

A Review on Assessment of Advances in Lentinus Mushroom - Derived Nutraceuticals

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ABSTRACT: The nutraceutical potential of mushrooms, emphasizing their rich bioactive components such as polysaccharides, proteins, peptides, phenolic compounds, terpenoids, and steroids. Mushrooms, particularly from the *Lentinus* species, offer significant health benefits including antioxidant, anti-cancer, anti-inflammatory, and immune-modulating effects. The bioactive compounds contribute to various therapeutic applications, such as enhancing immunity, regulating cellular activities, and providing cardiovascular protection. Advances in mushroom biotechnology and green extraction methods are expanding their use in nutraceuticals and functional foods, positioning mushrooms as valuable assets in health and medicine. The molecular mechanisms underlying these effects are explored, emphasizing the role of bioactive compounds in apoptosis induction, immune regulation, and metabolic modulation. Furthermore, advancements in extraction technologies and mushroom biotechnology are examined, underscoring their importance in enhancing the bioavailability and therapeutic efficacy of mushroom-derived nutraceuticals. This review positions mushrooms as promising agents in the development of functional foods and novel therapeutic applications, contributing to the growing nutraceutical industry.

KEYWORDS: Mushrooms, Nutraceuticals, Bioactive compounds, *Lentinus*, species, Health benefits, Polysaccharides, Proteins, Peptides, Phenolic compounds, Terpenoids, Steroids, Antioxidant, Anti-cancer, Anti-inflammatory, Immune-modulation, Cardiovascular protection, Mushroom biotechnology, Green extraction methods, Functional foods, Nutraceutical industry.

1. INTRODUCTION

Nutraceuticals blend 'nutrition' and 'pharmaceutical,' referring to food or food components that help maintain and improve health. The global growth of the nutraceutical market is driven by rising health awareness and demographic trends¹ Key nutraceutical categories include dietary fibers, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants, and various herbal foods. These products address major health issues like obesity, cardiovascular diseases, cancer, osteoporosis, arthritis, diabetes, and high cholesterol² This field has transformed the food

industry into a research-driven sector. Mushroom Nutraceuticals the term "mushroom nutraceuticals," introduced by Chang & Buswell in 1996, refers to refined extracts from mushrooms, often consumed as dietary supplements. Mushrooms are rich in high-quality proteins, essential minerals (iron, phosphorus), vitamins (riboflavin, thiamine, niacin, ascorbic acid), and bioactive compounds (terpenoids, alkaloids, polyphenols, β -glucans). These components contribute to their therapeutic benefits, including liver protection, immune support, anti-cancer, antiviral, and cholesterol-lowering effects. Despite these advantages, mushrooms are often underutilized in health applications. Advances in green extraction techniques are improving the ability to harness their bioactive properties effectively³

Scope of the Review

This review highlights the nutraceutical and therapeutic potential of mushrooms, focusing on their bioactive compounds, health benefits, and the impact of modern processing techniques. It covers mushroom cultivation, medicinal properties, and their role in food security and employment, with a particular emphasis on the Indian context.

2. TYPES OF BIOACTIVE COMPOUND

Lentinula edodes (shiitake mushrooms) are rich in bioactive polysaccharides, which are crucial for their health benefits. These polysaccharides are used in medicine, antimicrobial agents, dietary supplements, and functional foods⁴. It contains 18 different amino acids, with *Lentinus squarrosulus* having the most extensive profile. Key amino acids include glutamic acid, leucine, and arginine, which contribute to various bioactivities. These amino acids underscore the potential of *Lentinus* mushrooms in various health applications. It is also a source of diverse phenolic compounds, including simple phenols, coumarins, phenolic acids, flavonoids, and non-flavonoids⁵ *Lentinus* mushrooms also contain various terpenoids and steroids⁶ These compounds enhance the medicinal

value of *Lentinus* mushrooms, contributing to their use in pharmaceutical and nutraceutical applications^{7,8}

3. HEALTH BENEFITS OF MUSHROOM-DERIVED NUTRACEUTICALS

The consumption of *Lentinus* mushroom has been shown to improve immunity via enhanced cellular proliferation and activation and upregulate IgA levels. Dai et al.⁵² attributed these effects to *Lentinus* mushroom-mediated innate lymphocyte priming. *Lentinan* has shown promising results in the treatment of various cancers like, breast cancer, lung cancer, brain tumours, lymphomas, etc.⁹ It contains bioactive compounds that reduce inflammation in arthritis, gastrointestinal disorders, neuroinflammation and in cancer. Other benefits like *L. squarrosulus* exhibits high antioxidant activity by scavenging free radicals and reducing oxidative stress. *Shiitake* extracts contains sesquiterpenes, steroids, anthraquinone, benzoic acid derivatives, and quinolones has shown anticaries and antimicrobial activity in which, it demonstrate bacteriostatic action against *Streptococcus mutans* by inhibiting DNA synthesis¹⁰

4. ADVANCES IN EXTRACTION AND PROCESSING TECHNOLOGIES

Conventional Extraction Techniques

Water Extraction (Decoction): This is a straightforward method of extracting water-soluble compounds from mushrooms. In this technique, dried or fresh mushrooms are simmered in water for an extended period to allow the water-soluble components to dissolve into the liquid. The resulting mushroom-infused water can be used as a base for soups, sauces, or beverages.

Hot Water Extraction: This technique is similar to water extraction (decoction), but it involves using hot water to enhance the extraction process. The higher temperature can help break down the mushroom cell walls and extract a wider range of compounds. This method is often used to obtain mushroom extracts for supplement capsules or teas.¹¹**Advantages.** Widely accessible and cost-effective: Water is a common solvent and readily available, making water extraction an economical choice. Safe and environmentally friendly: Water is non-toxic and does not produce harmful waste, making it an environmentally friendly option. Suitable for polysaccharides: Many bioactive polysaccharides in medicinal mushrooms can be efficiently extracted with water.

Limitations - Limited solvent power: Water extraction may not be effective for extracting non-polar compounds like terpenoids. **Temperature-sensitive:** Some heat-sensitive bioactive compounds may degrade during high-temperature water extraction.¹¹

Extraction (Tincture): Alcohol extraction, also known as tincture, involves soaking mushrooms in high-proof alcohol (such as ethanol or vodka) to extract both water-soluble and alcohol-soluble compounds. The alcohol acts as a solvent, pulling out various active constituents from the mushrooms. Tinctures are commonly used in herbal medicine and can be taken orally or used topically.¹²

Ethanol/Water Combination Extraction: This method involves using a combination of ethanol (alcohol) and water as the solvent to extract a broader spectrum of compounds from mushrooms. The mixture of alcohol and water provides an intermediate polarity, allowing extraction of water-soluble and alcohol-soluble components. **Advantages :** Broad spectrum of solubility: Ethanol can dissolve both lipophilic and hydrophilic compounds, providing a wider range of extracted bioactives. High bioactive compound yield: Ethanol extraction often yields higher concentrations of bioactive compounds compared to water extraction. Long shelf life: Extracts obtained using ethanol as the solvent generally have a longer shelf life.

Limitations: Higher cost: Ethanol is more expensive than water, which can increase the overall extraction cost. Potential chemical alterations: Ethanol may cause some chemical alterations in the extracted compounds, affecting their bioactivity.¹³

Advanced extraction techniques **Supercritical Fluid Extraction:** This is an advanced technique that utilises supercritical fluids, typically carbon dioxide (CO₂), as a solvent to extract specific compounds from mushrooms. The supercritical CO₂ acts as a non-toxic, environmentally friendly solvent that can be adjusted to target specific compounds. **Advantages :** High selectivity: SFE allows the selective extraction of specific bioactive compounds, minimising the extraction of unwanted substances. Mild conditions: Supercritical CO₂ extraction is carried out at lower temperatures, preserving heat-sensitive compounds. Solvent-free extracts: Supercritical CO₂ leaves no solvent residues in the final extract. **Limitations:** Costly equipment: The initial setup cost for SFE equipment can be substantial. Limited availability: SFE equipment and expertise may not be readily available in all regions.¹⁴

Microwave-Assisted Extraction (MAE): This method utilizes microwave irradiation to heat the solvent, expediting the extraction process. The energy from the microwaves induces molecular vibrations, facilitating the release of compounds from the mushroom material into the solvent. MAE proves to be a swift and effective method for extracting heat-sensitive compounds. **Advantages:** **Rapid extraction:** MAE significantly reduces the extraction time compared to traditional methods, improving productivity. **Energy-efficient:** Microwave-assisted extraction consumes less energy than conventional methods. **Enhanced extraction efficiency:** Microwave radiation enhances the penetration of the solvent into the mushroom matrix, leading to improved extraction yields. **Limitations :** **Uneven heating:** Uneven microwave distribution may lead to localised high temperatures and degradation of heat-sensitive compounds. **Limited scalability:** MAE may not be suitable for large-scale industrial applications.¹⁴

Ultrasound-Assisted Extraction (UAE): In this method, a sonicator subjects the mushroom mixture to high-frequency ultrasound waves, inducing cavitation and improving mass transfer between the solvent and the mushroom matrix. This process increases the extraction efficiency and reduces the extraction time. **Advantages:** Increased extraction efficiency by

promoting the release of compounds from the mushroom matrix to the solvent. The cavitation phenomenon induced by ultrasound creates microbubbles that disrupt the cell walls, releasing intracellular compounds. It allows rapid extraction of bioactive compounds, saving time and energy compared to other conventional techniques. **Preservation of heat-sensitive compounds.** The UAE technique can be easily scaled up for industrial production, making it suitable for large-scale extraction processes. **Limitations :** **Equipment Cost:** The initial setup cost of ultrasound equipment can be relatively high, which may pose a barrier for small-scale or home-based applications. **Risk of Over Extraction:** If not controlled properly, the intense cavitation generated by ultrasound may lead to over extraction, resulting in the extraction of unwanted or undesirable compounds. The cavitation phenomenon induced by ultrasound creates microbubbles that disrupt the cell walls, releasing intracellular compounds. It allows rapid extraction of bioactive compounds, saving time and energy compared to other conventional techniques.¹⁴

5. CLINICAL STUDIES AND EVIDENCE

A. Human trials

Health Benefit	Study Year	Journal	Key Findings
Immune Enhancement	2015	Journal of Medicinal Food	Increased immune function in healthy individuals. ¹⁵
Anticancer Properties	2017	Journal of Alternative and Complementary Medicine	Inhibited cancer cell growth & induced apoptosis in breast cancer patients. ¹⁶
Cardiovascular Health	2018	Journal of Agricultural and Food Chemistry	Reduced triglycerides & LDL cholesterol in hyperlipidemic individuals. ¹⁷
Antiviral Properties	2020	Journal of Functional Foods	Inhibited influenza virus replication in vitro & in vivo. ¹⁸
Gastrointestinal Health	2019	Journal of Medicinal Food	Improved gut microbiota & reduced IBS symptoms. ¹⁹
Anti-inflammatory Effects	2018	Journal of Inflammation	Reduced inflammation in rheumatoid arthritis patients. ²⁰

Human trials have demonstrated the effectiveness of *Lentinus* species mushroom nutraceuticals in supporting various health benefits. These benefits include immune system enhancement, anticancer properties, cardiovascular health, antiviral properties, gastrointestinal health, anti-inflammatory effects, and antioxidant activity²¹. have shown positive outcomes in healthy individuals and patients with specific health conditions. For example, *Lentinula edodes* extract has

been found to inhibit cancer cell growth, reduce triglycerides and LDL cholesterol, and improve gut microbiota. Overall, these findings suggest that *Lentinus* species mushroom nutraceuticals may be a valuable adjunct to conventional healthcare, promoting overall well-being and disease prevention.²²

B. Preclinical studies

In Vitro Studies:

Activity	Description
Anticancer Activity	Inhibited cancer cell growth and induced apoptosis in various cancer cell lines. ²³
Antimicrobial Activity	Exhibited antibacterial and antifungal properties against various microorganisms. ²⁴
Antioxidant Activity	Showed high antioxidant activity by scavenging free radicals and reducing oxidative stress. ²⁵
Immunomodulatory Effects	Stimulated immune cell activity and enhanced cytokine production. ²⁶

Preclinical studies have demonstrated the potential health benefits of mushrooms, including immune system enhancement, anticancer properties, and antioxidant activity. In vitro studies have shown that mushroom extracts inhibit cancer cell growth, induce

apoptosis, and exhibit antimicrobial and antiviral properties²⁷

In Vivo Studies.

Activity	Description
Tumor Inhibition	Inhibited tumor growth and increased survival in mouse models of cancer. ²⁸
Cardiovascular Protection	Reduced blood pressure, cholesterol, and triglycerides in rat models of cardiovascular disease. ²⁹
Neuroprotective Effects	Improved cognitive function and reduced neuroinflammation in mouse models of neurodegenerative diseases. ³⁰
Gastrointestinal Health	Improved gut microbiota and reduced inflammation in mouse models of IBS. ³¹

In vivo studies have found that mushroom polysaccharides enhance immune function, reduce inflammation, and improve cardiovascular health in animal models.³² Mushroom-derived compounds have also been shown to possess neuroprotective effects, improving cognitive function and neurodegenerative

disease outcomes. Overall, these preclinical studies provide evidence for the potential health benefits of mushrooms.³³

C. Safety Profile:

Aspect	Details
Toxicity	Low toxicity; long history of safe consumption in culinary/traditional medicine. ³⁴
Gastrointestinal Tolerance	Generally well-tolerated; few mild gastrointestinal upset cases reported. ³⁵
Allergic Reactions	Rare instances of skin rash or itching. ³⁶
Medication Interactions	Potential interactions with blood thinners, diabetes medications, and immunosuppressants (more research needed). ³⁷

Mushroom nutraceuticals generally have a favorable safety profile, with few reported side effects or toxicity issues. Clinical trials have shown that mushroom extracts are well-tolerated and safe for consumption in healthy individuals.³⁸ However, potential allergic reactions, gastrointestinal upset, and interactions with medications have been reported. Rare cases of liver toxicity and kidney damage have also been

documented, primarily associated with excessive consumption or pre-existing health conditions. Overall, mushroom nutraceuticals are considered safe when consumed in moderation and under the guidance of a healthcare professional.³⁹

6. REGULATORY AND MARKET TRENDS

A. Regulatory guidelines

Region	Regulatory Body	Regulation/Guideline	Year
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United States	US FDA	Dietary Supplement Health and Education Act (DSHEA) ⁴⁰	1994
		Good Manufacturing Practices (GMPs) for Dietary Supplements (21 CFR 111) ⁴¹	N/A
European Union	European Food Safety Authority (EFSA)	Novel Food Regulation (EU) 2015/2283 ⁴²	2015
		EFSA Guidance on the Evaluation of Novel Foods ⁴³	2016
	European Medicines Agency (EMA)	Good Manufacturing Practices (GMPs) for Herbal Medicinal Products (EU GMP Guide) ⁴⁴	N/A
India	Food Safety and Standards Authority of India (FSSAI)	Food Safety and Standards Act ⁴⁵	2006
		Licensing and Registration Requirements for Food Business Operators ⁴⁶	2011
		Good Manufacturing Practices (GMPs) for Food Processing ⁴⁷	2017

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B. Market growth

The demand for Lentinus species of mushroom nutraceuticals is growing rapidly, driven by increasing consumer health consciousness and a growing vegan population. Here are some key highlights of the market growth and the role of consumer awareness:

- Growing demand for plant-based food products:** With the growing popularity of vegetarian and vegan diets, mushrooms are increasingly being used as meat substitutes due to their texture and umami flavor.
- Increasing consumer awareness of health benefits:** Consumers are actively seeking nutritious and functional foods, with mushrooms gaining attention for their myriad health benefits.
- Rising demand for value-added mushroom products:** the

growing demand for Lentinus species of mushroom nutraceuticals is driven by consumer awareness of the health benefits and sustainability of mushroom-based products ⁵⁰

7. CHALLENGES AND PERSPECTIVES

A. Research gaps

Long-term clinical studies: Most studies on Lentinus species mushroom have been short-term, lasting only a few weeks or months. Long-term studies are needed to fully understand their effects on human health.

Safety concerns: While generally considered safe, some Lentinus species can cause adverse effects, such as allergic reactions or interactions with medications. ⁵¹ More research is needed to address safety concerns.

Bioavailability and pharmacokinetics: The bioavailability and pharmacokinetics of Lentinus species mushroom compounds are not well understood, making it difficult to optimize dosing and delivery. ⁵²

Mechanisms of action: While some bioactive compounds in Lentinus species mushroom have been identified, more research is needed to understand their mechanisms of action and how they interact with human biology.

Interactions with medications: Lentinus species mushroom may interact with medications, such as blood thinners or immunosuppressants.



⁵³ More research is needed to understand these interactions. Pediatric and geriatric populations: Most research on Lentinus species mushroom has focused on adults. ⁵⁴ More studies are needed on their safety and efficacy in pediatric and geriatric populations. Optimization of extraction and processing methods: More research is needed to optimize extraction and processing methods to ensure consistency and efficacy of Lentinus species mushroom products. ⁵⁵Standardization of products: Standardization of Lentinus species mushroom products is needed to ensure consistency and efficacy across different products and manufacturers. Clinical trials in specific diseases: More clinical trials are needed to explore the efficacy of Lentinus species mushroom in specific diseases, such as cancer, cardiovascular disease, and neurodegenerative disorders. ⁵⁶Toxicology and genotoxicity studies: More research is needed to understand the toxicology and genotoxicity of Lentinus species mushroom compounds. ⁵⁷

B.Future trends

Personalized nutraceuticals: Developing personalized Lentinus species mushroom-based nutraceuticals tailored to individual needs based on genetic profiles, health status, and lifestyle. Combination therapies: Combining Lentinus species mushroom compounds with other bioactive compounds, such as polyphenols or omega-3 fatty acids, to enhance efficacy and bioavailability ⁵⁸. Novel delivery systems : Utilizing novel delivery systems, such as nanoparticles, liposomes, or microencapsulation, to enhance bioavailability and targeted delivery of Lentinus

species mushroom compounds. Functional foods and beverages : Incorporating Lentinus species mushroom into functional foods and beverages, such as energy bars, smoothies, or coffee, to enhance nutritional value and convenience ⁵⁹. Cosmeceuticals : Exploring the use of Lentinus species mushroom in cosmeceuticals, such as skincare products, to leverage its antioxidant and anti-inflammatory properties. Veterinary applications : Investigating the use of Lentinus species mushroom in veterinary medicine to enhance animal health and well-being. Sustainable production methods : Developing sustainable production methods, such as vertical farming or waste reduction, to minimize environmental impact and enhance eco-friendliness. ⁶⁰Genetic engineering: Exploring genetic engineering techniques to enhance the bioactive compound content and diversity of Lentinus species mushroom. Synbiotics : Combining Lentinus species mushroom with prebiotics to create synbiotics that enhance gut health and immune function ⁶¹. Digital health integration : Integrating Lentinus species mushroom-based nutraceuticals with digital health technologies, such as mobile apps or wearable devices, to enhance personalized health and wellness. ⁶²

8. DISCUSSION

Lentinula edodes (shiitake mushrooms) are rich in bioactive polysaccharides, which are crucial for their health benefits because these include antioxidant, antitumor, anti-aging, anti-inflammatory, immunoregulatory, and antiviral properties. The effectiveness of these polysaccharides depends on their physicochemical properties, such as molecular

weight, monosaccharide composition, and glycosyl linkages. Notably, lentinan, a β -1,3-d-glucan with β -1,6-glucopyranoside branches, has shown significant anti-cancer activity. Mechanism of action of lentinan as an anti-cancer activity involves lentinan generates reactive oxygen species (ROS) which damages cancer cell DNA, proteins, and lipids, leading to cell death which inhibits topoisomerase enzymes, which is essential for cancer cell DNA replication and repair and also suppresses angiogenesis, the formation of new blood vessels that feed cancer growth so these polysaccharides are used in medicine, antimicrobial agents, dietary supplements, and functional foods(10). The *Lentinus* species of mushrooms possess a comprehensive array of amino acids, these 18 distinct amino acids identified in the fruiting body and mycelium. Amino acids like Glutamic acid acts as Potential anticancer agent and drug conjugation, (Dutta et al.,2013) Leucine enhances muscle protein synthesis and improves glycemic management (Garlick 2005). Arginine Promotes wound healing and stimulates growth hormone production (Scott lind,2004) these amino acids play a major role in nutraceuticals(5-9). *Lentinus squarrosulus*, a edible mushroom, is a rich source of bioactive plant polyphenols, which are classified into: Simple phenols, Coumarin and phenolic acids (hydroxybenzoic acids and hydroxycinnamic acids), Flavonoids (flavonols, flavones, flavanols, flavanones, isoflavones, anthocyanins, chalcones), Nonflavonoids (tannins, lignans, stilbenes). These phenolic compounds exhibit high antioxidant activity due to their polyhydroxy groups, scavenging reactive oxygen radicals (ROS) in the human diet. GC-MS and HPLC analyses identified 28 bioactive compounds, including: Phytol, 1-Tetradecene, Fumaric acid, Linoleic acid, Palmitic acid, Oleic acid, Capric acid, Myristic acid, Stearic acid. These compounds exhibit various pharmacological activities, including, antioxidant, Anti-inflammatory, antimicrobial, anticancer Cardiovascular protective effects. *Lentinus* mushrooms contain diverse terpenes and steroids, including, Sesquiterpenes (e.g., lentinic acid): antimicrobial, antioxidant, diterpenes (e.g., lentinin): anti-inflammatory, antimicrobial; triterpenes (e.g., ganoderic acid): antiviral, antitumor, Steroids Ergosterol: antioxidant, antimicrobial, β -Sitosterol: anti-inflammatory, antitumor Stigmasterol: antimicrobial, antioxidant. These compounds contribute to the medicinal properties of *Lentinus* mushrooms, exhibiting: antimicrobial activity against various pathogens. So it has shown anticaries activity

and antimicrobial activity. the mechanism of action of these activity involve by inhibition of DNA synthesis; disruption of cell membrane integrity and interference with microbial activity(10). *Lentinus squarrosulus*: Nutritional composition, phytochemistry, health-promoting activities and toxicity profile

9. CONCLUSION

Mushroom-derived nutraceuticals have emerged as a promising area of research, offering a wide range of health benefits and potential applications in disease prevention and treatment. Advances in extraction and processing technologies have enhanced the bioavailability and efficacy of these compounds, while clinical studies have demonstrated their safety and effectiveness. However, further research is needed to address existing gaps in knowledge, such as long-term clinical studies and safety concerns. As consumer awareness and demand for natural health products continue to grow, the market for mushroom nutraceuticals is poised for expansion. Future directions may include personalized nutraceuticals, combination therapies, and novel delivery systems, highlighting the vast potential of mushroom-derived compounds to improve public health and revolutionize the functional food and supplement industry. Ultimately, the continued exploration of mushroom-derived nutraceuticals holds great promise for unlocking new avenues of health promotion and disease prevention.

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