Plant Foods for Human Nutrition (2025) 80:77
https://doi.org/10.1007/s11130-025-01316-9

REVIEW

Mycochemistry, Traditional Uses, and Nutraceutical Potential of *Laricifomes officinalis*: A Biotechnological and Pharmacological Perspective

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Accepted: 4 February 2025

Abstract

Laricifomes officinalis is a medicinal wood-inhabiting fungus renowned for its health benefits, particularly in traditional European medicine for the prevention and treatment of pulmonary conditions such as asthma, pneumonia, and tuberculosis. Beyond its therapeutic applications, *L. officinalis* plays an important ecological role by contributing to nutrient cycling in forest ecosystems. This review provides a comprehensive analysis of the current literature on *L. officinalis*, focusing on its phytochemical composition, traditional uses, pharmacological potential, and conservation status. The species is a rich source of bioactive compounds, including coumarin derivatives, indole compounds, phenolic compounds, polysaccharides, terpenoids and sterols, which exhibit a wide array of biological activities, such as antibacterial, anticancer, antifungal, anti-inflammatory, antioxidant, and antiviral effects. Drawing on extensive searches in scientific databases including Google Scholar, PubMed, Scopus, and Web of Science, this review examines the distribution, ecological significance, taxonomy, and pharmacological applications of *L. officinalis*. Given the growing threats of overexploitation and habitat loss, the conservation of *L. officinalis* is crucial. This review discusses various sustainable cultivation strategies, including establishing culture collections and regulating biosynthetic activity through LED and laser light techniques, show potential for preserving and enhancing the production of its bioactive compounds. Despite recent advances, further research is required to better understand the pharmacological efficacy and safety of *L. officinalis*, thereby unlocking its full medicinal potential for future therapeutic applications. This review underscores the necessity of integrating ecological conservation with pharmaceutical research, highlighting the dual importance of *L. officinalis* in natural ecosystems and therapeutic applications.

Keywords Bioactivity · Ethnomedicine · Fungal metabolites · Health benefits · Medicinal macrofungi · Sustainable cultivation

Introduction

Wood-inhabiting macrofungi are crucial to forest ecosystems, functioning as primary decomposers that break down lignin and cellulose to enrich soil and support plant growth, whether saprophytes feeding on dead organic matter or parasites infecting living trees [1, 2]. Their diverse fruiting bodies contribute to biodiversity, traditional medicine, food, and biotechnology [3–7]. Understanding the diversity and ecological roles of forest mushrooms is crucial for sustainable forest management. For example, knowledge of their decomposition processes can inform strategies to improve soil fertility and the resilience of forests to climate change. Growing interest in these macrofungi has stimulated the development of "mycosilviculture," a forestry practice that integrates mushroom cultivation with traditional silviculture to improve forest productivity while promoting mushroom availability [8]. Numerous wood-inhabiting macrofungi are valued for their medicinal properties, including *Ganoderma lucidum* (Reishi) [5, 9–12], *Inonotus obliquus* (Chaga) [13], *Phellinus linteus* (Black hoof mushroom) [14, 15] and *Trametes versicolor* (Turkey tail) [7, 8, 11, 16–18]. These species offer immune-boosting, anti-inflammatory, and antioxidant effects [9–19]. *G. lucidum*, known as Reishi or "the mushroom of immortality," has been used for thousands of years in traditional Chinese medicine, with triterpenoids and polysaccharides showing therapeutic potential [9, 11, 12]. Similarly, *P. linteus*, found on mulberry trees,

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Published online: 24 February 2025

is used in Chinese and Korean medicine for anticancer and immune-enhancing effects [14, 15]. *T. versicolor*, or Turkey tail, contains polysaccharopeptides that stimulate the immune system and are used as complementary cancer therapy [11, 17, 18]. *I. obliquus*, or Chaga, primarily grows on birch trees and is valued in Siberian and Scandinavian medicine for its high antioxidant content and immune support [13]. Often consumed as tea or extract, chaga exemplifies the connection between traditional knowledge and modern science.

Laricifomes (*Fomitopsidaceae*) consists of wood-decaying macrofungi mainly associated with coniferous trees, particularly larch (*Larix* spp.). These macrofungi have robust, woody fruiting bodies and function as decomposers, breaking down lignin and cellulose to support forest nutrient cycling [20]. *L. officinalis* (Vill.) Kotl. & Pouzar, commonly found on *Larix decidua* in mountainous areas, is a brown-rot agent known for its large, shelf-like fruiting bodies [20, 21]. Originally described by Elias Magnus Fries in 1821 as *Fomitopsis officinalis* (historically known as Agarikon), it was once widely distributed in temperate and boreal forests across Siberia, Europe, and North America [20–24]. Recent molecular studies have confirmed its unique taxonomic distinction, giving it the current designation *Laricifomes officinalis* [25]. This underlines its ecological role as a decomposer and its medicinal significance, particularly due to bioactive compounds with notable therapeutic potential [25].

Historically, *L. officinalis* has been recognized for its medicinal properties, especially in Siberian folk medicine, for its immune-boosting and anti-inflammatory effects [20, 21, 25–28]. It is also utilized in European, Chinese, and Tibetan medicine [20]. Recent studies have identified bioactive compounds such as agaricinic acid and chlorinated coumarins with antibacterial and antiviral properties, effective against gram-negative bacteria, *Mycobacterium tuberculosis*, herpes simplex virus, Orthopoxvirus, avian influenza (H5N1), and human influenza (H3N2) [27]. Furthermore, FOBP90-1, a purified polysaccharide from *L. officinalis*, displayed notable anticancer activity in zebrafish models [29], while other research has demonstrated that low-intensity laser light may serve as regulators of the biosynthetic activity of this species, influencing growth, polysaccharide synthesis, and total phenolic content [30]. In the early 20th century, overharvesting driven by pharmaceutical interest led to significant population declines of *L. officinalis*, exacerbated by deforestation [20]. As a result, it was classified as Endangered by the IUCN in 2019 [31], while in Lithuania it is considered to be extinct [32]. Additionally, Blanchette et al. [23] reported that *L. officinalis* is unique among brown rot fungi for producing large mycelial mats suitable for crafting items like wall pockets. The Tlingit people also used these mats for textiles, highlighting indigenous uses and potential spiritual significance associated with this fungus. Also, due to its medicinal significance, conservation efforts are a priority, including maintaining 14 strains in culture collections as per the World Federation of Culture Collections (WFCC) [33, 34]. Studying these strains supports taxonomic identification and biotechnological cultivation.

This review explores the phytochemistry, traditional uses, and pharmacological benefits of *Laricifomes officinalis*, focusing on its anticancer, anti-inflammatory, antimicrobial, and antioxidant properties, as well as its ecological importance and potential for nutraceutical and pharmaceutical applications. Additionally, it identifies research gaps and proposes future directions for drug discovery and therapeutic exploration.

Methodology

Data Collection and Analysis

To ensure a comprehensive understanding of *Laricifomes officinalis*, data were gathered from a wide range of sources, including research articles, monographs, and books from both indexed and non-indexed journals. A systematic research strategy was employed, utilizing multiple online bibliographic databases, such as Google, Google Scholar, PubMed, Scopus, Semantic Scholar, Springer, Web of Science, and ScienceDirect. The search focused on scientific articles using the keywords "*Laricifomes officinalis*" and its synonyms "*Fomitopsis officinalis*" and "*Fomes officinalis*" in combination with terms related to diversity, geographical distribution, habitat preferences, taxonomy, morphological characteristics, ethnomycological and ethnomedicinal significance, bioactive compounds and pharmacological properties.

In addition to these online resources, local libraries and personal documents were also consulted. The search covered publications available from 1992 to 2024, and identified over 100 scientific sources. Relevant studies were selected based on their contributions to understanding the species' diversity, geographical distribution, habitat preferences, taxonomy, morphological characteristics, ethnomycological and ethnomedicinal significance, bioactive compounds, therapeutic applications, antimicrobial properties, and overall value as a medicinal macrofungus. Furthermore, the reference lists of the 80 selected studies were reviewed to gather further detailed and accurate information. Data analysis involved synthesizing information from multiple languages, predominantly English, to ensure a thorough understanding of the topic. The analysis focused on the biological and ecological attributes of the species, as well as its ethnomycological and therapeutic importance.

Fig. 1 *Laricifomes officinalis*, Poland (Photo credit: Jacek Piętka)

Mycology, Distribution, and Ecology of *Laricifomes officinalis*

Laricifomes officinalis (Vill.) Kotl. & Pouzar (Fig. 1) has robust, woody, shelf-like fruiting bodies on larch trees, with a tough, fibrous texture and brown to dark surface. Belonging to the Fomitopsidaceae, it inhabits temperate and boreal forests, growing on dead or decaying larch. It plays a key role in wood decomposition, supporting nutrient cycling and forest health, while also having historical significance in traditional medicine.

Description: Basidiomata perennial, sessile, solitary, typically ungulate to columnar, up to 0.5 m in height. Upper surface chalky white to cream, aging to brownish or grey, often inhabited by green algae, sulcate, azonate or slightly zonate. Margin rounded, glabrous, matching upper surface. Hymenium cream to brownish, pores round, 4–5 per mm, dissepiments becoming lacerate with age. Context chalky white, yellowish when fresh, soft to hard with age, up to 12 cm thick. Tube layers concolorous, stratified, up to 1 cm thick per layer. Hyphal system dimitic; generative hyphae 2.5–7 µm wide, skeletal hyphae 5–6 µm wide, lactiferous hyphae abundant, up to 13 µm wide, staining in cotton blue. Sclerids present; cystidia absent, fusoid cystidioles present. Basidia clavate, 4-sterigmate, with a basal clamp. Basidiospores cylindrical to ellipsoid, 6–9 × 3–4 µm. This species is inedible, characterized by a floury smell and a notably bitter taste [20].

Distribution and Ecology: *L. officinalis* thrives in moist, shaded environments, primarily on larch but also on other conifers. It is found in temperate and boreal regions of the Northern Hemisphere, on *Larix* and *Cedrus* in Eurasia and North Africa, and on *Abies*, *Picea*, *Pinus*, *Pseudotsuga*, and *Tsuga* in North America. Common in Siberia and Europe, it decomposes wood, aiding nutrient cycling and ecosystem health, while interacting with various organisms [20, 35, 36].

Bioactive Metabolites and Mycochemistry of *Laricifomes officinalis*

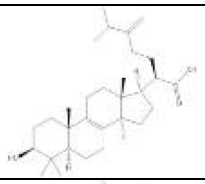
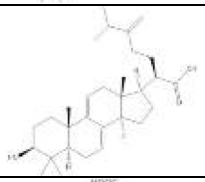
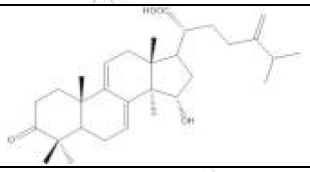
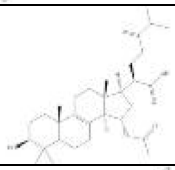
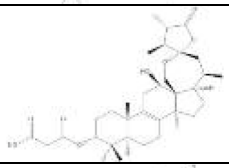
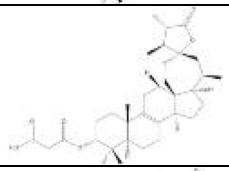
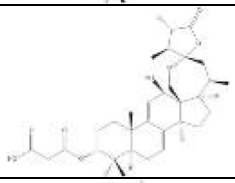
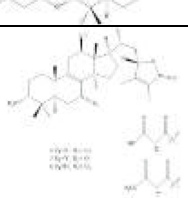
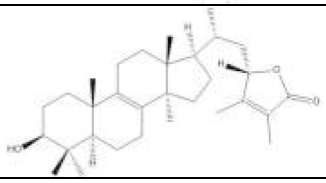
Recent studies have identified a variety of bioactive compounds in *L. officinalis*, including lanostane-type triterpenoids, sesquiterpenoids, sterol derivatives, polysaccharides, phenolics, and indole compounds (Table 1). These compounds contribute to its pharmacological potential and were identified using methods such as chromatographic techniques, Fourier Transform Infrared Spectroscopy (FTIR), and nuclear magnetic resonance (NMR) spectroscopy (Table 2) [20, 25–27, 29]. Key compounds include fefresin F-G acids, fomefficinic F-G acids, fomefficinols A-B, fomlactones A-C, laricinolic acid, ergosterol, and ergosta-7,22-dien-3-β-ol [37–42]. According to Wu et al. [43, 44], terpenes and steroid compounds are the primary active constituents of this species and likely account for the biological effects observed in its crude extracts. These primary and secondary metabolites, alongside essential minerals, are believed to be responsible for the fungus's antioxidant, antimicrobial, anticancer, and anti-inflammatory activities [25, 28]. This section provides a comprehensive overview of these metabolites and minerals in *L. officinalis*, highlighting their biological significance and therapeutic potential [20].

Primary Metabolites

Primary metabolites play a crucial role in the physiological processes of *L. officinalis*, encompassing essential vitamins, fatty acids, sterols, and amino acids [20]. Mykchaylova and Poyedinok [45] summarized the presence of various unsaturated fatty acids, including palmitic, oleic, linoleic, linolenic, and arachidonic acids, which are critical for maintaining cellular membrane structure and function. Furthermore, sterols such as ergosterol and ergosta-7,22-dien-3-β-ol were identified using various techniques, including gas chromatography–mass spectrometry (GC–MS), high-performance liquid chromatography (HPLC) and FTIR, contributing to the structural stability of fungal cell membranes [20].

The detection of B-group vitamins, along with vitamins E and A, in both the basidiomata and mycelium undersores their potential role in supporting metabolic functions and enhancing antioxidant defenses [45]. Furthermore, significant concentrations of phenylalanine were identified exclusively in the mycelium through high-performance liquid chromatography with diode-array detection (HPLC–DAD) analysis, with a measure concentration of 346.48 ± 4.0

Table 1 List of chemical compounds of *Laricifomes officinalis*

Class of compounds	Name of compound	Structure
Triterpenoids		
Lanostane-type triterpenes	Eburicoic acid	
	Dehydroeburicoic acid	
	3-Ketodehydrosulfurenic acid	
	Versisponic acid D	
	Officimalonic acid I	
	Officimalonic acid J	
	Officimalonic acid K	
	Officimalonic acid L-N	
	Officimalonic acid O	

mg/100 g dry weight (d.w.) [28]. Moreover, L-tryptophan was quantified at 70.08 mg/100 g in fruiting bodies and 8.06 mg/100 g in mycelium [28]. Recently, Spano et al. [46] tested dehydrated mycelia from four species, including *L. officinalis*, using NMR spectroscopy to identify and quantify amino acids and derivatives, sugars and polyols, organic

Table 1 (continued)

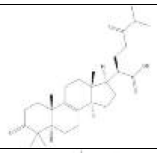
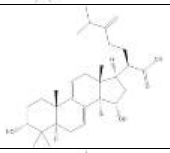
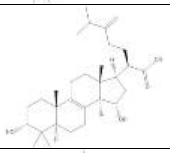
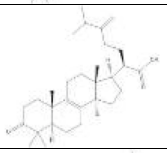
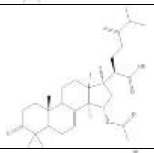
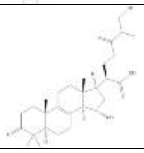
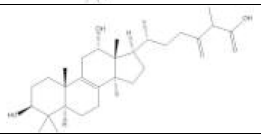
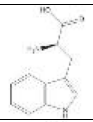
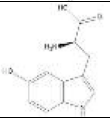
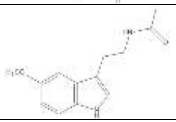
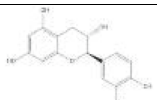
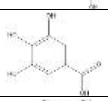
Sesquiterpenoids	Fomefficinic acid A	
	Fomefficinic acid B	
	Fomefficinic acid C	
	Fomefficinic acid D	
	Fomefficinic acid E	
	Fomefficinic acid F	
	Fomefficinic acid G	
Indoles		
	L-tryptophan	
	5-Hydroxy-L-tryptophan	
	Melatonin	
Phenolic compounds		
	Catechin	
	Gallic acid	
	p-Hydroxybenzoic acid	

Table 2 Mycochemical composition and pharmacological applications of *Laricifomes officinalis* across different regions

Country	Sample	Type of analysis	Class of compounds	Pharmacological property	References
China	MeOH extract	IR spectroscopy and ^{1}D and ^{2}D NMR	**Lanostane type triterpenoids**: officimalonic acids A-H and fomitopsin A	Anti-inflammatory activity measured by NO production inhibition, and cytotoxic	[48]
	EtOAc and *n*-BuOH extracts	IR spectroscopy	**Lanostane type triterpenoids**: officimalonic acids E, G, H	Cytotoxic	[48]
	Fruiting bodies extract	–	**Lanostane-type triterpenes**: fomitopsin C, 3-keto-dehydrosulfurenic acid, dehydroeburiconic acid, 3-acetyloxylanosta-8,24-dien-21-oic acid, pinicolic acid A, trametenolic acid B, and eburicoic acid	Anticancer	[47]
	Flavonoids	–	**Flavonoids**	Ex vivo antioxidant activity (CAT, GSH-Px and SOD) and anti-aging	[69]
	Homogeneous heteropolysaccharide (FOBP90-1)	FTIR, NMR and Congo red assay	**Heteropolysaccharide**: (→6)-α-D-Gal*p*-(1→, →2,6)-α-D-Gal*p*-(1→, →3)-α-L-Fuc*p*-(1→, →6)-β-D-Glc*p*-(1→, α-D-Man*p*-(1→, and 3-*O*-Me-α-L-Fuc*p*-(1→))	Cytotoxic, in vitro and in vivo antitumor	[29]
Italy	EtOH extracts of the hymenium, median, and apical parts of fruiting bodies	Total phenolic content (FC assay), LC–MS/MS-based metabolomics, HPLC-DAD	**Phenolics**: 27 phenolic compounds	Antioxidant, antibacterial and antifungal	[53]
Mongolia	Dried samples of fruiting body diluted in petroleum ether, $CHCl_3$, EtOAc, and *n*-butanol.	–	**Lanostane-type terpenoids**	Trypanocidal	[42]
	Hot water extract	GC–MS analysis	**Mannofucogalactan**	–	[51]
Poland	EtOH extracts prepared from dried fruiting bodies	FTIR and HPLC–DAD	**Phenolic compounds**: *p*-hydroxybenzoic acid, gallic acid, catechin; **Indolic compounds**: L-tryptophan, 6-methyl-D, L-tryptophan, melatonin, 5-hydroxy-L-tryptophan; **Sterols**: ergosterol, ergosterol peroxide; **Trace elements**	Antioxidant and antiproliferative	[28]
USA	EtOH extract	UV – Vis spectroscopy, FTIR, and NMR	**Chlorinated coumarins**: 6-chloro-4-phenyl-2 H-chromen-2-one, ethyl 6-chloro-2-oxo-4-phenyl-2 H-chromen-3-carboxylate, 7-chloro-4-phenyl-2 H-chromen-2-one, ethyl 7-chloro-2-oxo-4-phenyl-2 H-chromen-3-carboxylate	Antibacterial and cytotoxic	[49]

α-D-Galp α-D-Galactopyranose; *α-L-Fucp* α-L-Fucopyranose; *β-D-Glcp* β-D-Glucopyranose; *α-D-Manp* α-D-Manopyranose; *CAT* catalase; *EtOAc* ethylacetate extract; *EtOH* ethanolic extract; *n-BuOH* n-butanol extract; *MeOH* methanolic extract; *FC* Folin–Ciocalteu assay; *FTIR* Fourier Transform Infrared Spectroscopy; *GSH-Px* glutathione peroxidase; *HPLC* High-Performance Liquid Chromatography; *HPLC–DAD* High-performance liquid chromatography with diode-array detection; *IR spectroscopy* Infrared spectroscopy; *LC–MS/MS* Liquid Chromatography–Tandem Mass Spectrometry; *NMR* nuclear magnetic resonance; *NO* nitric oxide; *SOD* superoxide dismutase

acids, fatty acids, lipid polar heads, and nitrogen-containing compounds. *L. officinalis* was characterized by the highest levels of total amino acids (3644.9 mg/100 g d.w.), essential amino acids (1263.0 mg/100 g d.w.), and sweet amino acids (1994.3 mg/100 g d.w.), whereas the lowest contents of sugars and polyols were found in this sample.

Secondary Metabolites

Triterpenes and Sesquiterpenoids in *Laricifomes officinalis*

The secondary metabolites of *L. officinalis* play a crucial role in its pharmacological activities [20]. Among these, lanostane-type triterpenes are prominent, including eburicoic acid, dehydroeburicoic acid, sulfurenic acid, 3-ketodehydrosulfurenic acid, and versisponic acid D. These compounds exhibit significant antimicrobial, anti-inflammatory, and anticancer activities [20, 43, 47]. Five lanostane-type triterpenes, named fomefficinic acid A-E, were isolated from the dried sclerotium of *L. officinalis* and characterized using NMR spectroscopy (^{1}H, ^{13}C, HMQC, HMBC, NOESY), HR-EI-MS, infrared (IR) spectroscopy, ultraviolet-visible (UV–Vis) spectroscopy, and chromatographic techniques on silica gel and reversed-phase silica gel [38]. Five years later, the same group tested $CHCl_3$-soluble residue fraction of *L. officinalis* using column chromatography on silica gel and repeatedly reversed-phase silica gel, resulting in the isolation of four new triterpenes, fomefficinic acids F, G and fomefficinols A, B, along with seven known compounds. The known compounds were identified as officinalic acid, fomlactone A, fomlactone B, fomlactone C, laricinolic acid, ergosterol, as well as ergota-7,22,dien-3b-ol [39]. A sesquiterpenoid, fomeffic acid, and a triterpene lactone, fomefficinin, were isolated from the fungus *L. officinalis*, along with six known compounds: fomitopsin C, dehydrosulfurenic acid, dehydroeburiconic acid, dehydroeburicoic acid, 3-keto-dehydrosulfurenic acid, and laricinolic acid. Their structures and stereochemistry were determined using NMR and X-ray diffraction analyses [40]. After that, phytochemical investigation of the methanolic (MeOH) extract from the fruiting bodies of *L. officinalis* led to the isolation of eight 24-methyl-lanostane triterpenes, named officimalonic acids A-H. Their structures were elucidated through the analysis of spectroscopic data, single-crystal X-ray diffraction, and electronic circular dichroism. Officimalonic acid A (Table 1) represents a previously unknown triterpene with unusual structure, featuring a 24-methyl-7(8 → 9)*abeo*-lanostane skeleton. All of the compounds contain a malonate half-ester moiety at C-3 [48]. Recently, Han et al. [41] identified seven new 24-methyl-lanostane triterpenoids, referred to as officimalonic acids I – O. Officimalonic acids I-K are notable for their unique C-23 spirostructure moiety, while officimalonic acids L-O contain a 23,26-lactone unit, adding to the structural diversity of bioactive triterpenoids in *L. officinalis* [41] (Table 1). These structures were elucidated using spectroscopic techniques, including ^{1}D and ^{2}D NMR, High–Resolution Mass Spectrometry (HR-MS), IR and UV [41]. Seven lanostane-type triterpenoids as fomitopsin C, 3-keto-dehydrosulfurenic acid, dehydroeburiconic acid, 3-acetyloxylanosta-8,24-dien-21-oic acid, pinicolic acid A, trametenolic acid B, and eburicoic acid, were isolated from the fruiting bodies of *L. officinalis* and *Fomitopsis pinicola* [47].

Additionally, novel lanostane-type terpenoid acids, such as 12β,15α-dihydroxy-24-methyl-3,23-dioxo-lanosta-7,9(11)-dien-26-oic acid and 3α,12β-dihydroxy-24-methyl-7,23-dioxo-lanosta-8-en-26-oic acid, have been isolated from MeOH extracts, expanding the repertoire of known bioactive compounds in this species [25]. These structures were elucidated using spectroscopic techniques, including ^{1}D and ^{2}D NMR, as well as HR–MS [25].

Beyond triterpenes, *L. officinalis* also produces drimane sesquiterpenoids, including fomefficinic acids A-E and F-G, which exhibit significant antiviral and anticancer properties [38, 40].

Sterols and Other Compounds in *Laricifomes officinalis*

Sterols constitute an important group of secondary metabolites found in *L. officinalis*. Various compounds, including fefresin F-G acids, fomefficinols A-B, and fomlactones A-C, have been isolated from this species, contributing to its antimicrobial and anti-inflammatory properties [38–40]. Wu et al. [39] identified presence of ergosterol, and ergosta-7,22-dien-3β-ol in $CHCl_3$-soluble residue fraction of *L. officinalis*. Chlorinated coumarins, another class of secondary metabolites identified in this fungus, also display notable antiviral, anticancer, and anti-inflammatory activities [49]. Ethanolic (EtOH) extracts of *L. officinalis* were found to contain two chlorinated coumarins, 6-chloro-4-phenyl-2 H-chromen-2-one and ethyl 6-chloro-2-oxo-4-phenyl-2 H-chromen-3-carboxylate, along with their analogues, 7-chloro-4-phenyl-2 H-chromen-2-one and ethyl 7-chloro-2-oxo-4-phenyl-2 H-chromen-3-carboxylate. The structures of these compounds were confirmed using ab initio spectroscopic methods and ^{1}H NMR analysis [49].

Additionally, *L. officinalis* contains a variety of unsaturated fatty acids, such as palmitic, oleic, linoleic, and arachidonic acids, which are essential for maintaining cell membrane integrity and proper physiological function [45]. Other bioactive constituents identified include heteropolysaccharides, glucosamines, phospholipids, carotenoids, and essential oils, all of which play significant roles in the pharmacological activities attributed to this medicinal fungus [50].

Polysaccharides, Indole Compounds, and Phenolic Compounds in *Laricifomes officinalis*

Polysaccharides from *L. officinalis* have garnered considerable interest due to their anticancer and anti-inflammatory activities [29]. One example is mannofucogalactan, a key component of water-based extracts from fruiting bodies, structurally characterized and shown to exhibit anticancer properties [51, 52]. Golovchenko et al. [51] identified its branched structure in hot water extracts obtained from the fruiting bodies of *L. officinalis*. The backbone consists of partially 3-*O*-methylated 1,6-*O*-linked α-D-galactopyranosyl residues, with nearly every second residue substituted at *O*−2 by 3-*O*-α-D-mannopyranosyl-α-L-fucopyranosyl and β-D-galactopyranosyl residues, as determined by GC-MS analysis.

Four indole compounds, including L-tryptophan, 6-methyl-D, L-tryptophan, melatonin and 5-hydroxy-L-tryptophan, were found in both fruiting bodies and mycelium. Notably, 5-hydroxy-L-tryptophan, a precursor to serotonin, was identified and quantified only in the mycelium, where it was present in the highest amount among all identified compounds (517.99 ± 5.29 mg/100 g d.w.) [28]. Additionally, melatonin—recognized for its antioxidant effects and regulatory roles in sleep—was also identified in these extracts [28].

Among the phenolic compounds identified in *L. officinalis*, 21 were characterized using HPLC-DAD analysis. Catechin and gallic acid were confirmed as major constituents in the mycelium (58.37 ± 0.90 and 0.09 ± 0.00 mg/100 g d.w., respectively), while *p*-hydroxybenzoic acid was exclusively found in fruiting body extracts (0.07 ± 0.00 mg/100 g d.w.), significantly contributing to the antioxidant potential of this species [28]. Additionally, phenylalanine, an exogenous amino acid, was detected in in vitro cultures. Recently, Flores et al. [53]. used HPLC–DAD analysis to identify 27 phenolic compounds in EtOH extracts of various parts of the fruiting bodies of *L. officinalis*. Among them, flavonol quercetin was the most abundant compound in the extracts from the apical parts of the fruiting bodies (3.307 ± 0.251 µg/mg s.w.), followed by the flavanone hesperitin in the hymenium (1.880 ± 0.041 µg/mg d.w.) and the phenolic monoterpene thymol in the median part of fruiting body (1.682 ± 0.058 µg/mg d.w.). Other identified compounds were present in concentrations below 0.700 µg/mg d.w [53].

Minerals and Cytokinins in *Laricifomes officinalis*

In addition to a diverse array of organic compounds, *L. officinalis* serves as an abundant source of essential trace elements. Both the mycelium and fruiting bodies have demonstrated the ability to accumulate minerals such as zinc, copper, iron, and magnesium, identified using Flame Atomic Absorption Spectrometry (F–AAS). These minerals are essential for numerous enzymatic and antioxidant processes. Notably, mycelium contains significantly higher concentrations of zinc (15.34 mg/100 g) and iron (12.06 mg/100 g) compared to the fruiting bodies, while the latter exhibits elevated levels of copper [28]. Similarly, another study reported that the lowest amounts of magnesium and zinc were detected in the fruiting bodies of *L. officinalis* (132.1 and 15.3 mg/100 g d.w., respectively), while the highest amounts were observed in mycelium cultivated on a medium enriched with sulfate salts (1261 and 182.8 mg/100 g d.w., respectively) [26].

The cytokinin profile in *L. officinalis* mycelial biomass varies throughout distinct growth stages. Vedenicheva et al. [54] identified and quantified cytokinins in the mycelial biomass of 13 species, including *L. officinalis*, using high-performance liquid chromatography–mass spectrometry (HPLC–MS). Among the cytokinins, zeatin riboside and zeatin-*O*-glucoside were identified as the predominant cytokinin nucleosides, suggesting their key role in regulating mycelial growth and developmental processes [54].

Traditional Medicinal Applications of *Laricifomes officinalis*

Traditionally, *Laricifomes officinalis*, commonly known as Agarikon or Gharikon, has been used for its medicinal properties, particularly in the treatment of respiratory ailments, with historical references dating back to ancient Greece [55]. The earliest known documentation of Agarikon dates to the 1st century AD, when the Greek physician Dioscorides described its use in treating "consumption"—a term often associated with wasting diseases like tuberculosis [55]. In ancient Rome and Greece, this species was widely recognized as an effective remedy for tuberculosis, known then as 'agarikon' or 'agaricum' [20]. Agarikon has a long-standing global history in traditional medicine, where it has been valued for supporting respiratory, immune, and antimicrobial health (Fig. 2).

Figure 2 illustrates the diverse medicinal applications of *L. officinalis* across various cultures, highlighting its use in Europe for lung health, in North America for medicinal and spiritual purposes, and in the Middle East and Asia for treating respiratory and immune disorders. Furthermore, in Persian, *L. officinalis* (Agarikon) is known as "ghariqoun," with historical use in Arabic medicine for conditions like pulmonary tuberculosis [55, 57, 58]. Widely used in traditional medicine across Arab countries [59], Iran [58], Nigeria [60], and Mongolia [42], Agarikon's benefits were recorded by the 9th -century physician Ali ibn Abbas, who advocated its use as a purgative for cancer due to its detoxifying effects, earning it the name "*Boletus purgans*" [61, 62]. From the 9th to 10th centuries, it was used for pain, inflammation, jaundice, fever, bladder issues, sciatica, and rheumatism, with diuretic, anticoagulant, menstrual, and immune-boosting properties [55, 57, 61]. In the Middle Ages, Agarikon was used to treat

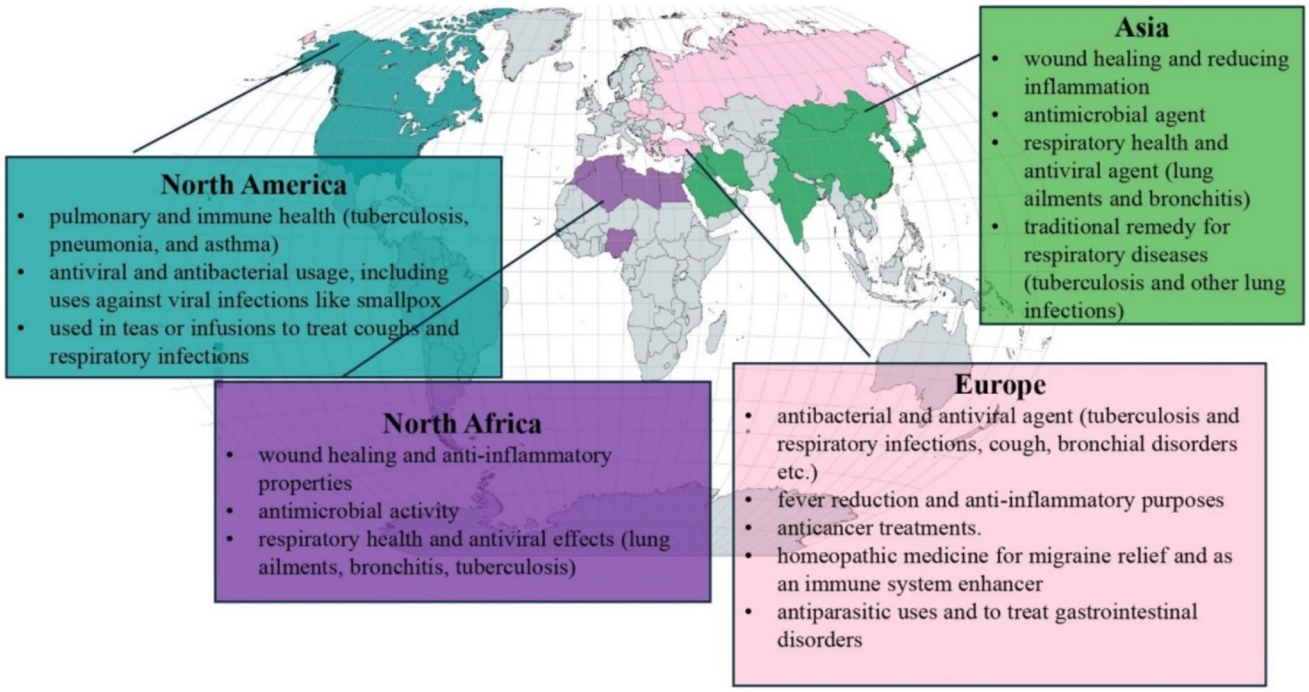


Fig. 2 Geographical distribution of traditional medicinal uses of *Laricifomes officinalis* globally (Map created using MapChart) [56])

battle wounds in Eastern Europe [57] and was recognized as a medicinal mushroom in 1613 by Syrenius in the *Cracovian Herbarium* [63]. It was also a component of Swedish Bitters in the 1730s, mixed with aloe juice, turmeric, and saffron [64]. Modern studies highlight its laxative, antiparasitic, and anti-inflammatory effects, especially for asthma and tuberculosis due to lanostane triterpenoids, valuable in light of antibiotic resistance concerns [42]. In homeopathy, it is used for migraines [65] and supports metabolism, weight management, bile production, and blood pressure regulation. Decoctions are used as sedatives for neurosis, headaches, and gout, and they also serve as mild sleep aids. Agarikon shows potential for cancer, liver disease, constipation, dysbiosis, and respiratory conditions like bronchitis and pleurisy; the powder also offers hemostatic and antimicrobial benefits [55, 66, 67].

The Agarikon pill (AGKP) is a traditional Uyghur medicine first recorded in the medicinal text *KarabadanKadiri* (1780) for treating lung ailments, phlegm, cough, and asthma. It is registered by the Uyghur Medical Hospital of Xinjiang (approval number M20041561) and included in the Drug Standard of the Chinese Ministry of Public Health's Uyghur medicine section. AGKP contains *L. officinalis* (formely *Fomes officinalis*) and five herbs: *Glycyrrhiza uralensis* L., *Citrullus colocynthis*, *Operculina turpethum*, *Aloe vera*, and *Astragalus sarcocolla* [68].

Heritage Crafts and Cultural Significance

The fruiting bodies of *L. officinalis* have historically played an important role in the cultural and spiritual practices of indigenous peoples in ancient North America. These fruiting bodies were used to craft ritual figurines believed to possess supernatural abilities, enabling communication with the spirit realm. Following the death of a Shaman, these figurines, known as "grave sentinels", were often placed at burial sites to ward off intruders, as it was believed that the Shaman's spirit resided within. Today, many of these figurines are preserved in museum collections, offering valuable insights into the cultural heritage and spiritual beliefs of these communities [22].

Veterinary Uses

In veterinary practice, the fruiting bodies of *L. officinalis* have been utilized for the prevention of various digestive disorders in cattle grazing in the Western Alps of Italy, including conditions such as indigestion, bloating, and gastric ulcers [62]. Traditionally, this species has been regarded as a panacea, employed in the treatment of a wide range of ailments, including cancer, digestive disturbances, dizziness, dysmenorrhea, excessive sweating, excretory diseases, hemorrhoids, respiratory conditions, and rheumatism. Moreover, it has been used as a helminthagogue, with high doses believed to induce emesis, whereas lower doses have been utilized for their diuretic effects [28].

Pharmacological Properties of *Laricifomes officinalis*

L. officinalis has shown substantial pharmacological potential, as highlighted by Gafforov et al. [20], who identified its antibacterial, antifungal, anti-inflammatory, antitumor, antiviral, and immunostimulatory activities (Table 2). This species has also been traditionally utilized to manage gastrointestinal disorders, respiratory conditions, and night sweats.

Antimicrobial Properties

The broad-spectrum antimicrobial properties of *L. officinalis* have been extensively documented. Girometta [27] reported its antibacterial and antiviral activities against pathogens such as *Mycobacterium tuberculosis*, *Yersinia pseudotuberculosis*, *Staphylococcus aureus*, and Ortho pox viruses. These effects are attributed to chlorinated coumarins in the mycelium and lanostane triterpenoids in the basidiomes, which contribute to its antibacterial, antiviral, and trypanocidal properties of *L. officinalis* [27]. Bold et al. [70] demonstrated that "Fomitop" gel, containing *L. officinalis* extracts (under synonym *Fomitopsis officinalis*), exhibits antibacterial properties against strains like *S. aureus* and *Enterococcus faecalis* and promotes faster healing in burn wounds compared to silver sulfadiazine, with full wound recovery observed by day 33 in treated mice.

Research on raw EtOH extracts from four medicinal basidiomycetes demonstrated that *L. officinalis* can inhibit certain bacterial strains, including Gram-positive bacteria (*Bacillus thuringiensis*, *S. aureus*) and Gram-negative bacteria (*Enterobacter aerogenes*, *Klebsiella pneumoniae*), albeit with high minimum inhibitory concentrations [71]. Chlorinated coumarins isolated from *L. officinalis* exhibited activity against *M. tuberculosis*, with minimum inhibitory concentrations (MICs) ranging from 20 to 50 µg/mL, demonstrating their potential as anti-tuberculosis agent [49]. Coumarin compounds derived from this species demonstrated inhibitory activity against various bacterial and fungal strains, including *Agrobacterium tumefaciens*, *B. cereus*, *B. subtilis*, *Escherichia coli*, *Salmonella typhimurium*, and *S. aureus*. However, they exhibited weaker effects against *Acinetobacter baumannii*, *Candida albicans*, *E. faecalis*, *M. smegmatis*, *M. tuberculosis*, *Pseudomonas aeruginosa*, and *Streptococcus pneumonia* [72].

Several isolated compounds, such as 6-chloro-4-phenylcoumarin and ethyl 6-chloro-2-oxo-4-phenyl-2 H-chromen-3-carboxylate, exhibited considerable antimicrobial potential [49, 64]. Sidorenko and Buzoleva [73] also confirmed the antibacterial activity of mycelium extracts, suggesting potential utility in treating pseudotuberculosis and infections caused by *Pseudomonas* spp. Mykchaylova and Poyedinok [45] found that ethylacetate (EtOAc) extracts from *L. officinalis* strongly inhibited *S. aureus* (15–25 mm inhibition zones) and moderately inhibited *K. pneumoniae*, with no activity against *B. subtilis*, *E. coli*, or *P. aeruginosa*.

Antiviral Properties

L. officinalis is well-recognized for its antiviral properties [62]. Studies from the United States have identified significant antiviral activity among almost 100 mushroom species, including *L. officinalis*, particularly against the varicella-zoster virus. In traditional Iranian medicine, it has also been used to combat smallpox, influenza H5N1, and hepatitis C, with antiviral effects largely attributed to lanostane-type triterpenoids [57]. Specific compounds such as fomitopsin D have demonstrated activity against herpes simplex virus type 1 (HSV-1), while fomitopsin F has shown efficacy against *B. cereus* [28]. Extracts of *L. officinalis* have also shown direct antiviral effects against the cowpox virus [28].

Even at low concentrations (1–2%), extracts of *L. officinalis* have been shown to inhibit virus-induced cell damage by 50%. Furthermore, crude extracts diluted to a 1:106 ratio have demonstrated efficacy against influenza A and B viruses, as well as herpes viruses, potentially preventing neuropathies linked to herpes and hepatitis C infections [74].

Antiparasitic Properties

Lanostane-type terpenoids derived from *L. officinalis* have demonstrated inhibitory effects on *Trypanosoma congolense*, the causative agent of nagana, a disease that affects livestock. These findings underscore the potential applications of *L. officinalis* in treating parasitic infections, though further research is needed [40, 42, 49, 60].

Antioxidant and Anticancer Properties

Free radicals, such as like superoxide anion and hydroxyl radicals, contribute to oxidative stress and cellular damage. While the body`s enzymatic defenses (e.g., superoxide dismutase, catalase), help mitigate these effects, antioxidant supplements can provide additional protection [11, 16]. Certain macrofungi, including *L. officinalis*, have demonstrated the ability to inhibit cancer cell proliferation [25, 29, 40, 47, 52, 75].

For instance, Feng et al. [40] isolated a novel sesquiterpenoid (fomeffic acid) and a new triterpene lactone (fomefficinin) from *L. officinalis*, both of which exhibited significant cytotoxic activity against cancer cell lines such as HL-60, Bel-7402, and KB. Another group of triterpenes, officimalonic acids A-H (Fig. 3), demonstrated anti-inflammatory and cytotoxic properties against human cancer cells, including H460, HepG2, and BGC-823 [25].

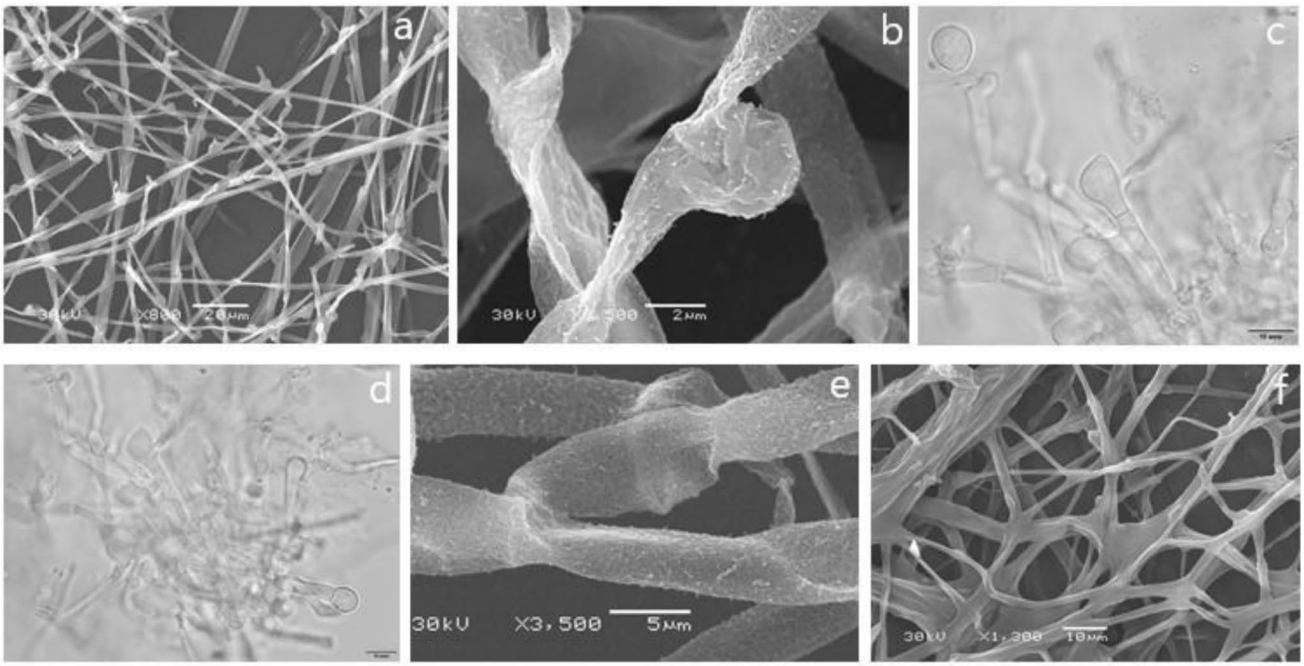


Fig. 3 Micromorphology of *Laricifomes officinalis*: **a** vegetative mycelium with clamp connections (SEM, ×8000); **b** clamp connections (SEM, ×6500); **c**, **d** apical blastoconidia on hyphae (×100); **e** hyphae with crystals (SEM, ×3500); **f** mycelial cords and mycelial films (SEM, ×1300) [33]

Neuroprotective and Anti-inflammatory Properties

An in vivo study showed that flavonoids from *L. officinalis* exhibit anti-aging effects in mice by boosting antioxidant activity in the brain, spleen, and thymus, elevating brain glutathione peroxidase, and increasing liver catalase and superoxide dismutase levels [69]. Although evidence directly linking these compounds to improved brain function is limited, Sha [69] reported that six weeks of daily flavonoid administration reduced oxidative stress in aging mice brains, potentially benefiting conditions like Alzheimer's, Parkinson's, multiple sclerosis, and Huntington's disease [11].

The antioxidant activity of *L. officinalis* may benefit conditions related to oxidative stress, such as epilepsy and depression [76]. Flavonoids in *L. officinalis* may enhance brain function by activating intracellular kinases that regulate CREB (cAMP response element-binding protein), essential for synaptic plasticity [77]. Recent studies also suggest that flavonoid activation of the CREB-BDNF pathway may contribute to anti-epileptic effects [77].

Han et al. [41] evaluated the anti-inflammatory activity of seven newly isolated 24-methyl-lanostane triterpenoids by assessing their effects on NO production in LPS-induced RAW264.7 cells. The anti-inflammatory assay showed that officimalonic acids K and M significantly inhibited NO production and cyclooxygenase (COX-2) in LPS-induced RAW 264.7 cells [41]. Dehydrosulfurenic acid, a unique triterpenoid found in *L. officinalis*, has been patented for the treatment of ischemic stroke, demonstrating potential in reducing motor deficits and neuronal injury in a rat model [78]. Eburicoic acid (Table 1), a lanostane triterpenoid, exhibits anti-inflammatory effects by inhibiting pro-inflammatory cytokines in macrophages without cytotoxicity, potentially offering antidepressant benefits due to the link between inflammation and depression [20].

Micromorphology, Cultural Characteristics of Pure Cultures of *L. officinalis*

Current efforts to ensure the conservation of genetic diversity and biotechnological application of *L. officinalis* include the maintenance of strains of different geographical origins in culture collections [33, 79]. These collections provide crucial resources for studying the morphological and cultural characteristics of the strains, supporting taxonomic identification and enabling biotechnological cultivation aimed at producing mycelial biomass and biologically active compounds. Existing data on the morphological and cultural characteristics of *L. officinalis* have been gathered to support these conservation efforts [33, 34]. Micromorphological analysis of *L. officinalis* vegetative mycelium was conducted using a scanning electron microscope (SEM) (Fig. 3). The vegetative mycelium consists of thin-walled, septate, and branching hyphae with diameters ranging from 1.2 to 3.5 µm. Numerous single clamp

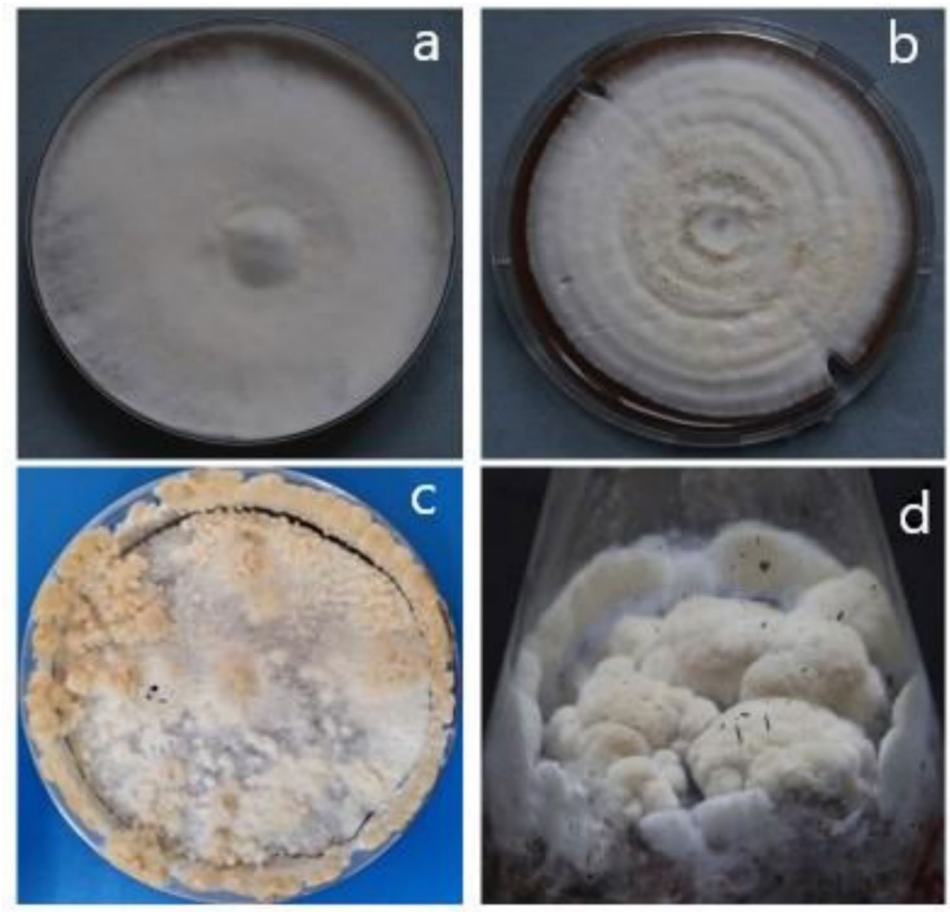


Fig. 4 Morphology of *Laricifomes officinalis* mycelial colonies grown on agar nutrient media and plant substrates: **a** malt extract agar (MEA), after 20 days of cultivation; **b** MEA, after 30 days of cultivation; **c** glucose-peptone-yeast agar, after 30 days of cultivation; **d** plant substrate (larch sawdust), after 40 days of cultivation [33]

connections are observed on the hyphae, along with a small number of anastomoses, mycelial cords, and films. Hyphal incrustation in the form of thin villi was also noted (Fig. 3a-b, d). Thick-walled, ellipsoid-shaped blastoconidia are formed on the vegetative mycelium, measuring between 5.21 and 5.57 µm in length and 4.135 to 4.61 µm in width (Fig. 3c-d). On the 30th day of cultivation, blastoconidia concentrations ranged from $6.1 \pm 0.3 \times 10^7$ to $7.5 \pm 0.3 \times 10^8$ pieces/cm².

The morphology of mycelial colonies reveals dense, woolly growth (Fig. 4a). As the colonies age, they become powdery and occasionally take on a light cream hue (Fig. 4c). Colony edges are smooth and slightly raised above the substrate, and over time, exudate may form (Fig. 4b). The reverse side of the colonies mirrors the color of the medium. Colonies produce a faint mushroom-like or slightly fruity odor. Primordia formation may occur under specific conditions, such as light exposure (Fig. 4c, d). The rate of radial growth on agar media ranges from 1.9 to 3.2 mm per day, with an optimal cultivation temperature of 26 °C and a critical upper temperature limit of 41 °C The conservation of *L. officinalis* is vital due to its declining population and pharmacological importance. Currently, culture collections are essential for preserving genetic diversity, supporting species protection, and enabling biotechnological applications. Understanding the micromorphology and growth characteristics of *L. officinalis* is a key to successful conservation and restoration efforts, which aim to exploit its bioactive properties for therapeutic purposes while preserving this important fungal species in its natural habitat.

New Approaches to Light-mediated Regulation of Biomass and Metabolite Synthesis in *L. officinalis*

Biotechnology for the cultivation of medicinal macrofungi is a promising tool for achieving several UN global Sustainable Development Goals (SDGs) related to food security, health and environmental protection [4]. Since 2000, medicinal mushroom components, such as L-ergothioneine, lycopene, and β-glucans, have been recognized as novel foods, prompting ongoing searches for new species like *L. officinalis* [4, 11] The development of new intensive biotechnologies using innovative cultivation methods allows us to fully utilize the natural potential of producer strains for the production of natural biologically active compounds, expanding the range of their application in the food industry, pharmacology and medicine [80]. Of particular relevance is the development of scientifically sound methods for enhancing the synthesis of biologically active substances using environmentally friendly physical factors,

in particular low-intensity artificial light [30]. Light has proven to be a promising growth regulator for enhancing the synthesis of certain bioactive compounds during cultivation. The spectral sensitivity of *L. officinalis* for synthesizing mycelial mass, polysaccharides, and fatty acids was investigated using laser and LED irradiation at different wavelengths [30]. LEDs emitted light at 470 nm (blue), 530 nm (green), and 650 nm (red), while an argon laser emitted coherent light at 488 nm. Low-intensity light irradiation increased biomass and polysaccharide production, with blue light (470–488 nm) yielding the highest biomass (> 14.7 g/l by day 12). All wavelengths promoted exo- and endopolysaccharide synthesis, with blue light providing the highest increases. Red and green LED irradiation also altered the fatty acid profile, increasing linolenic acid (C18:2 ω−6) and pentadecenoic acid (C15:1), while reducing palmitic acid (C16:0) and oleic acid (C18:1 ω−9). These findings suggest that low-intensity LED light is a viable tool for regulating the biosynthetic activity of *L. officinalis* [30].

Conclusion and Future Perspectives

Laricifomes officinalis is a valuable medicinal and nutritional resource with significant applications in traditional medicine. This review highlights its ethnomycological importance and pharmacological potential, focusing on its antibacterial, anticancer, antifungal, anti-inflammatory, and antioxidant activities, as well as its use as a dietary supplement Conservation efforts for *L. officinalis* are crucial due to overexploitation and habitat loss, requiring targeted strategies. New approaches, such as maintaining genetic resources in culture collections and regulating biosynthetic activity using LEDs and low-intensity laser light, show promise for sustainable cultivation and optimization production of bioactive compounds. The decline in the transfer of traditional knowledge highlights the need for further phytochemical and pharmacological research to value the full potential of *L. officinalis* Future studies should prioritize innovative preservation techniques, advanced biotechnological interventions, and pharmaceutical development to effectively exploit the therapeutic properties of *Laricifomes officinalis*. Specific molecular mechanisms, such as regulation of inflammatory pathways (e.g., NF-κB, COX-2) and apoptosis-related proteins (e.g., caspases, Bcl-2 family), merit further investigation to elucidate the biological effects of the bioactive compounds. Additionally, omics-based approaches, including metabolomics and proteomics, could unveil novel secondary metabolites and their biosynthetic pathways, thereby expanding our understanding of the species' pharmacological potential Advanced extraction techniques, such as supercritical fluid extraction and ultrasound-assisted extraction, should be explored to improve the eco-friendliness and efficiency of isolating bioactive compounds. The application of biotechnological tools, such as LED and laser light technology, could be further optimized to regulate the biosynthesis of valuable metabolites under controlled conditions. This review recommends focusing future research efforts on the conservation and sustainable use of *L. officinalis* to achieve the development of innovative pharmaceutical and cosmetic products, including fungal bioactives and mushroom-enriched food products. By integrating these advanced methods, the full medicinal and biotechnological potential of *L. officinalis* can be exploited.

Acknowledgements The authors gratefully acknowledge Dr. Sándor Farkas from the International Centre for Genetic Engineering and Biotechnology, Trieste (Italy), for his help in preparing the chemical structures of selected compounds.

Author Contributions YG: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Supervision, Writing – original draft, Writing – review and editing; MR: Methodology, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review and editing; OM: Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review and editing; SR: Validation, Investigation, Resources, Writing – review and editing; MK: Visualization, Writing – review and editing; JM: Investigation, Visualization, Writing – review and editing; Şİ: Investigation, Writing – review and editing; MY: Investigation, Writing – review and editing; AMA: Writing – review and editing; SG: Formal analysis, Writing – review and editing.

Funding The research was financed by Agency for Innovative Development under the Ministry of Higher Education, Science, and Innovation of the Republic of Uzbekistan (No AL-8724052922-R3) and CAS PIFI (Grant no. 2022VBA0021), Institute of Botany (IBK) Mushroom Culture Collection and Biological Activity of Strains of the Mushroom Culture Collection of IBK (Project No. 0120U10111).

Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical Approval and Consent to Participate Not applicable.

Consent for Publication All authors agreed to participate in the paper.

Competing Interests The authors declare no competing interests.

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