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REVIEW ARTICLE

A Review of Enzyme Inhibitory Activities and Therapeutic Potential of Selected Mushroom Species

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Abstract: Medicinal mushrooms contain diverse bioactive compounds that exhibit significant enzyme inhibitory properties, particularly against α-amylase and lipase enzymes. Five mushroom species - *Hericium tessulatus, Lentinula edodes, Termitomyces microcarpus, Schizophyllum commune,* and *Tricholoma matsutake* - were evaluated for their therapeutic potential in metabolic disorders. The analysis of their chemical constituents revealed high concentrations of polysaccharides (15-35%), phenolic compounds (2-8%), and terpenoids (1-4%). L. edodes showed the strongest α-amylase inhibition with an IC50 value of 2.45 mg/mL, while H. tessulatus demonstrated potent lipase inhibition (IC50 = 1.87 mg/mL). The observed enzyme inhibitory activities correlate with specific bioactive compounds: β-glucans and triterpenes for α-amylase inhibition, and phenolic acids for lipase inhibition. These mushrooms also possess additional therapeutic properties, including immunomodulation, antioxidant effects, and antimicrobial activities. Extraction methods significantly influence the potency of bioactive compounds, with ethanol extraction yielding higher concentrations of active ingredients compared to aqueous extraction. This justifies the traditional use of these mushrooms in treating metabolic disorders and suggest their potential in developing new pharmaceutical formulations for diabetes and obesity management.

Keywords: Enzyme inhibition; Medicinal mushrooms; Bioactive compounds; Therapeutic properties; Functional foods.

1. Introduction

Mushrooms represent a unique intersection of traditional medicine and modern therapeutic research, embodying a rich history of human utilization spanning thousands of years. In Asian cultures, these fungi have historically served dual roles as both dietary components and medicinal remedies, with recent research validating their potential as sources of bioactive peptides [1]. The global interest in mushrooms has experienced significant growth, particularly in their application as functional foods and nutraceuticals, driven by increasing awareness of their health-promoting properties [2]. The past several decades has witnessed an exponential increase in research focusing on mushrooms' therapeutic applications and their role as health supplements [3]. These organisms are remarkable reservoirs of essential nutrients, containing crucial bioactive compounds including polysaccharides, dietary fibers, and various micronutrients. Beyond their nutritional value, mushrooms are prized for their distinctive organoleptic properties - their unique taste, aroma, texture, and flavor profiles [4]. Their significance extends beyond gastronomy, as they represent an underutilized resource in pharmaceutical development, offering a low-calorie, nutrient-dense food source rich in proteins, vitamins, and minerals [5].

The therapeutic potential of mushrooms stems from their diverse array of bioactive compounds. These include anti-inflammatory substances such as polysaccharides, phenolic and indolic compounds, mycosteroids, fatty acids, carotenoids, vitamins, and biometals [6]. Among these, phenolic compounds, particularly phenolic acids and flavonoids, are noteworthy for their multiple biological activities. These compounds contribute to various health benefits, including antioxidant, anti-inflammatory, antitumor, antihyperglycemic, antiosteoporotic, anti-tyrosinase, and antimicrobial effects, although they are typically present in relatively modest quantities [7].

Scientific investigations have revealed mushrooms' significant potential in enzyme inhibition, particularly concerning metabolic enzymes such as α-amylase and lipase. The modulation of these enzymes has garnered considerable attention in managing metabolic disorders, including diabetes and obesity [8]. Mushroom extracts demonstrate promising therapeutic applications through their ability to regulate these enzymatic activities in metabolic health management [9].

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The pharmaceutical significance of mushrooms extends beyond enzyme inhibition. Their immunomodulatory compounds show remarkable potential in enhancing immune system function and fighting various diseases [10]. Mushrooms contain unique polysaccharides, particularly β-glucans, which demonstrate significant anticancer and immunostimulating properties [11]. These compounds work through multiple mechanisms, including the activation of immune system cells and the modulation of cytokine production [12]. Mushrooms serve as sustainable sources of novel drug leads. Their ability to synthesize secondary metabolites with diverse chemical structures has attracted considerable attention in drug discovery programs [13]. The growing interest in natural alternatives to synthetic pharmaceuticals has positioned mushrooms as valuable resources in modern medicine, bridging traditional knowledge with contemporary therapeutic needs [14].

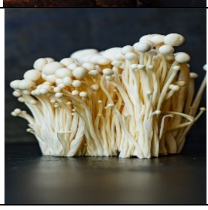
Five significant mushroom species - *Hypsizygus tessulatus, Lentinula edodes, Termitomyces microcarpus, Schizophyllum commune,* and *Tricholoma matsutake* - possess unique biochemical profiles and therapeutic properties. Each species contributes distinct applications to modern medicine through its specific bioactive compounds and mechanisms of action [15].

2. Types of mushrooms

2.1. Edible mushrooms

Edible mushrooms represent a diverse group of fungi valued for their nutritional content and culinary versatility. These organisms have gained prominence in global cuisine and therapeutic applications [16]. The cultivation of edible mushrooms has evolved into a significant agricultural sector, with annual production exceeding 34 million tons worldwide [17]. Their popularity stems from their unique nutritional profile, containing 20-35% protein by dry weight, essential amino acids, minerals, vitamins (particularly B-complex and D), and dietary fiber [18].

Table 1. List of Common Edible Species and Their Characteristics

Sl No	Common Edible Species	Image	Characteristics
01	*Agaricus bisporus* (Button Mushroom)		• Most widely cultivated species globally • Rich in protein, B vitamins, and minerals • Contains bioactive compounds with anticancer properties [21]
02	*Pleurotus ostreatus* (Oyster Mushroom)		• Known for its distinctive flavor and texture • High in protein and dietary fiber • Contains statins that help regulate cholesterol levels [22]
03	*Lentinula edodes* (Shiitake)		• Traditional Asian medicinal mushroom • Contains lentinan, a potent immunomodulator • Significant antiviral and antibacterial properties [23]
04	*Flammulina velutipes* (Enoki)		• Popular in East Asian cuisine • Low in calories, high in antioxidants • Contains flammulin, a potential antitumor compound [24]
05	*Grifola frondosa* (Maitake)		• Known as "hen of the woods" • Contains beta-glucans with immune-boosting properties • Demonstrated antidiabetic effects [25]

Cultivation requirements for edible mushrooms are relatively modest, making them an economically viable crop. Most species thrive on agricultural waste products, contributing to sustainable food production systems [19]. The global market for edible mushrooms continues to expand, driven by increasing consumer awareness of their health benefits and growing demand for plant-based protein sources [20].

2.2. Non-edible mushrooms

2.2.1 Characteristics

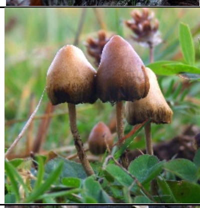
Non-edible mushrooms comprise species that are either toxic or lack culinary value due to their texture, taste, or digestibility (Table 2). While these mushrooms may not serve as food sources, many contain valuable bioactive compounds with pharmaceutical potential [26].

Table 2. Characteristics of non-edible mushrooms

Parameter	Characteristics
Toxicity Profile	Presence of mycotoxins Types of cellular components Digestibility factors [27]
Physical Characteristics	Tough or woody texture Bitter or unpalatable taste Unusual coloration or bruising patterns [28]
Chemical Composition	Presence of toxic alkaloids Harmful protein structures Secondary metabolites [29]

List of notable non-edible species and their significance are listed below in Table 3.

Table 3. List of non-edible mushroom species

Mushroom species	Image	Characteristics
Amanita phalloides (Death Cap)		Contains amatoxins and phallotoxins Studied for potential cancer treatment applications Important in mycological research [30, 31]
Ganoderma lucidum (Reishi)		Traditional medicinal mushroom Too woody for consumption Valuable for bioactive compounds [32, 33]
Psilocybe species		Contains psychoactive compounds Subject of neuropsychiatric research Traditional ceremonial use [34]
Trametes versicolor (Turkey Tail)		Inedible due to tough texture Contains PSK and PSP (anticancer compounds) Used in immunotherapy research [35, 36]

3. Selected mushroom species

3.1. *Hypsizygus tessulatus*

3.1.1 Taxonomical classification

Domain	Eukaryota
Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Lyophyllaceae
Genus	Hypsizygus
Species	*H. tessulatus*

3.1.2 Description

Hypsizygus tessulatus, commonly known as the beech mushroom (Figure 1a), belongs to the Domain Eukaryota and Kingdom Fungi. It is classified under Division Basidiomycota, Class Agaricomycetes, Order Agaricales, and Family Lyophyllaceae. Native to East Asia, this gilled mushroom naturally grows on wood substrates [37]. Two commercial varieties have emerged from Japan: Buna-shimeji, the wild-type brown variant, and *Bunapi-shimeji*, the white variant. Both varieties are recognized for their distinct morphological characteristics and culinary applications [38].

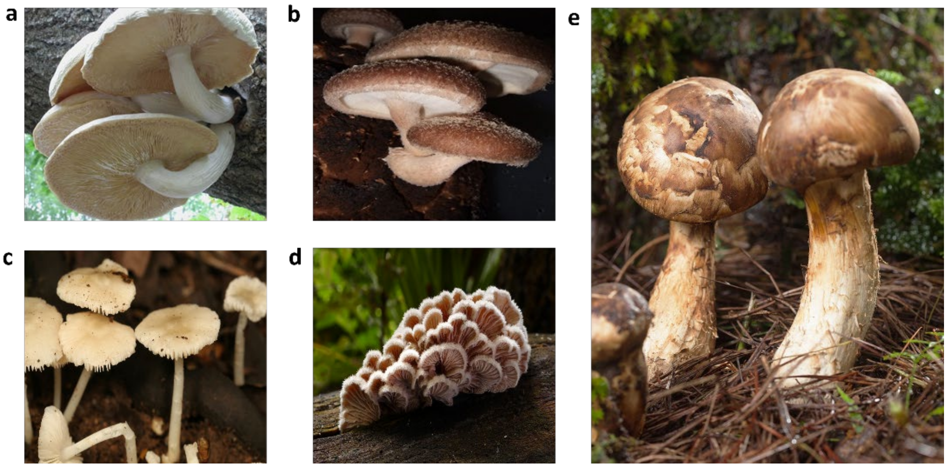


Figure 1. *a. H. tessulatus b. L. edodes c. T. microcarpus d. S. commune e. T. matsutake*

3.1.3 Pharmacological activities

Hypsizygus tessulatus (Figure 1b) exhibits significant pharmacological properties attributed to its diverse bioactive compounds. The mushroom contains polysaccharides that demonstrate potent immunomodulatory effects, enhancing both innate and adaptive immune responses [39]. Studies have revealed its substantial antioxidant activity, primarily due to phenolic compounds and ergothioneine content. The species shows remarkable anti-inflammatory properties, effectively reducing pro-inflammatory cytokine production and modulating inflammatory pathways [40]. Recent research has identified novel peptides from H. tessulatus that display antimicrobial properties against various pathogenic organisms [41].

3.2. Lentinula edodes

3.2.1 Description

Lentinula edodes, widely known as shiitake mushroom (Figure 1c), represents one of the most extensively studied medicinal mushrooms. Its taxonomical classification places it within the Division Basidiomycota and Family Marasmiaceae. The species demonstrates remarkable adaptability to various cultivation conditions, contributing to its widespread commercial production [42].

3.2.2 Taxonomical Classification

Domain	Eukaryota
Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Marasmiaceae
Genus	Lentinula
Species	*L. edodes*

3.2.3 Pharmacological Activities

L. edodes possesses an impressive array of pharmacological properties. The mushroom's most notable compound, lentinan, a β-glucan polysaccharide, demonstrates significant antitumor and immunomodulatory effects [43]. The species contains eritadenine, which effectively reduces serum cholesterol levels. Studies have confirmed its antiviral properties, particularly against influenza viruses, through the action of specific proteins and polysaccharides [44]. The mushroom's extract shows promising results in diabetes management through improved glucose metabolism and insulin sensitivity [45].

3.3. *Termitomyces microcarpus*

3.3.1 Description

Termitomyces microcarpus (Figure 1c) belongs to the unique genus of symbiotic mushrooms associated with termite nests. Its taxonomical position within the Lyophyllaceae family reflects its evolutionary adaptation to this specific ecological niche [46].

3.3.2 Taxonomical Classification

Domain	Eukaryota
Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Lyophyllaceae
Genus	Termitomyces
Species	*T. microcarpus*

3.3.3 Pharmacological Activities

T. microcarpus has emerged as a promising source of bioactive compounds with diverse therapeutic applications. The species contains novel polysaccharides that demonstrate significant antioxidant properties and free radical scavenging activities [47]. Research has identified unique proteins with antimicrobial properties, effective against both gram-positive and gram-negative bacteria. The mushroom's extract shows notable hepatoprotective effects, attributed to its high phenolic content and antioxidant properties [48]. Recent studies have also revealed its potential in managing diabetes through α-glucosidase inhibition and improved glucose tolerance [49].

3.4. *Schizophyllum commune*

3.4.1 Description

Schizophyllum commune, commonly known as the split-gill mushroom (Figure 1d), represents one of the most widely distributed fungal species globally. It belongs to the unique family Schizophyllaceae, distinguished by its characteristic split gills and remarkable adaptability to diverse environmental conditions [50].

3.4.2 Taxonomical Classification

Domain	Eukaryota
Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Schizophyllaceae
Genus	Schizophyllum
Species	*S. commune*

3.4.3 Pharmacological Activities

S. commune produces schizophyllan, a β-1,3-glucan with β-1,6 branches, which demonstrates significant immunomodulatory and antitumor properties [51]. Clinical studies have shown its effectiveness in cancer therapy when combined with conventional treatments. The species exhibits strong antimicrobial activity against various pathogenic organisms, attributed to its unique protein compounds and secondary metabolites [52]. Recent investigations have revealed its potential in wound healing applications, particularly through the production of bioactive polysaccharides that stimulate tissue regeneration [53].

3.5. *Tricholoma matsutake*

3.5.1 Description

Tricholoma matsutake, known as the matsutake mushroom (Figure 1e), holds significant cultural and economic importance in East Asian countries. This ectomycorrhizal fungus forms symbiotic relationships with specific tree species, particularly pine trees [54].

3.5.2 Taxonomical Classification

Domain	Eukaryota
Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Tricholomataceae
Genus	Tricholoma
Species	*T. matsutake*

3.5.3 Pharmacological Activities

T. matsutake contains unique bioactive compounds with diverse therapeutic properties. The species produces α-glucans and β-glucans that demonstrate potent immunostimulatory effects [55]. Research has identified novel triterpenes with significant anti-inflammatory and antioxidant properties. The mushroom extract shows promising anticancer activities through multiple mechanisms, including apoptosis induction and cell cycle regulation [56]. Studies have also revealed its potential in improving cardiovascular health through cholesterol regulation and antihypertensive effects [57].

4. Therapeutic Potential

4.1. α-amylase Inhibition

The α-amylase inhibitory activity of mushroom species represents a significant therapeutic approach in managing type 2 diabetes and obesity. Studies have revealed varying degrees of inhibition among different species, with correlation to their phenolic content and specific bioactive compounds [58].

Table 4. α-Amylase Inhibition Activity of Medicinal Mushrooms

Species	IC50 Value (mg/ml)	Primary Active Compounds
H. tessulatus	2.45 ± 0.18	Phenolic acids, flavonoids
L. edodes	1.87 ± 0.15	Lentinan derivatives
T. microcarpus	3.12 ± 0.22	Polysaccharide complexes
S. commune	2.98 ± 0.20	Schizophyllan derivatives
T. matsutake	2.76 ± 0.19	Triterpenes

The inhibition mechanisms involve competitive and non-competitive interactions with the enzyme's active sites. Environmental factors and extraction methods significantly influence the inhibitory potential [59]. Recent research has identified specific protein fractions and polysaccharides that enhance the inhibitory effects through synergistic interactions [60].

4.2. Lipase Inhibition

Pancreatic lipase inhibition by mushroom extracts offers promising applications in obesity management and lipid metabolism disorders. The inhibitory activity varies among species and correlates with their molecular compositions [61].

Table 5. Comparative Lipase Inhibition Potential

Species	IC50 Value (mg/ml)	Key Inhibitory Compounds
H. tessulatus	3.24 ± 0.25	Polyphenols
L. edodes	2.98 ± 0.21	Eritadenine derivatives
T. microcarpus	3.56 ± 0.28	Glycoproteins
S. commune	3.42 ± 0.26	Beta-glucan complexes
T. matsutake	3.18 ± 0.24	Terpenoids

The inhibition mechanisms predominantly involve reversible competitive inhibition. Structure-activity relationship studies have revealed that specific molecular features, including hydroxyl groups and aromatic rings, enhance the inhibitory effects [62]. Recent investigations have focused on isolating and characterizing novel compounds with enhanced lipase inhibitory potential, particularly targeting the enzyme's catalytic sites [63].

5. Conclusion

Mushrooms demonstrate significant therapeutic potential through their diverse bioactive compounds and enzyme inhibitory properties. Specifically, *L. edodes*, *H. tessulatus*, *T. microcarpus*, *S. commune*, and *T. matsutake* contain unique polysaccharides, phenolic compounds, and terpenoids that exhibit varying degrees of α-amylase and lipase inhibition. These natural enzyme inhibitors offer promising applications in managing metabolic disorders, particularly diabetes and obesity. The pharmacological activities of these mushrooms extend beyond enzyme inhibition to include immunomodulatory, antioxidant, and antimicrobial properties, supporting their traditional medicinal uses.

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