CHAPTER 2

REVIEW OF LITERATURE

Ayurveda emphasizes in keeping a balance between soul, body and mind, as well as correcting doshas like Kapha, Pitta, and Vatta to attain a healthy lifestyle, the regime of which is natural and differ from person to person. Similarly, in traditional Chinese medicine the body and mind are considered as a miniature cosmos where every individual is treated as an independent entity whose health is dependent on the Yin-Yang balance. According to this, Emperors of great dynasties consumed tea prepared from mushrooms, particularly Lingzhi, in order to achieve immortality. Mushrooms are also administered to alleviate kapha, though not as frequently as other fruits and vegetables (Varghese et al., 2019).

In India, several substantiated evidences on traditional mushroom use have been discovered, including Baiga tribes of Central India to cure asthma by utilizing *Ganoderma lucidum*, *Lycoperdon pusillum* to heal gum bleeding and wounds and *Agaricus* sp. to treat goitre (Rai et al., 2005). Various tribes in West Bengal, particularly in Darjeeling, consume *Cordyceps sinensis*, *Daldinia concentric*, *Pisolithus arhizus*, *Schizophyllum commune* and *Termitomyces clypeatus* as medicine to treat minor skin infections, as well as an anti-aging, revitalising, and invigorating tonic. Assamese tribes such as the Adivashis, Bodos, Gaos and Rajbangshis ate wild edible mushrooms. While mushrooms like *Astraeus hygrometricus, Lycoperdon* sp., *Geastrum* sp., *Russala* sp., *Lactarius* sp., *Termitomyces reticulates, Tuber* sp. and *Volvariella* sp. are used not only as food but also as medicine by the Bhuyan and Kharia tribes of Odisha (Panda and Tayung, 2015). Macro-fungi are thus recognised as a highly sought-after category of fungus that can be cherished as culinary food and medicine with ethnic knowledge. Macro-fungi have been found to have various therapeutic potential like anticancer, antioxidant, immunomodulating, cardiovascular, anti-inflammatory, antiviral, antimicrobial, hepatoprotective and antidiabetic properties (Wasser, 2014) (**Fig 2.1**).

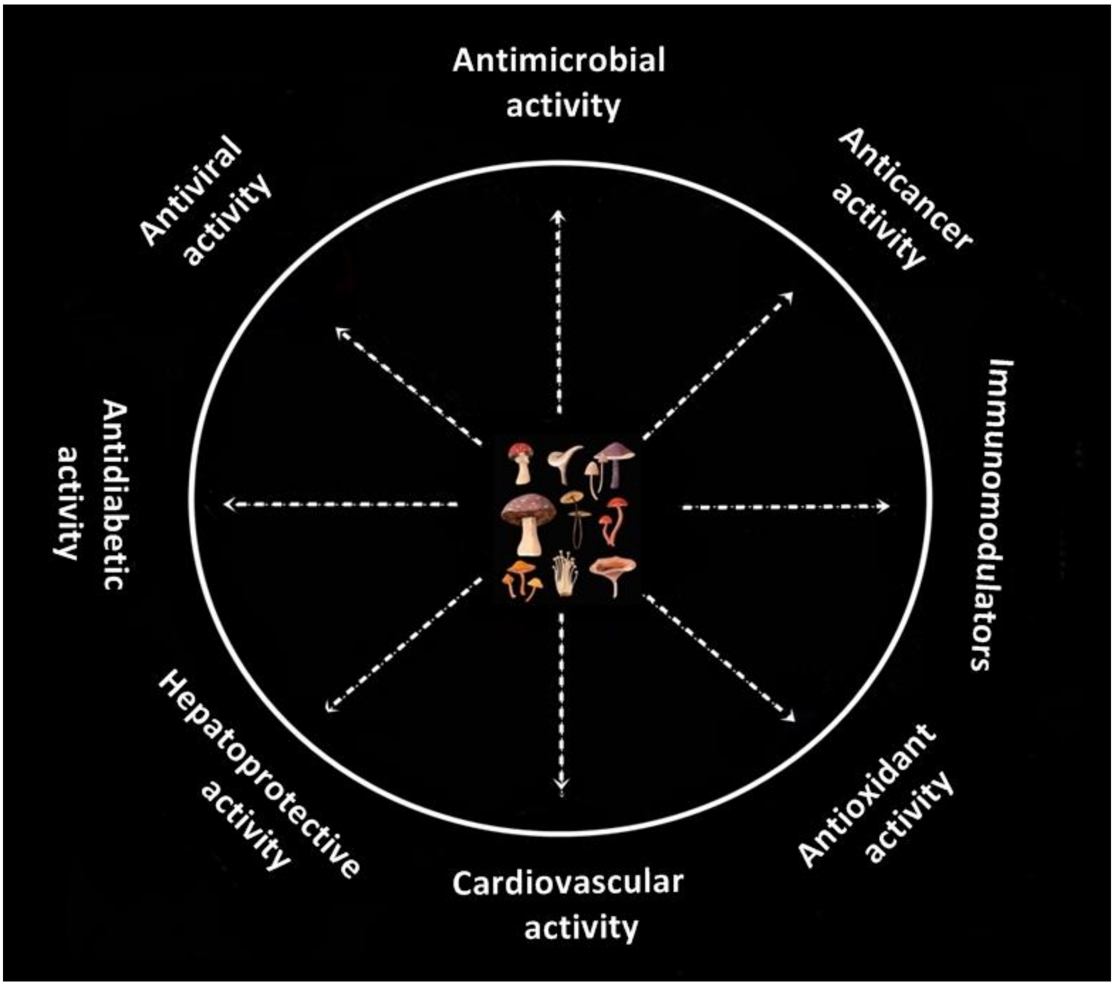

Fig. 2.1: Schematic illustration of therapeutic applications of macro-fungi

2.1. Antioxidant

Reactive oxygen and nitrogen species (ROS and RON) produced by healthy cellular metabolism interact with wide range of chemical molecules that can be harmful to biological systems. Because of the presence of various bioactive constituents like polysaccharides, polyphenols, tocopherols, vitamins, carotenoids and minerals, certain edible macro-fungi have strong antioxidant effects (Yadav and Negi, 2021). Antioxidants are universally acknowledged as providing protection against disease by scavenging the harmful free radicals as ROS (Kothari et al., 2018). The antioxidant potential of macro-fungi is arbitrated by lipid peroxidation inhibition, free radical scavenging and activation of catalase, glutathione peroxidase and superoxide dismutase (Kozarski et al., 2015). The antioxidant potential of different macro-fungi has been shown in **Table 2.1**.

2.2. Anti-inflammatory

Inflammation, which is characterised by dolor (pain), calor (heat), rubor (redness) and tumour, can occur as a result of a disruption in immunologic or metabolic pathways. They can cause chronic diseases like cancer, diabetes, colitis and nerve damage if they are not restrained (Kothari et al., 2018). The most well-known β-glucan, lentinan, extracted from *Lentinus edodes* was reported to be used in the treatment of inflammation. Inflammatory symptoms, body weight, levels of myeloperoxidase (MPO), disease activity index (DAI), MDA, NO, and the expression of pro-inflammatory markers were used to assess the anti-inflammatory efficacy of this β-glucan (Nishitani et al., 2013). Linear β-glucan extracted from *Cordyceps militaris* exhibits anti-inflammatory characteristics both in vitro and in vivo. *C. militaris* glucan suppressed THP-1 cell inflammation in vitro by inhibiting IL-1, COX-2 and TNF-α, production. In an LPS-induced inflammation mouse model, β-glucan effectively suppressed the phase of inflammation in formalin-persuaded nociceptive reaction in vivo (Smiderle et al., 2014). Glucans extracted from *Inonotus obliquus* inhibited the signalling pathways of COX-2, nuclear factor-B (NF-B) and iNOS, resulting in anti-inflammatory properties (Ma et al., 2013). According to the studies of Castro-Alves and do Nascimento, (2018), α- and β-glucans retrived from *Pleurotus albidus* substantially control pro-inflammatory lipid-loaded macrophage production and lipid-induced inflammation in THP-1 cells. In another study, the anti-inflammatory potential was reported from the *Pleurotus florida* extract in rat model which was confirmed by hot plate method, formalin induced pain, tail flick method and acetic acid-induced writhing (Ganeshpurkar and Rai, 2013).

Table 2.1: Anti-oxidative potential of various macro-fungi

Fungi	Efficacy	Compound/Extract	Reference
Agaricus silvaticus	DPPH radical-scavenging activity: 83.7±2.1%	Phenolic compounds and organic acids	Gąsecka et al., 2018
Armillaria mellea	DPPH radical-scavenging activity, IC_{50}:1.32± 0.09 mg/ml	Methanolic extracts	Erbiai et al., 2021
Auricularia auricula-judae	ABTS scavenging activity: 78.01%; DPPH radical-scavenging activity: 47.79%	Polysaccharides	Cai et al., 2015
Cantharellus cibarius	DPPH radical-scavenging activity: 35.23%; ABTS scavenging activity: 40.70%, IC_{50}: 7.8624 mg/ml	Phenolic compounds and flavonoids	Zhao et al., 2018
Clitocybe geotropa	DPPH radical-scavenging activity, IC_{50}: 246.58 µg/ml	Phenolic compounds	Kosanić et al., 2020
Coriolus versicolor	DPPH radical-scavenging activity: 80.66%	Phenolic compounds	Stojanova et al., 2021
Flammulina velutipes	DPPH radical-scavenging activity, IC_{50}:0.202 mg/ml; H_2O_2 radical-scavenging activity, IC_{50}: 0.622 mg/ml	Phenolic compounds	Ukaegbu et al., 2020
Fuscoporia torulosa	DPPH radical-scavenging activity, IC_{50}: 0.02±0.00 mg/ml; Chelating Fe^{3+} ions, IC_{50}: 1.59±0.02 mg/ml Reduction of Fe^{3+} ions, IC_{50}: 0.09 ±0.03 mg/ml	Aqueous extract	Stojanova et al., 2021
Ganoderma lucidum	DPPH radical-scavenging activity, IC_{50}: 8.51±0.24 µg/ml; ABTS scavenging activity IC_{50}: 10.06 ±0.13 µg/ml	Ethyl acetate extract	Kebaili et al., 2021
Macrolepiota procera	DPPH radical-scavenging activity, IC_{50}: 1.3 ±0.05 mg/ml	Methanolic extracts	Erbiai et al., 2021
Pleurotus cystidiosus	DPPH Radical Scavenging activity: 79.01%	Ethanolic extract	Garcia et al., 2020
Pleurotus djamor	DPPH radical scavenging activity, IC_{50}: 3.83 mg/ml; Hydroxide radical scavenging activity, IC_{50}: 1.681 mg/ml; ABTS radical scavenging activity, IC_{50}: 0.816	water-soluble galactoglucan	Maity et al., 2021

	mg/ml		
Pleurotus ostreatus	DPPH radical-scavenging activity, IC_{50}: 0.321 mg/ml	β-D-Glucan Lectin, glycoproteins, homogentisic acid, β-Glucans, gallic acid, naringin, tocopherols, myricetin,	Bakir et al., 2018
Schizophyllum commune	DPPH radical-scavenging activity: 58.15 ± 0.86 %	α- and β-Glucans, phenolic compounds	Basso et al., 2020
Trametes versicolor	DPPH radical-scavenging activity, IC_{50}: 0.04±0.00 mg/ml; Chelating Fe^{3+} ions, IC_{50}: 2.26±0.02 mg/ml; Reduction of Fe^{3+} ions, IC_{50}: 0.30 ± 0.05 mg/ml	Aqueous extract	Stojanova et al., 2021

2.3. Hepatoprotective

By minimising exposure to chemical pollution such as medications during disease, the liver plays a crucial role in the detoxification and metabolism of such hazardous substances (Chaturvedi et al., 2018). By disrupting the pro-oxidant and antioxidant equilibrium, ionising radiations, oxidising chemicals and mutagens cause liver damage. As a result, alternative medications for the treatment of liver illnesses are required. In this regard, the preventive benefits of various fungal metabolites against hepatic inflammation have been examined (Kothari et al., 2018). Secondary metabolites of mushrooms, like steroids, terpenes, phenolics and key cell wall components, have anti-hepatic properties (Chaturvedi et al., 2018).

In a rat model of CCl_4-induced acute liver injury, polysaccharides from *Flammulina velutipes* displayed hepatoprotective effects (Zhang et al., 2018a). In one more study, alkali soluble and water soluble polysaccharides extracted from *Russula vinosa* have been investigated for hepatoprotective potential on CCl_4-persuaded acute liver grievance of mice (Liu et al., 2014). In hyperlipidemic mice, Xu and colleagues found that zinc polysaccharides derived from mycelial of *Pleurotus eryngii* var. *tuoliensis* through enzymatic method had hepatoprotective properties (Xu et al., 2017). Liu et al., (2017) isolated alkali soluble and water-soluble polysaccharides from *Oudemansiella radicata*, application of which was led to decrease level of aspartate aminotransferase and serum alanine aminotransferase and increase level of glutathione peroxidase and hepatic superoxide dismutase. The hepatoprotective activity was reported in hypercholesterolemic rats using the compounds extracted from *Lentinus edodes* (Nisar et al., 2017).

Antrodin A, a compound produced from *Antrodia camphorata*, has been found to improve the anti-inflammatory properties of the liver (Yi et al., 2020). According to the study of Wang et al., (2019), the hepatoprotective properties were observed in alcohol-persuaded liver injured mice using the treatment with peptide-polysaccharides extracted from *Trametes versicolor* having the dose of 80 and 160 mg/kg/day. Two novel fungal immunomodulatory proteins extracted from *Lentinus tigrinus* have been shown to protect the liver from necrosis by lowering the concentration of serum aminotransferases and thereby improving the liver histology (Gao et al., 2019).

2.4. Anti-cancer

Cancer is the leading cause of mortality in the world, and its prevalence is increasing in lockstep with other pollutions. After the harmful side effects and pharmaceutical tolerance, natural anticancer therapies are being sought. Multiple assays like MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide), BrdU, 5-bromo-2'-deoxyuridine, and LDH, lactate dehydrogenase and various techniques like Western blotting, PCR and flow cytometry have been utilized to evaluate the anticancer effectiveness of macro-fungi in clinical trials. Modern approaches for cancer treatment involving fungal products are being investigated, for example, DNA vaccinotherapy inclusive of mushroom immunomodulatory adjuvants, the development of nanovectors, the development of prodrugs with lectins derived from mushroom which are able to recognize glycoconjugates on the cancerous cell surface and so on (Kothari et al., 2018). Because the considerable anticancer effects of numerous extracts and constituents derived from macro-fungi were reported in cancerous cell line assays and animal models (**Table 2.2**), the search for new antitumor constituents from macro-fungi and assessment for their medicinal efficacy is becoming a legitimate research topic (Yadav and Negi, 2021).

Table 2.2: Anticancer potential of extracts or compounds from different macro-fungi

Fungi	Extract/Compound	Type of cancer	Cell line studied	Reference
Taiwanofungus camphoratus	Mycelia broth	Adenocarcinoma	A549	Wang et al., 2017b
Termitomyces clypeatus	Water-soluble extract	Astrocytoma	U373MG	Mondal et al., 2016
Phellinus linteus	Ethanol extract	Bladder cancer	T24	Konno et al., 2015
Cordyceps militaris	Cordycepin-rich ethanol extract	Breast cancer	MCF-7 and MDA-MB-231	Wu et al., 2019
Fomes fomentarius	Ethanol extract	Breast cancer	MDA-MB-231	Lee et al., 2019
Ganoderma lucidum	Spore oil	Breast cancer	MDA-MB-231	Jiao et al., 2020
Innotus obliquus	Hot water extracts	Breast cancer	DMBA	Fang et al., 2020
Marasmius oreades	Ethanol extract	Breast cancer	MCF-7 and MDA-MB-231	Shomali et al., 2019
Phellinus igniarius	Ethanol extract	Breast cancer	MCF-7	Wang et al., 2017
Pleurotus ostreatus	Methanol extract	Breast cancer	MCF-7	Khan et al., 2016
Xylaria Hill	Hexane, ethyl acetate, and methanol extracts	Breast cancer	MDA-MB-231 and MCF-7	Ramesh et al., 2015
Auricularia auricula-judae	Dichloromethane extract	Bronchoalveolar	NCI H358	Reza et al., 2014
Lentinula edodes	Hot water extract	Carcinoma	CT26	Ishikawa et al., 2016
Hexagonia glabra	Ethanol, ethyl acetate, and water extracts	Cervical cancer	HeLa, SiHa and CaSki	Ghosh et al., 2020
Lentinellus Cochleatus, Kuehneromyces Mutabilis, Lactarius quietus	Water and organic extracts	Cervix cancer	HeLa	Vanyolos et al., 2015
Innotus obliquus	Ethanol extract, Water extracts	Colon cancer	HT-29, HCT-116	Lee et al., 2015; Tsai et al., 2017
Marasmius oreades	Ethanol extract	Colon cancer	HT-29	Shomali et al., 2019
Trametes versicolor	Ethanol extract	Colon cancer	LS174	Knežević et al., 2018
Ganoderma applanatum	80% methanol extract	Colorectal cancer	Caco-2	Elkhateeb et al., 2018
Pleurotus sajor-caju	N-hexane extract	Colorectal cancer	HCT116	Finimundy et al., 2018
Ganoderma tsugae	Ethanol extract	Endometrial cancer	AN3 CA, HEC-1-A and KLE	Tsai et al., 2021
Pleurotus eryngii var. ferulae	Ethanol extract	Esophageal cancer	Eca-109	Yang et al., 2018

Phellinus igniarius	Ethanol extract	Gastric cancer	MGC-803	Wang et al., 2017
Ganoderma lucidum	Methanol extract	Gastric cancer	AGS	Reis et al., 2015
Coprinus comatus	Water and ethanol extracts	Glioblastoma	U87MG and LN-18	Nowakowski et al., 2021
Inonotus baumii	Ethanol extract	Hepatocarcinoma	SMMC-772	Yang et al., 2019b
Pleurotus eryngii var. ferulae	Ethanol extract	Hepatocarcinoma	H22 and HepG2	Yang et al., 2019b
Pleurotus ostreatus	Extract	Leukemia	Jurkat and KG-1	Ebrahimi et al., 2018
Macrolepiota procera	Mycelial extract	Lung cancer	A549	Seçme et al., 2018
Agaricus lanipes	Methanol extract	Lung cancer	A549	Kaygusuz et al., 2017
Calvatia gigantea	Methanol extract	Lung cancer	A549	Eroğlu et al., 2016
Trametes gibbosa, Trametes hirsuta, Trametes versicolor	Ethanol extract	Lung cancer	A549	Knežević et al., 2018
Xylaria Hill	Hexane, ethyl acetate, and methanol extracts	Lung cancer	A549	Ramesh et al., 2015
Hypsizygus ulmarius	Ethanol extracts	Lymphoma	DLA	Greeshma et al., 2016
Antrodia cinnamonea	Ethanol extract	Melanoma	B16-F0	Wang et al., 2017a
Agaricus brasiliensis	ethanol and water extracts	Oral cancer	CAL 27	Fan et al., 2011
Antrodia salmonea	Fermented culture broth	Ovarian cancer	SKOV-3 and A2780	Yang et al., 2019
Calocybe indica	Ethanol extract	Pancreatic cancer	PANC-1 and MIAPaCa2	Ghosh and Sanyal, 2020
Agaricus bisporus	Ethanol extract	Prostate cancer	PC3	French et al., 2019
Fomitopsis pinicola	Ethanol extract	Prostate cancer	PCa	Kao et al., 2020
Termitomyces clypeatus	Water-soluble extract	Retinoblastoma	Y-79	Mondal et al., 2016
Agaricus brasiliensis	Mycelia extract obtained from solid state fermentation	Sarcoma	S180	Rubel et al., 2018

2.5. Immunomodulators

Immunomodulators are crucial elements in modern health-care systems, and function in conjugation with the immune system as the main barrier against the primary infection. They are commonly classified as immune stimulants, immunological suppressants or immune adjuvants in clinical practise. Because immunomodulators of macro-fungi stimulate both the innate and adaptive immune systems, immunomodulation is the most important therapeutic feature utilised for macro-fungi globally. The components extracted from macro-fungi increase the expression and excretion of cytokines by proliferating and stimulating the components of innate immune system like macrophages, natural killer (NK) cells and neutrophils. These cytokines boost adaptive immunity by activating the β-cells for excretion and stimulation of antibodies and differentiation of T cell as well (Yadav and Negi, 2021). The four key types of immune modulators identified from macro-fungi that was reported to efficiently suppress the production of cytokine, are lectins, polysaccharides, terpenes, terpenoids, and fungal proteins (Zhao et al., 2020).

Various compounds extracted from macro-fungi act as potent immunomodulators and immunotherapeutic in numerous research studies. Some of these macro-fungi and their important compounds include: *Ganoderma annulare* (Applanoxidic acid A); *Ganoderma lucidum* (ganoderic acids, ganodermanontriol, ganoderiol F, ganopoly and ganosporeric acid A); *Ganoderma pfeifferi* (applanoxidic acid G, ganodermadiol and lucidadiol); *Grifola frondosa* (ergosterol); *Hericium coralloides* (Erinacin E); *Inonotus hispidus* (Hispidin and hispolon); *Laricifomes officinalis* (Dehydrotrametenolic acid); *Lentinula edodes* (eritadenine); *Lenzites betulina* (Betulinan A); *Schizophyllum commune* (Schizophyllan); *Wolfiporia cocos*

(Dehydrotrametenolic acid) and *Trametes versicolor* (Coriolan) (Arunachalam et al., 2022).

Two lectins i.e. TML-1 and TML-2 derived from *Tricholoma mongolicum*, have been shown to have immunomodulating potential by enhancing macrophage- activating factors and thereby inhibit the propagation of mouse lymphoblast cells by elevating tumor necrosis factor (TNF- α) and nitrite (Zhao et al., 2020). High amounts of triterpenoids like lanostane, which has anti-infective and immunomodulating properties, are found in *Ganoderama applanatum* and *Ganoderma lucidum* (Chakraborty et al., 2019). *Lentinula edodes* has been shown to promote non-specific cytotoxicity and increase cytokine production in macrophages (Morales et al., 2020).

2.6. Antidiabetic

Diabetes mellitus, a metabolic disorder originated due to high level of blood glucose, affects millions of people. It can lead to life-threatening consequences, organ failure, and fatality if not adequately controlled. Diabetes can be prevented and managed, according to research, by living a healthy lifestyle that includes nutrition and exercise. Although there are a number of synthetic medications available to treat this problem, long-term use is linked to a slew of negative side effects. As a result, research has switched to medicinal plants and herbs, which are regarded to be quite harmless (Khursheed et al., 2020). Consumption of mushroom reduced triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) whereas increased the high-density lipoprotein cholesterol (HDL-C). Mushrooms also have a lot of fibre and water. They are high in natural insulin-like enzymes, which aid in the breakdown of glucose in foods while also lowering insulin resistance (IR). Most medicinal mushrooms like *Sparassis crispa*, *Poria cocos*, *Pleurotus* sp., *Phellinus linteus*, *Inonotus obliquus* and *Ganoderma lucidum* have demonstrated to be effective in curing the diabetes mellitus (De Silva et al., 2012). Polysaccharide derived from macro-fungi was found to dramatically lower the concentration of blood glucose and enhance the metabolism of lipid in diabetic mice. Furthermore, the pancreatic islets were prevented from damage (Yang et al., 2019a). Supplementing *Agaricus blazei* extract along with metformin and gliclazide for 12 weeks improved insulin resistance (IR) in patients having type 2 diabetes mellitus (Hsu et al., 2007). Antidiabetic potential reported from various macro-fungi has been shown in **Table 2.3**.

Table 2.3: Antidiabetic potential of different macro-fungi

Fungi	Blood glucose level before mg/dl	Blood glucose level after mg/dl	Reference
Pleurotus pulmonarius	163.11	116.54	Balaji et al., 2020
Coprinus comatus	331.25	274.75	Ratnaningtyas et al., 2019
Agaricus bisporus	230	130	Ekowati et al., 2018
Auricularia auricular	540	216	Hu et al., 2017
Calvatia gigantea	280	160	Ogbole et al., 2019
Tuber melanosporum	220	140	Zhang et al., 2018
Grifola frondosa	268.2	189	Kou et al., 2019

2.7. Cardiovascular diseases

The presence of low levels of HDL (high-density lipoprotein) and high levels of LDL (low-density lipoprotein) is associated with cardiovascular disease, raising the ratio of total to HDL cholesterol, which is the primary cause of cardiovascular disease (Chaturvedi et al., 2018). Medicinal mushrooms *Pleurotus eryngii*, *Hypsizygus marmoreus* and *Grifola frondosa* have been utilised as biological markers for atherosclerosis-prone C57BL/6J mice, which lower the concentration of total cholesterol in the human body (Fombang et al., 2016). The extract of *Tricholoma matsutake* and *Agaricus bisporus* contains inhibitory peptides which block the activity of enzyme angiotensin responsible for cardiovascular illness and hypertension (Geng et al., 2016; Lau et al., 2014). By preventing platelet aggregation, the ethanolic extract of *Hericium erinaceus* boosts the metabolism of lipid. It also serves as a therapeutic agent for a variety of vascular disorders and aids in the reduction of TGA and LDL levels while increasing HDL levels, resulting in a hypocholesterolemic effect (Khan et al., 2013; Koh et al., 2003).

2.8. Antimicrobial

Macro-fungi produce several anti-fungal and antibacterial agents for their survival in nature (Waithaka et al., 2021). These natural antimicrobials are becoming more relevant as an alternative to synthetic additives whose health consequences are still contested (Olatunde and Benjakul, 2018). Various macro-fungi were reported as potent antimicrobial against *Mycobacterium tuberculosis*, and a reduction in the quantity of *M. tuberculosis* bacteria by fungal extract offers a novel approach in the treatment of tuberculosis, instead of using available commercial cytotoxic drugs (Patel et al., 2021). The antimicrobial potential of different macro-fungi has been shown in **Table 2.4**.

Table 2.4: Antimicrobial potential of different macro-fungi

Fungi	Crude extract/ fraction	Antimicrobial activity	Reference
Agaricus bisporus	Methanolic extract	Antifungal activity against *Candida* sp.	Jose Alves et al., 2013
Auricularia auricula-judae	Crude polysaccharides	Antibacterial against the food-borne *Staphylococcus aureus* and *Escherichia coli*	Cai et al., 2015
Craterellus cornucopioides	Acetone extract	Antibacterial activity against *E. coli*, *Proteus mirabilis*, *Bacillus cereus*, *B. subtilis*, and *S. aureus*	Kosanić et al., 2019
Gandoderma lucidum	Sulfated polysaccharide	Antibacterial activity against *E. coli*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Salmonella*, *Listeria monocytogenes*, *Shigella sonnei*, *S. aureus* and *S. epidermidis*,	Wan-Mohtar et al., 2016
Lactarius deliciosus	Hydroalcoholic extract	Antifungal activity against *Monilinia fructicola*	Volcão et al., 2022
Lentinula edodes	Aqueous extract	Antibacterial activity against *Klebsiella pneumonia*, *S. aureus*	Garcia et al., 2021
Leucoagaricus leucothites	Ethanol extract	Antibacterial activity against *E. coli*, *P. aeruginosa*, *Enterococcus faecalis* and *S. aureus*	Sevindik et al., 2018
Pleurotus ostreatus var. florida, P. ostreatus, P. salmoneostramineus and P. cornucopiae var. citrinopileatus	Aqueous extract	Antifungal activity against *Trichoderma harzianum*, *Pythium* sp. and *Verticillium* sp.	Owaid et al., 2017

2.9. Anti-viral

The CCK-8 and TZM-bl pseudovirus tests were used to explore the in vitro cytotoxicity and antagonistic to HIV-1 activities of aqueous extract from *Cordyceps sinensis* (Zhu et al., 2016). The in vitro antagonistic to dengue infection serotype 2

(DENV-2) tests used various macro-fungi like *Cordyceps sinensis*, *Schizophyllum commune, Ganoderma lucidium, Pleurotus giganteus, Hericium erinaceus* and *Lignosus rhinocerotis* (Ellan et al., 2019). The polysaccharides extracted from *Inonotus obliquus* exhibited anti-Feline calicivirus activity. By blocking viral binding and absorption, it initiates its inhibitory activities directly on infectious particles. (Tian et al., 2017). In comparison to the benchmark inhibitor 1,8- Dihydroxy-4,5-dinitroanthraquinone, *In-silico* examination of 4-triterpenoids from *Ganoderma lucidum*, namely Ganoderic acid C2, Ganodermanontriol, Ganosporeric acid A and Lucidumol A revealed viral protease inhibitory activities suggested that *G. lucidum* could be useful in the designing of new drugs to cure DENV-associated disorders (Bharadwaj et al., 2019). In vitro tests revealed that polysaccharide extracted from *Gandoderma frondosa* inhibited enterovirus 71 which is the root cause of foot, hand and mouth infection; induced apoptosis and smothered viral protein articulation (Zhao et al., 2016). *Hericium erinaceus* has been shown to have antiviral properties by restoring mucosal resistance in Muscovy duck reovirus-damaged ducklings (Wu et al., 2018). Moreover, plaque reduction studies revealed suppression of adherence/invasion and reduction in viral outflow articulation as well, indicating that *H. erinaceus* was able to nutralise Dengue virus infection in vitro (Ellan et al., 2019). Polysaccharide components of ethanol and water extracts of *Pleurotus pulmonarius* exhibited antiviral action against influenza A virus (VA et al., 2020). A varied range of macro-fungi have been shown antiviral actions against numerous viruses as shown in **Table 2.5**.

Table 2.5: Antiviral activities of various macro-fungi

Fungi	Compound/Extract	Antiviral activity against	Reference
Agaricus brasiliensis	Sulfated polysaccharides	Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2)	de Sousa Cardozo et al., 2014
Agaricus bisporus	Tyrosinases - protein	Hepatitis C virus	Lopez-Tejedor et al., 2021
Ganoderma lucidum	Proteoglycan	HSV-1 and HSV-2	Liu et al., 2004
Inonotus obliquus	polysaccharides	Human immunodeficiency virus type 1 (HIV-1), hepatitis C virus, HSV	Pan et al., 2013; Shibnev et al., 2015; Tian et al., 2017
Lentinula edodes	Culture extract polysaccharide	anti-influenza virus activity, Poliovirus type 1 and bovine herpes virus type 1	Kuroki et al., 2018; Rincão et al., 2012
Lentinus edodes	lentinan	IHNV infection	Ren et al., 2018
Phellinus baumii	Polyphenols (hispidin, hypholomine B, inoscavin A, davallialactone and phelligridin D)	Influenza A virus (H1N1, H5N1, and H3N2)	Hwang et al., 2015

2.10. Anti-Covid

Coronaviruses (CoVs) are single-stranded, positive-sense, enveloped, un-segmented, RNA viruses of the family Coronaviridae belonging to the order Nidovirales (Cui et al., 2019). In December 2019, several unusual pneumonia cases were documented in Wuhan city of China. These cases arose due to a new Severe Acute Respiratory Syndrome (SARS)-CoV-2, and are now called as Covid-19 infection (Benvenuto et al., 2020; Wu et al., 2020). Person affected with CoVs shows symptoms like temperature, common cold and cough, nasal congestion, sore throat, headache, muscle pain and severe acute respiratory failure. The World Health Organization (WHO) in March 2020 declared that the SARS-CoV-2 eruption as a “pandemic” because it has spread afterward throughout China and the whole world and caused nearly 3% mortality rate (Zhang et al., 2020).

Various studies on the immune-enhancing potential of a variety of therapeutic mushrooms may have examined at COVID-19 treatment (Rangsinth et al., 2021). Basidiomycetes macro-fungi may be helpful as therapeutic or preventative add-on therapies for the infection of COVID-19, for the detrimental inflammation and immunological reaction linked with COVID-19 as well (Hetland et al., 2021). Rangsinth et al., (2021) discovered six low-toxic/nontoxic compounds in mushrooms inhibited the SARS-CoV-2 protease. Similarly, Chaga mushrooms, which have a powerful enzymatic and defensive system due to their parasitic lifestyle, showed promising results in reducing COVID-19-related inflammatory reactions (Shahzad et al., 2020). A combination of two mushrooms i.e. *Fomitopsis officinalis* and *Trametes versicolor* have physiologically coherent immuno-modulating properties against SARS-CoV-2 (Arunachalam et al., 2022). The medicinal mushrooms, *Agaricus blazei*, *Grifola frondosa*, *Hericium erinaceus* and *Hericium erinaceus* may have importance as therapeutic and prophylactic add-on therapies during the infection of COVID-19. They can be used particularly as antidotes to pneumococcal super-infection, especially when instigated by multi-resistant bacteria, and to the immunological overreaction and inflammatory damage associated with COVID-19 infection (Shahzad et al., 2020; Hetland et al., 2021).

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