophages, and natural killer cells. They also cause the production of cytokines such as IFN-, IL-2, IL-4, IL-10, and TNF-. Similarly, mushrooms have been shown to have probiotic properties that can help to flatten the curve.

INTRODUCTION

Coronavirus 2 (SARS-CoV-2)-caused COVID-19 viral respiratory illnesses are spreading rapidly. SARS-CoV-2 enters the body through inhalation or contact with an infected person's respiratory droplets. The infection progresses in three stages: (1) asymptomatic phase (lasts about 1-2 days), the virus multiplies in the upper respiratory tract; (2) non-severe symptomatic phase (lasts 2-14 days), with common symptoms such as fever, dry cough, pharyngitis, shortness of breath, joint pain, and tiredness, increases the risk of community spread; (3) severe respiratory symptomatic phase, virus moves to lower airways, triggers a strong innate immune response, develops acute respiratory disease/multi-organ failure and death in worst scenario.^[1]

Besides the progress of antiviral drugs, preventative public health practices such as lifestyle and appropriate nutrition are limiting the spread of infections during stage-2 and counteracting the SARS-CoV-2 infection during stage-1.^[2] Recent studies highlight the potential roles of micronutrients, trace elements, dietary components antioxidants and probiotics in the development and maintenance of an effective immune system and reducing chronic inflammations during COVID 19,^[3,4] also noticed that high energy diet and diabetes increase the risk factor of Coronavirus attack and subsequent spreading.^[5] This postulates the necessity of a balanced food with low calories and adequate immune-supportive functions. Mushrooms are a type of 'functional food,' meaning they have a high nutritional value as well as health advantages.

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According to our earlier research on the “ethnomedicinal applications and ecology of wild mushrooms among selected tribal societies of the Western Ghats”^[6], tribes are well-versed in the concept of “mushroom as food with specific health purposes.” Aside from taste, tribes consume/use mushrooms for a variety of therapeutic purposes, including respiratory ailments, including cough, cold, and asthma symptoms. Patients with SARS-CoV-2 infection experience similar symptoms, which is why the study was conducted. The immunomodulatory, anti-inflammatory, antioxidant, antiviral, and probiotic activity of ethnomedicinal mushrooms may contribute to COVID-19 preventive effectiveness, according to this hypothesis.

Ethnomedicinal Knowledge of Wild Edible Mushrooms from Kerala's the Western Ghats'

The mushrooms chosen (Fig. 1) are based on our prior study, 'ethnomedicinal knowledge of wild edible mushrooms from Kerala's the Western Ghats', which have long been used for immunity and to treat respiratory difficulties. Disease classification was based on data collected from each community during the ethnomycological survey and reliability testing using Informant Consensus Factors (ICF).^[6]

Retrieval of Evidence for the Potential use of Selected Wild Mushrooms

Using the phrases “mushroom name” AND antiviral/respiratory support/antioxidant/immune potential/relaxant/probiotic, etc., We conducted a bibliographic search in Google Scholar, PubMed, Web of Science, WHO database, and Science Direct. These mushrooms were also investigated for possible nutritional and health-promoting properties. The year of publication (between 2010 and 2021) and the dependability of research (*in-vitro/in-vivo*/case studies) were utilised to narrow the scope of the investigation.

Immune Stimulatory Activity of Mushrooms

The immune response during COVID-19 is a double-edged sword: it maintains immunity, but the excessive and incorrect generation of inflammatory cytokines can cause cytokine storm syndrome, which can lead to organ immuno-pathology, complications, and mortality.^[7] Two therapeutic approaches are currently in use: the first involves the use of immune suppressors to reduce the hyper inflammation caused by a viral infection, and the second involves the use of immune potentiators, which can eradicate the virus by stimulating the host's innate and adaptive immune responses.

Medicinal mushrooms are natural immune modulators because they stimulate both innate and adaptive immune systems and include a variety of immune-regulatory substances such as polysaccharides, and fungal immunomodulatory proteins (FIPs), terpenes, and terpenoids. Activation of immunological effector cells such



Fig. 1: Ethnomedicinal mushrooms from the Western Ghats of Kerala.

as lymphocytes, macrophages, and natural killer cells are examples of immune-modulating effects. They also cause the production of cytokines such as IFN-, IL-2, IL-4, IL-10, and TNF- (Table 1).

Pleurotus ostreatus,^[8-10] *Ganoderma lucidum*,^[15] and *Auricularia auricula* polysaccharides enhance natural killer (NK) cell count, neutrophils, and macrophages, as well as induce cytokine expression and release.^[16-17] PS-G (polysaccharide produced from *Ganoderma lucidum*) has the ability to modulate immunological responses by activating and maturing immature dendritic cells (DCs).^[14] Schizophyllan (Polysaccharide from *Schizophyllum commune*) promotes the expression of genes coding for proteins in the nuclear factor (NF)-kB pathway and modulates immune system functions, according to a study by Yelithao and coworkers.^[16]

Antioxidants and Anti-inflammatory Activity of Wild Mushrooms

Antioxidant supplementation has been shown in clinical trials to improve immune responses. Mushrooms, as an antioxidant source, may help maintain oxidative equilibrium.^[19] Mushroom antioxidants provide protection throughout their life cycle through a variety of ways (Table 2).



Table 1: Immunomodulatory activity of mushrooms.

Mushroom	Extract/compound	Pattern of effect	Reference
<i>P. ostreatus</i>	β -(1,3/1,6) glucan	Increase natural killer (NK) cell count, neutrophils, macrophages, stimulate cytokines expression and secretion	[8-10]
<i>G. lucidum</i>	Fungal Immunomodulatory Protein FIP-SN15	Stimulate immune cells to produce a variety of cytokines	[11,12]
<i>G. lucidum</i>	Mycelial extract	(NF)- κ B activation	[13]
<i>G. lucidum</i>	Ganoderma derived Polysaccharide(PSG)	Activate immature dendritic cells (DCs), induce a significant proliferation of T-cells	[14]
<i>G. lucidum</i>	Polysaccharide	Increase natural killer (NK) cell count, neutrophils, macrophages, stimulate cytokines expression and secretion	[15]
<i>S. commune</i> <i>S. commune</i>	Polysaccharide(Glycomannans) β (1-3) and β (1-6) D-glucan	Activate of nuclear factor-kappa (NF- κ B) and mitogen-activated protein kinase (MAPK) stimulate immune cells to produce a variety of cytokines	[16] [17]
<i>A. auricula</i>	Polysaccharide AAP	Stimulate IFN- γ , IL-2, IL-4, IL-10, and TNF- α levels in the serum	[18]

Table 2: Ethnomedicinal mushrooms' anti-inflammatory and antioxidant properties.

Mushroom	Extract/compound	Pattern of effect	Reference
<i>P. ostreatus</i>	Pleuran	Prevent TNF- α mediated inflammation	
<i>P. ostreatus</i>	Mushroom concentrate	Inhibit proliferation and secretion of interferon- γ (IFN- γ), IL-2, and IL-6 in mice	[20]
<i>G. lucidum</i>	Mushroom extract	Suppress growth and proliferation of tumors by Jak-STAT signaling pathway, T cell receptor signaling pathway and PI3K-Akt signaling pathway in mouse	[9]
<i>C. cibarius</i>	Polysaccharide (CC-1)	Proliferation effect on B cells	[21]
<i>C. cibarius</i>	Mushroom extract	Lower expression of cyclooxygenase-2 in rats	[22]
<i>S. commune</i>	Homogeneous protein bound heteropolysaccharide	<i>In-vitro</i> antioxidant activity. inhibits the production of nitric oxide (NO), induce nitric oxide synthase (iNOS), and 5-lipoxygenase (5-LOX) from macrophages in RAW 264.7 murine macrophages	[23]
<i>Phlebopus portentosus</i>	Pulvinic acid derivatives	Cytotoxic activity against human mammalian cell lines	[24]
<i>A. auricula</i>	Fruit body extract	Reduced expressions of inflammatory cytokines (IL-6, TNF- α and IL-1 β)	[25]
<i>Coprinellus species</i>	Ergothioneine	<i>In-vitro</i> antioxidant activity Diminish ROS and NO	[26]
<i>Termitomyces heimii</i>	β -glucan	<i>In-vitro</i> antioxidant activity: Diminish ROS and NO	[27]
<i>T. microcarpus</i>	Polyphenol	<i>In-vitro</i> antioxidant activity: Diminish ROS and NO	[28]
<i>A. auricula</i>	polysaccharides	Anti-oxidant up-regulate stress-resistance-related enzymes including superoxide dismutase (SOD)	[29]
<i>T. microcarpus</i>	Crude extract	DPPH radical scavenging activity	[30]

They are involved in chain breaking, free radical scavenging, lipid hydroperoxide inhibition or breakdown, primary antioxidant renewal, and singlet oxygen (102) quenching. Antioxidants can serve as inducers, causing changes in gene expression and the activation of enzymes that remove reactive oxygen species (ROS) in the body. With different polysaccharides and polyphenols,

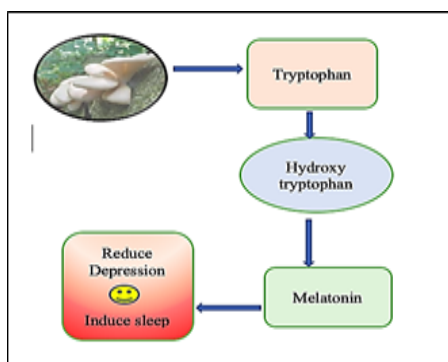
alterations in the redox state lead to anti-inflammatory effects.

Probiotic Activity of Wild Mushrooms

The review here addresses the key areas in mushrooms that govern gut microbiota in the health of the host. Probiotics have been shown in studies to flatten the curve

Table 3: Antiviral activity of mushrooms

Mushroom	Extract/compound	Pattern of effect	Virus strains	Reference
<i>P. ostreatus</i>	β -glucan pleuran	Increase proinflammatory cytokines (IL-1 β , IL-6, and TNF- α)	HSV-1 and HSV-2	[34]
<i>A. auricula</i>	Mycelial extract	Inhibit influenza virus type H1N1 and herpes simplex virus type 2 (HSV-2),	H1N1 and herpes simplex virus type 2 (HSV-2),	[35]
<i>G. lucidum</i>	Proteoglycan	Inhibit herpes simplex virus	herpes simplex virus 1 HSV1, HSV 2	[36]
<i>Ganoderma</i>	Triterpenoids	Inhibitors of Dengue virus DENV NS2B-NS3 protease,	Dengue virus DENV	[37]
<i>S. commune</i>	Extract	By interfering with the initial stage of DENV-2 infection,	DENV-2	[38]
<i>P. ostreatus</i>	Lectin	Hepatitis B virus tolerance via TLR6 signaling	Hepatitis B virus	[39]

**Fig. 2:** Sleep inducing action of mushroom.

of the coronavirus disease COVID-19 by reducing bacterial and viral infections, including RTIs.^[31] The mushrooms in this investigation are also looking for probiotic functions. Various polysaccharides found in the fruit body, mycelia, and water extract of mushrooms suppress endogenous pathogens in the GI tract, allowing the immune system to be more capable of resisting external pathogens (Table 3). *G. lucidum* is a probiotic mushroom that has a wide range of benefits. The anti-obesity polysaccharide xylan degrading bacterium *bacteroides* promotes by the and glucan content of this mushroom decreases obesity in mice.^[13,14] The extracts of *G. lucidum* and *P. ostreatus* boost the immune system.

Antiviral Activity of Mushrooms

Mushrooms and their active chemicals have been widely recognised a rich reservoir and used as a traditional medicinal medicine for many chronic infections, including viral disorders, since ancient times.^[33] Mycelia extracts and other isolated compounds have been found to have antiviral properties in mushrooms. Polysaccharides, carbohydrate-binding proteins, peptides, enzymes, polyphenols, triterpenoids, and other mushroom components help to fight viral infections. These drugs primarily target viral entrance, uncoating, replication, assembly, release, and immune cell modulation. Antiviral effects of mushrooms against herpes simplex virus types 1 and 2 (HSV-1 and 2)

have been described utilising β -glucan extracted from *P. ostreatus*,^[34] mycelial extract of *Auricularia auricula*,^[35] and *G. lucidum* Proteoglycan.^[36] Dengue virus (DENV) is inhibited by *G. lucidum* triterpenoids^[37] and *S. commune* extract.^[38] However, the action of mushroom components is distinct. *P. ostreatus* lectin has antiviral action against the hepatitis B virus.^[39] Table 3 summarizes the research on mushrooms' antiviral properties

Sleep Inducing Activity of Mushrooms

COVID-19 has negative effects on sleep, including sleep disturbances, mental diseases, and physiologic ailments, particularly during quarantine.^[40] Sleep-inducing qualities include indoleamine (5-hydroxytryptophan, serotonin, and melatonin), which is produced from dietary tryptophan, as well as appropriate vitamin D levels (Fig. 2). Serotonin and its precursor, 5-hydroxytryptophan, are abundant in *C. cibarius* and *P. ostreatus*. In rats, *G. lucidum* extract (GLE) increases total sleep time and non-rapid eye movement (NREM) sleep time, implying that mushrooms may have sleep-inducing properties.^[43]

Nutritional and Biochemical Components of Mushroom

Various micronutrients and dietary components have important roles in the development and maintenance of a healthy immune system that can help to reduce chronic inflammation. Except for *Ganoderma* and *Auricularia*, the nutrient profile of ethnomedicinal mushrooms from the Western Ghats has been published in our previous studies^[44] which revealed the high protein, crude fibre, and low fat and salt content are relevant from a pharmacological standpoint. In addition, the antioxidant activities of *Lentinus bambusinus* and *Coprinellus micaceus* as measured by DPPH (IC₅₀) ranged from 3.38 0.10 to 9.790.14 mg/mL. These data also indicate the mushrooms' considerable immune-boosting properties.

Summary

Mushroom consumption has antiviral, immune-boosting, and cholesterol-lowering benefits, according to several pathways. The wild mushroom extracts investigated



potentially have therapeutic effects against problems including lung inflammation and consequences that typically follow COVID-19 infection. More extensive chemical and pharmacological investigations of particular substances are recommended to complete the information. *L. bambusinus*, *C. micaceous*, and *Termitomyces* are poorly explored wild mushroom species found in the Western Ghats

CONFLICT OF INTEREST

The authors have no conflict of interests

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