

Emerging Insights into the Medicinal Properties of *Lentinula edodes*: Bioactive Compounds and Mechanisms

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Abstract:

Lentinula edodes (shiitake mushroom) is a widely consumed edible and medicinal fungus known for its diverse pharmacological properties. It contains a rich array of bioactive compounds, including polysaccharides (notably lentinan), phenolic compounds, sterols, terpenoids, and proteins. These compounds exhibit significant biological activities such as immunomodulatory, anticancer, antioxidant, anti-inflammatory, antimicrobial, and metabolic regulatory effects. Recent advances have elucidated molecular mechanisms underlying these effects, including modulation of immune receptors, apoptosis pathways, oxidative stress signaling, and gene–protein interaction networks. This review comprehensively summarizes the bioactive compounds of *L. edodes*, their mechanisms of action, pharmacological properties, and future therapeutic potential. Emphasis is placed on recent research developments and emerging applications in nutraceuticals and drug discovery.

Keywords: *Lentinula edodes*, lentinan, β -glucans, medicinal mushrooms, immunomodulation, anticancer, bioactive compounds

1. Introduction:

Medicinal mushrooms have long been integral to traditional medicine, particularly in East Asia. Among these, *Lentinula edodes* has gained global recognition due to its dual role as a functional food and therapeutic agent. It is the second most widely cultivated edible mushroom worldwide and is rich in nutrients and pharmacologically active compounds (Lindequist, 2024). *Lentinula edodes* (Shiitake mushrooms) is one of the most cultivated edible mushrooms (Liu et al. 2020). *L. edodes*, also known as flower mushroom, Shiitake, winter mushroom, golden oak mushroom, emperor mushroom, and Chinese black mushroom has been cultivated for thousands of years (Ponnusamy et al. 2022). Bioactive polysaccharides obtained from *L. edodes* have shown an important role as free radical scavengers in the prevention of oxidative damage and can be explored as for its new potential as a natural antioxidant (Muñoz-Castiblanco et al. 2022). Modern scientific investigations have validated many traditional claims, revealing that *L. edodes* contains bioactive molecules capable of modulating immune responses, inhibiting tumor growth, and reducing oxidative stress. With increasing interest in natural therapeutics, this mushroom has emerged as a promising candidate for drug development and nutraceutical applications. *L. edodes* contains about 68-78% of carbohydrates (mono-, di-, tri-, and polysaccharides), exogenous amino acids (including arginine, histidine, leucine, isoleucine, lysine, methionine,

phenylalanine, threonine, valine, and tryptophan), lipids (5-8% of dry matter), vitamins (including B1, B2, B12, C, D, E), minerals (including Ca, K, Mg, Mn, P, Zn, and Na), fiber, and numerous substances with antibacterial, antiviral, and antifungal properties (Bisen et al. 2010; Finimundy et al. 2014; Roszczyk et al. 2022).

A large number of pharmacological and clinical studies have shown that lentinan that one of the active shiitake mushroom extracts, has antioxidant, immunomodulatory, anti-tumor, anti-cancer, hypoglycemic, hypolipidemic and other biological activities (Maeda and Chihara 1971; Suzuki et al. 1994; Meng et al. 2020, Sheng et al. 2021; Zohu et al. 2024). This review summarizes the major bioactive constituents of *L. edodes*, their mechanisms of action, and their therapeutic potential. Emphasis is placed on recent advances in molecular mechanisms, including immune signaling pathways, oxidative stress modulation, and network pharmacology.

Compounds of *Lentinula edodes*:

L. edodes is reportedly contained several classes of bioactive compounds, such as carbohydrates, proteins, fiber, lipids, and ash, vitamins, folates, niacin, and minerals, making it a high protein and low-fat food (Sheng et al. 2021). Over the last two decades, increasing scientific attention has been directed toward the nutritional significance and pharmacological potential of *L. edodes* (shiitake mushroom). Among its diverse bioactive constituents like polysaccharides, polysaccharopeptides, lectins, and other secondary molecules, with polysaccharides, particularly β -glucans, are considered to be the major functional components responsible for several of its health-promoting properties (Gaitán-Hernández et al., 2019). Polysaccharides have been isolated and characterized from different biological sources of *L. edodes*, including the fruiting bodies, mycelium, and submerged-fermentation cultures. Fruiting bodies have been investigated as an important source of bioactive polysaccharide fractions, whereas mycelial cultures and fermentation systems have been explored for the production of intracellular and extracellular polysaccharides (Gregori et al., 2012; Feng et al., 2010; Li et al., 2018). The biological effects of *L. edodes* polysaccharides are closely associated with their physicochemical and structural characteristics. Parameters such as molecular weight, monosaccharide composition, degree of branching, glycosidic linkage pattern, and three-dimensional conformation can substantially influence their biological activities. Reported activities include antioxidant, antitumor, anti-inflammatory, anti-aging, immunomodulatory, and antiviral effects, although the magnitude and mechanism of these activities may vary according to the structural characteristics of individual polysaccharide fractions (Sheng et al., 2021). One of the best-characterized polysaccharides of *L. edodes* is lentinan, a high-molecular-weight β -(1 $\rightarrow$ 3)-D-glucan containing β -(1 $\rightarrow$ 6)-linked glucopyranosyl branches. Lentinan has attracted considerable interest because of its host-mediated immunomodulatory and antitumor effects. Its biological activity has been associated with its characteristic β -glucan structure and its ability to modulate immune responses (Zhang et al., 2011). Because of their diverse biological properties, *L. edodes* polysaccharides have considerable potential for applications in pharmaceutical and nutraceutical products, functional foods, dietary supplements, and as bioactive or antimicrobial ingredients. Their therapeutic and functional-food applications have therefore become an important area of research, with ongoing studies focusing on extraction, purification, structural characterization, structure activity relationships, and mechanisms of action (Roszczyk et al., 2022).

Table-1: Main Compounds found in *L. edodes* (Heleno et al. 2012; Reis et al. 2012; Chandra et al. 2011)

Fatty Acids	Free Sugars	Polysaccharides	Amino Acids	
Linoleic	Arabinose	Heteroglycans	Glutamate	Leucine
Palmitic	Glycerol	Heterogalactans	Threonine	Valine
Oleic	Arabinol	Heteromannans	Arginine	Alanine
Stearic	Mannose	Heteroglycans	Cystine	Glycine
Myristic	Mannitol	Xyloglucans	Histidine	Lysine
Arachidic	Glucose	Polyuronide	Aspartate	Serine
Linolenic	Fructose	α -glucan	Isoleucine	Proline
Tetradecenoic	Trehalose	Chitin	Phenylalanine	Tyrosine

Major bioactive compounds of *L. edodes*:

Over the past two decades, extensive research has established *Lentinula edodes* (shiitake mushroom) as an important source of nutritionally and pharmacologically valuable bioactive compounds. Its biological properties are attributed to a diverse range of constituents, including polysaccharides, β -glucans, eritadenine, phenolic compounds, sulfur-containing metabolites, sterols, terpenoid-related compounds, ergothioneine, proteins, peptides, and lectins (Gaitán-Hernández et al., 2019; Fukushima-Sakuno, 2020; Sheng et al., 2021). Recent reviews further emphasize that the biological effects of *L. edodes* may arise from interactions among multiple classes of compounds rather than from a single constituent alone (Makkar et al., 2026).

Polysaccharides and β -glucans:

Polysaccharides represent one of the most extensively studied groups of bioactive constituents in *L. edodes*. They have been isolated from fruiting bodies, mycelial biomass, and submerged fermentation cultures, and considerable attention has been devoted to their extraction, purification, structural characterization, and biological activities (Feng et al., 2010; Gregori et al., 2012). *L. edodes* polysaccharides are predominantly β -glucans, although heteropolysaccharides and other carbohydrate fractions have also been reported. Their biological activities are strongly influenced by physicochemical and structural characteristics, including molecular weight, monosaccharide composition, degree of branching, glycosidic linkage, and higher-order conformation. Several biological activities have been reported for *L. edodes* polysaccharides, including antioxidant, antitumor, anti-inflammatory, immunomodulatory, antiviral, anti-aging, and hepatoprotective effects (Sheng et al., 2021). In particular, β -(1 $\rightarrow$ 3)-glucans containing β -(1 $\rightarrow$ 6)-linked side chains have been associated with important immunomodulatory effects. Recent research has further highlighted the role of mushroom β -glucans in regulating inflammatory and immune responses through interactions with specific immune-cell receptors and downstream signaling pathways (Mizuno and Minato, 2024).

Lentinan:

Among the polysaccharides of *L. edodes*, lentinan is one of the most extensively investigated. It is a high-molecular-weight β -(1 $\rightarrow$ 3)-D-glucan possessing β -(1 $\rightarrow$ 6)-linked glucosyl branches. Its structural characteristics are considered important determinants of its biological activity, particularly its

immunomodulatory and host-mediated antitumor effects (Zhang et al., 2011). Recent studies continue to investigate improved extraction and purification technologies for lentinan, including ultrasound-assisted and other advanced extraction approaches, with the objective of increasing yield while preserving its structural and biological properties (Sheng et al., 2021).

1. **Eritadenine:** **Eritadenine**, also known as lentinacin, is an important low-molecular-weight bioactive compound characteristic of *L. edodes*. It has attracted considerable interest because of its reported effects on lipid metabolism, particularly its hypocholesterolemic potential. Studies have investigated the occurrence of eritadenine in shiitake, as well as the influence of cooking, processing, digestion, and extraction conditions on its availability (Morales et al., 2018). The compound is therefore of particular interest in the development of functional foods and nutraceutical preparations based on *L. edodes*.
2. **Phenolic compounds:** Phenolic compounds constitute another group of secondary metabolites contributing to the antioxidant properties of *L. edodes*. Various phenolic and aromatic compounds have been detected in shiitake extracts, and their contribution to antioxidant activity has been investigated along with polysaccharides and other constituents. The overall antioxidant capacity of *L. edodes* is therefore likely to result from the combined contribution of phenolic compounds, polysaccharides, ergothioneine, and other reducing or radical-scavenging molecules (Sheng et al., 2021; Fukushima-Sakuno, 2020).
3. **Sulfur-containing compounds:** Sulfur-containing metabolites are particularly characteristic of *L. edodes* and contribute substantially to its distinctive aroma and flavor. **Lenthionine** is one of the best-known sulfur-containing compounds associated with shiitake. In addition to their sensory significance, several sulfur-containing compounds and polyacetylenes isolated from *L. edodes* have demonstrated antimicrobial activity, making this group relevant to the pharmacological potential of the mushroom (Fukushima-Sakuno, 2020).
4. **Sterols:** *L. edodes* also contains biologically important sterols, particularly **ergosterol**, which is a major fungal sterol. Ergosterol is nutritionally relevant because it can serve as a precursor of vitamin D₂ following exposure to ultraviolet radiation. Sterols, together with polysaccharides and other low-molecular-weight compounds, contribute to the nutritional and functional-food value of shiitake (Gaitán-Hernández et al., 2019).
5. **Ergothioneine:** Ergothioneine is a sulfur-containing amino-acid derivative that has attracted increasing attention because of its antioxidant and nutritional properties. It is naturally present in edible mushrooms and has been identified as one of the potentially important health-promoting constituents of *L. edodes*. Recent research has considered ergothioneine together with eritadenine and polysaccharides as part of the complex bioactive matrix of shiitake (Makkar et al., 2026).
6. **Proteins, peptides and lectins:** In addition to carbohydrate and low-molecular-weight metabolites, *L. edodes* contains biologically active proteins and peptides, including lectin-like proteins. These compounds have been investigated for their potential immunomodulatory, antimicrobial and other pharmacological activities. Consequently, proteins and peptides should also be considered when evaluating the overall medicinal potential of *L. edodes* rather than focusing exclusively on polysaccharides (Gaitán-Hernández et al., 2019; Sheng et al., 2021).

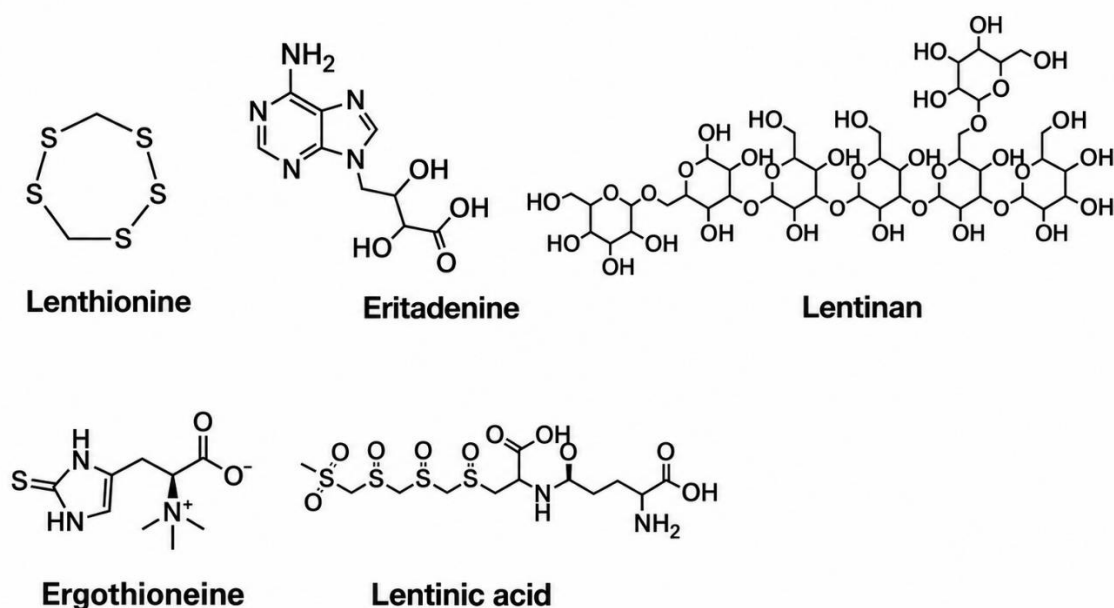


Fig.1: Some prominent bioactive molecules found in the mycelium of the *L. edodes* (Baral, 2025)

Pharmacological Activities of Bioactive Compounds of *L. edodes*:

L. edodes contains a complex mixture of high- and low-molecular-weight bioactive constituents, including β -glucans and other polysaccharides, lentinan, proteins and peptides, eritadenine, ergothioneine, phenolic compounds, sulfur-containing metabolites, polyacetylenes, sterols, terpenoids and other secondary metabolites. Current evidence indicates that the biological effects of *L. edodes* are likely to result from the combined action of these constituents rather than from a single compound. A recent comprehensive review specifically emphasizes the importance of considering *L. edodes* as a multicomponent food matrix in which polysaccharides, phenolics, terpenoids, eritadenine, ergothioneine and peptides may interact with the gut microbiota and host metabolism (Makkar et al., 2026).

1. Antitumor and anticancer activity: The **antitumor activity** of *L. edodes* has been studied particularly extensively in relation to polysaccharides and β -glucans. Among these, lentinan, a high-molecular-weight β -(1 $\rightarrow$ 3)-D-glucan with β -(1 $\rightarrow$ 6)-linked branches, is one of the best-characterized bioactive constituents. Its anticancer effects are generally considered to involve host-mediated immunomodulation, rather than simple direct cytotoxicity. β -glucans can interact with pattern-recognition receptors on immune cells and influence macrophages, dendritic cells, natural killer cells and T lymphocytes (Roszczyk et al., 2022). Recent experimental work has provided additional evidence for the direct anticancer effects of lentinan. Park et al. (2024) investigated lentinan against gastric and colon cancer cell lines and reported inhibition of cell proliferation, migration, colony formation and wound-healing capacity. The treatment was associated with G2/M cell-cycle arrest, increased reactive oxygen species (ROS), increased phospho-p38 and decreased ERK1/2 signaling, indicating involvement of stress- and apoptosis-related pathways. The immunological mechanism has also been demonstrated using *L. edodes* mycelial extract. Kajiyama et al. (2023) reported that the extract increased MHC-I, MHC-II, CD80, CD86 and CD40 expression in dendritic cells and enhanced IL-12 production. These activated dendritic cells promoted IFN- γ production by CD8⁺ T

cells and their differentiation into effector cells. In a melanoma-bearing mouse model, the extract prevented tumor-associated deterioration of antigen-presenting-cell function. Increased granzyme-B and Ki-67 expression in tumor-infiltrating CD8⁺ T cells were observed, and changes in gut microbial composition were also reported. The study further indicated that antibiotic treatment abolished the additional antitumor effect, suggesting a role for the gut microbiome in this response. Thus, the anticancer potential of *L. edodes* involves both direct effects on cancer-cell behavior and indirect enhancement of host antitumor immunity. However, evidence from cell and animal models should not be interpreted as proof of clinical efficacy in humans.

2. **Immunomodulatory activity:** Immunomodulation is one of the most extensively documented pharmacological properties of *L. edodes* polysaccharides. β -(1→3)-glucans with β -(1→6) branches are particularly important in this context. Their biological effects are associated with recognition by immune receptors and subsequent activation of signaling cascades involved in innate and adaptive immunity (Mizuno and Minato, 2024). Polysaccharides from *L. edodes* can influence macrophages, dendritic cells, natural killer cells and T lymphocytes. Activation of macrophages may increase the production of cytokines and other mediators, whereas dendritic-cell activation can enhance antigen presentation and subsequent T-cell responses. The precise effect depends on polysaccharide structure, molecular weight, branching degree and extraction procedure (Roszczyk et al., 2022). Kajiyama et al. (2023) demonstrated that *L. edodes* mycelial extract stimulated antigen-presenting cells and increased IL-12 production while suppressing IL-10 and TGF- β production in macrophages. The findings suggest a shift toward a more immunostimulatory/M1-like macrophage phenotype and enhanced cytotoxic T-cell activity. These findings provide a mechanistic basis for the traditional association of shiitake with immune support, although the magnitude and clinical relevance of these effects depend on the preparation, dose and biological context.
3. **Antioxidant activity:** The antioxidant properties of *L. edodes* are associated with several groups of constituents, particularly polysaccharides, phenolic compounds and ergothioneine. Muñoz-Castiblanco et al. (2022) demonstrated concentration-dependent antioxidant activity of crude *L. edodes* polysaccharides against DPPH, ABTS, hydroxyl and superoxide radicals. The polysaccharides also inhibited lipid peroxidation in a methyl-linoleate model. These findings indicate that polysaccharide fractions can act through both direct radical scavenging and inhibition of oxidative lipid damage. Phenolic constituents provide an additional antioxidant component. Ergothioneine, a sulfur-containing amino-acid derivative, is another important antioxidant constituent. Its biological properties include radical scavenging, metal chelation and protection against oxidative damage (Cheah and Hallwell, 2025). Recent research has further linked ergothioneine to regulation of oxidative stress, lipid peroxidation, mitochondrial dysfunction and inflammatory responses. Importantly, an ergothioneine-rich *L. edodes* extract was shown to improve mitochondrial function in senescent HT22 neuronal cells, with evidence suggesting involvement of the Nrf2 signaling pathway. This provides preliminary evidence for a potential neuroprotective role, although further in-vivo and clinical studies are required (Feriani et al., 2020).
4. **Anti-inflammatory activity:** The anti-inflammatory properties of *L. edodes* are particularly associated with β -glucans and other polysaccharide fractions. Mushroom β -glucans can interact with

innate immune receptors and influence inflammatory signaling pathways. Mizuno and Minato (2024) reviewed evidence indicating that β -(1 $\rightarrow$ 3)-glucans with β -(1 $\rightarrow$ 6) branches can modulate immune responses and inflammatory cascades. Experimental studies have provided evidence for suppression of inflammatory mediators. For example, *L. edodes* polysaccharides were investigated in a mouse model of acute lung injury and were associated with reductions in TNF- α , IL-1 β and IL-6, together with increased activities of antioxidant enzymes such as SOD and CAT. These results suggest that the protective activity may involve simultaneous regulation of oxidative stress and inflammation. Lentinan and mycelial extracts may therefore have anti-inflammatory effects through modulation of macrophages, cytokine production and immune-cell signaling (Maity et al., 2013).

5. **Antimicrobial activity:** The antimicrobial properties of *L. edodes* are associated with both high-molecular-weight polysaccharides and low-molecular-weight secondary metabolites. Sulfur-containing compounds are particularly characteristic of shiitake. Lenthionine (1,2,3,5,6-pentathiepane) is a major sulfur-containing compound responsible for the characteristic aroma of the mushroom. Research has demonstrated significant antimicrobial activity of lenthionine, particularly against yeasts and fungi. In one study, lenthionine exhibited MIC values of approximately 2–8 μ g/mL against several fungal/yeast organisms tested (Kupcová et al., 2018). *L. edodes* also produces polyacetylenes, including lentinamycin and related compounds. These metabolites have demonstrated antibacterial and antifungal activities in experimental systems. Recent reviews describe activity against both Gram-positive and Gram-negative bacteria as well as fungi and yeasts. Thus, sulfur-containing compounds and polyacetylenes may contribute to the mushroom's ecological defense against competing microorganisms and potentially provide leads for antimicrobial compound discovery. Antiviral activity has been reported mainly for polysaccharide-rich extracts and other mushroom fractions. An experimental study investigating aqueous extract, ethanol extract and polysaccharide fractions of *L. edodes* against poliovirus type 1 and bovine herpesvirus type 1 found that the tested preparations affected early stages of viral replication. *L. edodes* polysaccharides have consequently identified antiviral activity as one of the major reported biological properties, although the available evidence is predominantly experimental and should not be interpreted as evidence that shiitake preparations are clinically effective antiviral drugs. The antiviral effects of crude aqueous or ethanolic extracts were found in vitro, e.g., against poliovirus type 1 (PV-1), bovine herpes virus type 1 (BoHV-1) (Rincao et al., 2012), herpes simplex virus-2 (HSV-2) (Spim et al. 2021), and SARS CoV-2 (Elhusseiny et al. 2022). The mycelial preparation LEM inhibits influenza virus by interfering with virus entry into the host cells and activation of the immune response through the type I IFN pathway (Kuroki et al., 2018).
6. **Hepatoprotective activity:** Hepatoprotective activity has been reported for *L. edodes* extracts and polysaccharide fractions. Earlier experimental work demonstrated that methanolic *L. edodes* extract reduced biochemical indicators of liver injury in mice exposed to paracetamol-induced hepatotoxicity, including serum transaminases and bilirubin. Song et al. (2021) investigated polysaccharides obtained from an acidic-hydrolysis residue of *L. edodes* in a mouse model of LPS-induced liver injury. The study specifically evaluated both antioxidant and hepatoprotective effects, providing evidence that polysaccharide fractions may contribute to liver protection (Akramiene et al., 2007).

7. **Neuroprotective and anti-aging potential:** The antioxidant and mitochondrial effects of *L. edodes* constituents provide a potential basis for neuroprotective and anti-aging activities. Ergothioneine is particularly interesting because of its ability to accumulate in tissues through the OCTN1 transporter and protect cells from oxidative stress. An ethanolic extract of *L. edodes* and a cosmetic cream formulation incorporated with the extract inhibited the production of the inflammatory mediator nitric oxide (NO) by lipopolysaccharide (LPS)-stimulated macrophages and thus showed anti-inflammatory activity. In addition, both the extracts as the cream exhibited antibacterial effects against *Enterococcus faecalis* and methicillin-sensitive and methicillin-resistant *Staphylococcus aureus* (Taofiq et al., 2016).
8. **Antihypertensive potential:** Eritadenine and other low-molecular-weight constituents have been associated with potential cardiovascular effects. Some reviews report angiotensin-converting enzyme (ACE) inhibitory activity among the bioactivities associated with *L. edodes* constituents. However, this area is considerably less established than the immunomodulatory activity of polysaccharides. Therefore, ACE inhibition should be presented as a reported experimental property, rather than as evidence that *L. edodes* itself is an antihypertensive therapy (Gil-Ramirez et al., 2016; Moroles et al., 2021).
9. **Immunotherapeutic and gut-immune effects:** An emerging area of *L. edodes* research is the interaction between mushroom bioactives, the gut microbiota and host immune system. High-molecular-weight polysaccharides may resist digestion in the upper gastrointestinal tract and subsequently undergo microbial fermentation in the colon. The resulting metabolites and microbial changes may contribute to systemic immunological effects. This concept is particularly important for *L. edodes* because recent research indicates that its biological effects cannot always be explained by direct absorption of individual compounds. Makkar et al. (2026) proposed a diet-microbe-host framework in which β -glucans, heteropolysaccharides, phenolics, terpenoids, eritadenine, ergothioneine and peptides interact within the whole mushroom matrix.

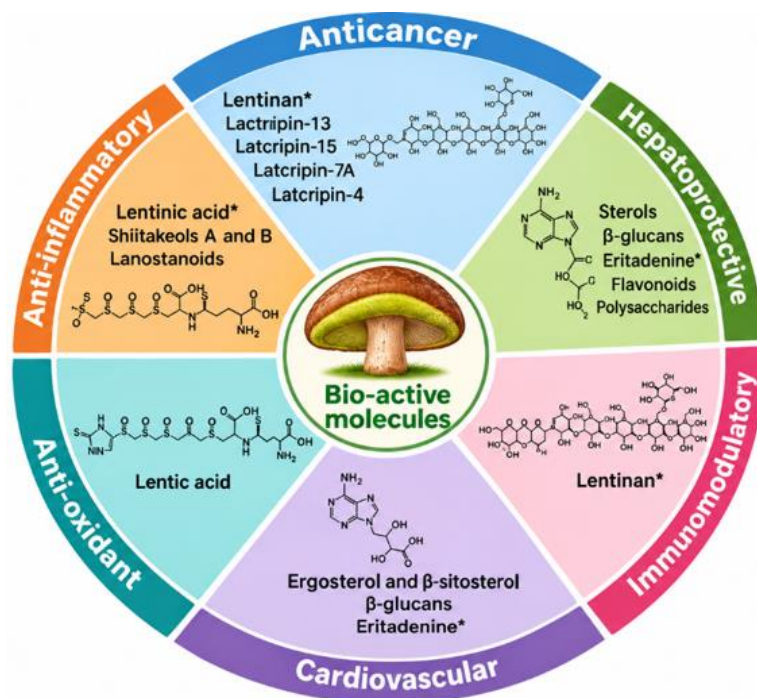


Fig.2: Bioactive compounds and pharmacological activity (Baral, 2025)

Table-2: Summary of pharmacological activities (Roszczyk et al. 2022)

Bioactive component	Major pharmacological activity	Main proposed mechanism/effect	Evidence level
Lentianin	Antitumor, immunomodulatory	β-glucan–immune receptor interaction; cytokine modulation; immune-cell activation	In vitro + animal + clinical background
Other β-glucans	Immunomodulatory, anti-inflammatory	Dectin-1/other PRR signaling; macrophage/DC activation	Mainly experimental
Polysaccharides	Antioxidant	Radical scavenging; inhibition of lipid peroxidation	In vitro
Polysaccharides	Hepatoprotective	Antioxidant and anti-inflammatory effects	Animal
Polysaccharides	Antiviral	Interference with early viral replication	In vitro
Polysaccharides	Antidiabetic potential	α-Amylase inhibition; glucose-utilization pathways	In vitro
Eritadenine	Hypocholesterolemic/lipid-	Modulation of	Experimental

	regulating	cholesterol metabolism	
Ergothioneine	Antioxidant/neuroprotective	ROS protection, metal chelation, Nrf2 and mitochondrial effects	Cellular + biochemical
Phenolic compounds	Antioxidant	Radical scavenging and redox regulation	Chemical/cellular
Lenthionine	Antimicrobial	Inhibition of microbial growth	In vitro
Polyacetylenes	Antibacterial/antifungal	Direct antimicrobial effects	In vitro
Proteins/lectins	Antifungal, cytotoxic, immunomodulatory	Protein-specific molecular interactions	Experimental
Terpenoids/phenolic meroterpenoids	Antioxidant, immunomodulatory	Compound-specific molecular mechanisms	Chemical/cellular
Mycelial extracts	Immunomodulatory/antitumor	APC activation, IL-12, CD8 ⁺ T-cell responses	Cellular + animal
Whole mushroom/extracts	Antioxidant, hepatoprotective	Combined action of multiple bioactives	In vitro + animal

2. Conclusion:

Lentinula edodes represents a promising medicinal mushroom with a diverse array of biologically active constituents, including polysaccharides, particularly lentinan, phenolic compounds, terpenoids, sulfur-containing compounds, amino acids, sterols, and other secondary metabolites. These compounds contribute to its broad range of reported biological activities, including antioxidant, antimicrobial, anti-inflammatory, immunomodulatory, antitumour, antidiabetic, and cardioprotective effects. Among these constituents, lentinan has received particular attention because of its well-documented immunomodulatory and therapeutic potential. Despite substantial progress in understanding the phytochemical composition and biological activities of *L. edodes*, further studies are required to establish structure–activity relationships, precise molecular mechanisms, bioavailability, pharmacokinetics, safety, and clinical efficacy of individual compounds and their combinations. Future research integrating metabolomics, molecular biology, advanced extraction technologies, and well-designed clinical studies could facilitate the development of standardized *L. edodes*-derived nutraceuticals and therapeutic products. Thus, *L. edodes* holds considerable potential as a valuable source of natural bioactive molecules for pharmaceutical, nutraceutical, and functional-food applications. Last but not least, shiitake mushrooms are not only an excellent tasting food to enjoy, but also provide humans with substances valuable to health, e.g., dietary fiber, essential amino acids, and precursors of vitamin D, even when used in this way.

References:

1. Akramiene, D., Kondrotas, A., Didziapetriene, J., and Kevelaitis, E. (2007). Effects of beta-glucans on the immune system. *Medicina*, 43, 597-606.
2. Baral, B. (2025). Holistic Evaluation of Shiitake mushrooms (*Lentinula edodes*): Unraveling Its Medicinal and Therapeutic Potentials. *Chemistry & Biodiversity*, 22(12), e01244. <https://doi.org/10.1002/cbdv.202501244>.
3. Bisen, P.S., Baghel, R.K., Sanodiya, B.S., Thakur, G.S., and Prasad, G.B. (2010). *Lentinus edodes*: A macrofungus with pharmacological activities. *Curr. Med. Chem.* 17: 2419-2430.
4. Chandra, L.C., Smith, B.J., Clarke, S.L., Marlow, D., D'Offay, J.M., and Kuvibidila S.R. (2011). Differential effects of shiitake- and white button mushroom supplemented diets on hepatic steatosis in C57BL/6 mice. *Food and chemical toxicology: An international journal published for the British Industrial Biological Research Association*. 49(12), 3074-3080.
5. Cheah, I. K., and Halliwell, B. (2025). Ergothioneine as a promising natural antioxidant: Bioactivities, therapeutic potential, and industrial applications. *Food & Function*. <https://doi.org/10.1039/D5FO02337H>
6. Elhusseiny, S.M., El-Mahdy, T.S., Elleboudy, N.S., Yahia, I.S., and Farag, M.M.S., Ismail, N.S.M., Yassien, M.A., Aboshanab, K.M. (2022). In vitro anti SARS-CoV-2 activity and docking analysis of *Pleurotus ostreatus*, *Lentinula edodes* and *Agaricus bisporus* edible mushrooms. *Infect. Drug Resist.*, 15, 3459-3475.
7. Feng, Y.L., Li, W.Q., Wu, X.Q., Cheng, J.W., and Ma, S.Y. (2010). Statistical optimization of media for mycelial growth and exo-polysaccharide production by *Lentinus edodes* and a kinetic model study of two growth morphologies. *Biochemical Engineering Journal*, 49(1), 104-112. <https://doi.org/10.1016/j.bej.2009.12.002>.
8. Feriani, A., Tir, M., Hamed, M., Sila, A., Nahdi, S., Alwasel, S., Harrath, A.H., and Tlili, N. (2020). Multidirectional insights on polysaccharides from *Schinus terebinthifolius* and *Schinus molle* fruits: Physicochemical and functional profiles, in vitro antioxidant, antigenotoxicity, antidiabetic, and antihemolytic capacities, and in vivo anti-inflammatory. *Int. J. Biol. Macromol.*, 165, 2576-2587
9. Finimundy, T., Dillon, A., Henriques, J., and Ely, M. (2014). A Review on General Nutritional Compounds and Pharmacological Properties of the *Lentinula edodes* Mushroom. *Food Nutr. Sci.*, 5, 1095-1105.
10. Fukushima-Sakuno, E. (2020). Bioactive small secondary metabolites from the mushrooms *Lentinula edodes* and *Flammulina velutipes*. *The Journal of Antibiotics*, 73, 687-696. <https://doi.org/10.1038/s41429-020-0354-x>.
11. Gaitán-Hernández, R., López-Peña, D., Esqueda, M., and Gutiérrez, A. (2019). Review of bioactive molecules production, biomass, and basidiomata of shiitake culinary-medicinal mushrooms, *Lentinus edodes* (Agaricomycetes). *International Journal of Medicinal Mushrooms*, 21(9), 841-850.
12. Gil-Ramirez, A., Caz, V., Smiderle, F.R., Martin-Hernandez, R., Largo, C., Tabernero, M., Marin, F.R., Iacomini, M., Reglero, G., and Soler-Rivas, C. (2016). Water-soluble compounds from *Lentinula edodes* influencing the HMG-CoA reductase activity and the expression of genes involved in the cholesterol metabolism. *J. Agric. Food Chem.*, 64, 1910-1920.
13. Gregori, A., Kretschmer, N., Wagner, S., Boechzelt, H., Klinar, D., Bauer, R., and Pohleven, F. (2012). Influence of olive oil press cakes on shiitake culinary-medicinal mushroom, *Lentinus*

- edodes, fruiting bodies production and effect of their crude polysaccharides on CCRF-CEM cell proliferation. *International Journal of Medicinal Mushrooms*, 14(4), 419-424.
14. Heleno, S.A, Barros, L., Martins, A., Queiroz, M.J., Santos-Buelga, C., and Ferreira I.C. 2012. Phenolic, polysaccharidic, and lipidic fractions of mushrooms from northeastern Portugal: chemical compounds with antioxidant properties. *J. Agric. Food Chem.*, 60(18): 4634-4640.
15. Kajiyama, S., Nagatake, T., Ishikawa, S., et al. (2023). *Lentinula edodes* mycelia extract regulates the function of antigen-presenting cells to activate immune cells and prevent tumor-induced deterioration of immune function. *BMC Complementary Medicine and Therapies*, 23, 281. <https://doi.org/10.1186/s12906-023-04106-5>.
16. Kupcová, K., Stefanová, I., Plavcová, Z., Hošek, J., Hrouzek, P., and Kubec, R. (2018). Antimicrobial, cytotoxic, anti-inflammatory, and antioxidant activity of culinary processed shiitake medicinal mushroom (*Lentinus edodes*, Agaricomycetes) and its major sulfur sensory-active compound-lenthionine. *International Journal of Medicinal Mushrooms*, 20(2), 165–175.
17. Kuroki, T., Lee, S., Hirohama, M., Taku, T., Kumakura, M., Haruyama, T., Nagata, K., and Kawaguchi, A. (2018). Inhibition of influenza virus infection by *Lentinus edodes* mycelia extract through its direct action and immunopotentiating activity. *Front. Microbiol.*, 9, 1164.
18. Li, Q., Lei, Y., Hu, G., Lei, Y., and Dan, D. (2018). Effects of Tween 80 on the liquid fermentation of *Lentinus edodes*. *Food Science and Biotechnology*, 27(4), 1103-1109. <https://doi.org/10.1007/s10068-018-0339-8>.
19. Lindequist, U. (2024). Medicinal Mushrooms as Multicomponent Mixtures-Demonstrated with the Example of *Lentinula edodes*. *Journal of Fungi*, 10(2), 153. <https://doi.org/10.3390/jof10020153>
20. Liu, Y., Luo, M., Liu, F., Feng, X., Ibrahim, S.A., Cheng, L., and Huang, W. (2020). Effects of freeze drying and hot-air drying on the physicochemical properties and bioactivities of polysaccharides from *Lentinula edodes*. *Int. J. Biol. Macromol.*, 145, 476-483.
21. Maeda, Y.Y., and Chihara G. (1971). *Lentinan*, a new immuno-accelerator of cell-mediated responses. *Nature.*, 229(5287), 634. <https://doi.org/10.1038/229634a0>.
22. Maity, S., Kar Mandal, E., Maity, K., Bhunia, S.K., Behera, B., Maiti, T.K., Mallick, P., Sikdar, S.R., and Islam, S.S. (2013). Structural study of an immunoenhancing polysaccharide isolated from an edible hybrid mushroom of *Pleurotus florida* and *Lentinula edodes*. *Bioact. Carbohydr. Diet. Fibre*, 1, 72–80
23. Makkar, S., Nehra, K., Makker, J., Kaur, H., Annepu, S.K., Sindhu, A., and Singh, A. (2026). Macromolecular organization in *Lentinula edodes*: Integrating co-occurring bioactives for structure–function relationships across gut microbiota and host metabolism. *Comprehensive Reviews in Food Science and Food Safety*, 25(4), e70536. <https://doi.org/10.1111/1541-4337.70536>
24. Meng, Y., Lyu, F., Xu, X., and Zhang, L. (2020). Recent advances in chain conformation and bioactivities of triple-helix polysaccharides. *Biomacromol.*, 21(5):1653–77. <https://doi.org/10.1021/acs.biomac.9b01644>.
25. Mizuno, M., and Minato, K.I. (2024). Anti-inflammatory and immunomodulatory properties of polysaccharides in mushrooms. *Current Opinion in Biotechnology*, 86, 103076. <https://doi.org/10.1016/j.copbio.2024.103076>.
26. Morales, D., Tabernero, M., Largo, C., Polo, G., Jiménez Piris, A., and Soler-Rivas, C. (2018). Effect of traditional and modern culinary processing, bioaccessibility, biosafety and bioavailability

- of eritadenine, a hypocholesterolemic compound from edible mushrooms. *Food & Function*, 9(12), 6360-6368. <https://doi.org/10.1039/C8FO01704B>
27. Morales, D., Shetty, S.A., Lopez-Plaza, B., Gomez-Candela, C., Smidt, H., Marín, F.R., and Soler-Rivas, C. (2021). Modulation of human intestinal microbiota in a clinical trial by consumption of a s-D-glucan-enriched extract obtained from *Lentinula edodes*. *Eur. J. Nutr.*, 60, 3249-3265.
28. Muñoz-Castiblanco, T., Mejía-Giraldo, J. C., and Puertas-Mejía, M.Á. (2022). *Lentinula edodes*, a novel source of polysaccharides with antioxidant power. *Antioxidants*, 11(9), 1770. <https://doi.org/10.3390/antiox11091770>.
29. Park, G. S., Shin, J., Hong, S., Gopal, J., and Oh, J.W. (2024). Anticarcinogenic potential of the mushroom polysaccharide lentinan on gastric and colon cancer cells: Antiproliferative, antitumorigenic, Mu-2-related death-inducing gene, MUDENG ramifications. *Journal of Industrial and Engineering Chemistry*, 135, 122-130. <https://doi.org/10.1016/j.jiec.2024.01.024>.
30. Ponnusamy, C., Uddand Rao, V.V.S., Pudhupalayam, S.P., Singaravel, S., Periyasamy, T., Ponnusamy, P., Prabhu, P., Sasikumar, V., and Ganapathy. S. (2022). *Lentinula Edodes* (Edible Mushroom) as a Nutraceutical: A Review. *Biosciences Biotechnology Research Asia*, 19(1): 1-11. <http://dx.doi.org/10.13005/bbra/2964>
31. Reis, F.S., Martins, A., Barros, L., and Ferreira, I.C. (2012). Antioxidant properties and phenolic profile of the most widely appreciated cultivated mushrooms: a comparative study between in vivo and in vitro samples. *Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association*. 50(5): 1201-1207.
32. Rincão, V.P., Yamamoto, K.A., Ricardo, N.M., Soares, S.A., Meirelles, L.D., Nozawa, C., and Linhares, R.E. (2012). Polysaccharide and extracts from *Lentinula edodes*: Structural features and antiviral activity. *Virol. J.*, 9, 37.
33. Roszczyk, A., Turło, J., Zagożdżon, R., and Kaleta, B. (2022). Immunomodulatory properties of polysaccharides from *Lentinula edodes*. *International Journal of Molecular Sciences*, 23(16), 8980. <https://doi.org/10.3390/ijms23168980>
34. Sheng, K., Wang, C., Chen, B., Kang, M., Wang, M., Liu, K., and Wang, M. (2021). Recent advances in polysaccharides from *Lentinus edodes* (Berk.): Isolation, structures and bioactivities. *Food Chemistry*, 358, 129883.
35. Song, X., Cai, W., Ren, Z., Jia, L., and Zhang, J. (2021). Antioxidant and hepatoprotective effects of acidic-hydrolysis residue polysaccharides from shiitake culinary-medicinal mushroom *Lentinus edodes* in mice. *International Journal of Medicinal Mushrooms*, 23(2), 85-96.
36. Spim, S.R.V., Holtz Pistila, A.M., Pickle, T.B., Silva, M.T., and Grotto, D. (2021). Effects of Shiitake culinary-medicinal mushroom, *Lentinus edodes* (Agaricomycetes), bars on lipid and antioxidant profiles in individuals with borderline high cholesterol: A double-blind randomized clinical trial. *Int. J. Med. Mushrooms* 2021, 23, 1-12.
37. Suzuki, M., Takatsuki, F., Maeda, Y.Y., Hamuro, J., and Chihara, G. (1994). Antitumor and immunological activity of lentinan in comparison with LPS. *Int J Immunopharmacol.*, 16(5-6), 463-8. [https://doi.org/10.1016/0192-0561\(94\)90037-x](https://doi.org/10.1016/0192-0561(94)90037-x).
38. Taofiq, O., Heleno, S.A., Calhella, R.C., Alves, M.J., Barros, L., Barreiro, M.F., González-Paramás, A.M., and Ferreira, C.F.R. (2016). Development of mushroom-based cosmeceutical formulations with anti-inflammatory, anti-tyrosinase, antioxidant, and antibacterial properties. *Molecules*, 21, 1372.

39. Zhang, Y., Li, S., Wang, X., Zhang, L., and Cheung, P.C.K. (2011). Advances in lentinan: Isolation, structure, chain conformation and bioactivities. *Food Hydrocolloids*, 25(2), 196-206.
<https://doi.org/10.1016/j.foodhyd.2010.02.001>.
40. Zhao, Z.Z., Zhang, F., Zhao, Q.L., Zhao, J., He, H.-R., Liu, H.J., Liu, K.K., and Chen, H. (2026). Unusual prenylated phenols with antioxidant and immunosuppressive activities from the edible mushroom *Lentinula edodes*. *RSC Advances*, 16(14), 12295–12301.
<https://doi.org/10.1039/D5RA09796G>
41. Zhou, G., Liu, H., Yuan, Y., Wang, Q., Wang, L., and Wu, J., (2024). Lentinan progress in inflammatory diseases and tumor diseases. *European Journal of Medical Research* (2024) 29:8
<https://doi.org/10.1186/s40001-023-01585-7>.