



REVIEW ARTICLE

THE MYCOLOGICAL ARSENAL: UNVEILING THE ANTICANCER POTENTIAL OF MUSHROOMS

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Received: Jun 16 2025; **Accepted:** Jul 26;2025; **Published:** Aug.16,2025

Abstract

Fungi have long been recognized in traditional medicine for their healing properties, and contemporary research increasingly points to their significant potential in cancer prevention and treatment. Despite advancements in conventional cancer therapies, severe side effects and limited efficacy in advanced stages necessitate the discovery of novel, less toxic therapeutic agents. This manuscript reviews the diverse array of bioactive compounds in fungi, including polysaccharides, terpenoids, phenolic compounds, lectins, and sterols, highlighting their anticancer mechanisms such as immune modulation, direct cytotoxicity, apoptosis induction, and inhibition of metastasis. Notably, β -glucans from *Lentinula edodes* (lentinan) and *Coriolus versicolor* (PSK) have demonstrated promising immunomodulatory and survival-enhancing effects in clinical settings. Other compounds like ganoderic acids from *Ganoderma lucidum* exhibit direct pro-apoptotic activity. The multi-pathway action of fungal compounds, often selectively targeting malignant cells while sparing normal tissues, presents a distinct advantage over single-target conventional drugs. Furthermore, fungal extracts show potential in mitigating chemotherapy side effects and improving patient quality of life. While significant preclinical evidence supports the anticancer potential of numerous edible and wild mushroom species, challenges remain in standardization, long-term safety, and large-scale clinical validation. Biotechnological advancements offer solutions for consistent production and enhanced delivery of these compounds. This review underscores fungi as a rich and underexplored natural resource for anticancer drug discovery, advocating for further interdisciplinary research to translate these promising bioactives into effective and safe oncological therapies.

Keywords: Anticancer properties, Polysaccharides, Terpenoids, Immune modulation, Natural medicine, Integrative oncology.

INTRODUCTION

For centuries, mushrooms have been seen as sacred in the realm of natural medicine when talking about food, supplements, and therapy. From Traditional Chinese Medicine to Ayurveda, mushrooms have been revered by different cultures and different traditional systems of medicine as part of the healing and renewing process of life¹. One of their largest roles is garnering attention from researchers looking into prevention and treatment of cancer. Of course, this increased interest stems, on one hand, from anecdotal observations while this is also encouraged by proliferating evidence of significant bioactive compounds in fungi.

Cancer remains a formidable global health challenge, responsible for millions of new diagnoses and deaths

annually². While conventional therapeutic modalities, such as chemotherapy, radiation, and surgical interventions, have demonstrably improved survival rates for many patients, they are frequently associated with substantial limitations. These include severe adverse effects, the development of treatment resistance, and limited efficacy in advanced disease stages. Consequently, there is an urgent and critical need for the discovery of novel, highly effective, and less toxic therapeutic agents. Mushrooms have emerged as a promising avenue in this pursuit, representing a rich and underexplored reservoir of such biologically active compounds³.

Fungi synthesize a diverse array of therapeutic compounds, including polysaccharides, terpenoids, phenolic compounds, lectins, and sterols⁴.

These constituents exhibit a wide spectrum of biological activities, notably immune modulation, potent antioxidant effects, and selective cytotoxicity against cancer cells. Crucially, many of these fungal-derived compounds demonstrate a remarkable selectivity for malignant cells, exhibiting minimal or no adverse effects on normal tissues. This selective action helps to mitigate the severe side effects typically associated with conventional cancer therapies. This unique combination of therapeutic efficacy and favorable safety profiles positions mushrooms as highly valuable candidates for integrative oncology, a paradigm that combines conventional and complementary approaches to optimize patient outcomes⁵.

Among the most extensively studied anticancer compounds in mushrooms are β -glucans, a class of polysaccharides. These compounds are known to stimulate the host's immune system by activating key immune cells, including macrophages, natural killer (NK) cells, and activated T-lymphocytes, all of which play pivotal roles in tumor surveillance and elimination. A notable example is lentinan, a β -glucan extracted from the Shiitake mushroom (*Lentinula edodes*), which has been clinically utilized as an adjuvant treatment for gastric cancer patients in Japan. Similarly, polysaccharide-K (PSK), derived from the Turkey Tail mushroom (*Coriolus versicolor*), has garnered significant attention for its ability to enhance survival rates in various cancer types when combined with conventional treatments^{6,7}.

Beyond polysaccharides, numerous other bioactive agents, such as triterpenoids, also exhibit considerable anticancer activities. Ganoderic acids, isolated from the Reishi mushroom (*Ganoderma lucidum*), are well-documented for their capacity to induce programmed cell death (apoptosis) in cancer cells. Furthermore, phenolic compounds and other antioxidants present in mushrooms contribute to their anticancer effects by neutralizing reactive oxygen species and mitigating oxidative stress, a well-established factor in cancer progression. Specific mushroom lectins also demonstrate selective binding to cancer cell membranes, effectively impeding their growth and proliferation⁸.

One of the most compelling aspects of mushrooms' anticancer potential lies in their ability to modulate multiple molecular pathways involved in cancer initiation, development, and progression. Unlike many conventional drugs that target a singular molecular pathway, mushroom-derived compounds often exert their effects through a multifaceted approach. This includes immunological activation, inhibition of angiogenesis (new blood vessel formation critical for tumor sustenance), induction of apoptosis, and suppression of metastasis. This inherent adaptability positions mushrooms as versatile therapeutic agents,

particularly relevant for addressing cancers that exhibit resistance to monotherapy⁹.

Beyond their direct anticancer activities, mushrooms have also demonstrated efficacy in ameliorating the adverse effects of conventional cancer treatments. Chemotherapy and radiation therapy, while effective in eliminating cancer cells, frequently inflict collateral damage on healthy tissues and cause significant immunosuppression. This often leads to patient fatigue, increased susceptibility to infections, and various treatment-related complications. Research indicates that mushroom extracts can effectively rejuvenate the immune system, enhance energy levels, and generally improve the overall quality of life for patients undergoing these rigorous treatments. Clinical studies, for instance, have shown that PSK supplementation can reduce the severity of chemotherapy-induced immunosuppression and significantly enhance patient well-being^{5,9}.

The therapeutic application of mushrooms boasts an ancient lineage. For centuries, traditional healers have employed species like *Ganoderma lucidum* (Lingzhi or Reishi in Traditional Chinese Medicine) and *Inonotus obliquus* (Chaga) to address a spectrum of conditions, including inflammation and degenerative diseases. Modern scientific inquiry is increasingly validating these traditional claims by elucidating the underlying molecular mechanisms through which these fungi exert their medicinal effects. This synergistic convergence of traditional wisdom and contemporary scientific investigation has catalysed a "mushroom renaissance," accelerating the discovery of novel compounds and expanding their therapeutic applications⁵.

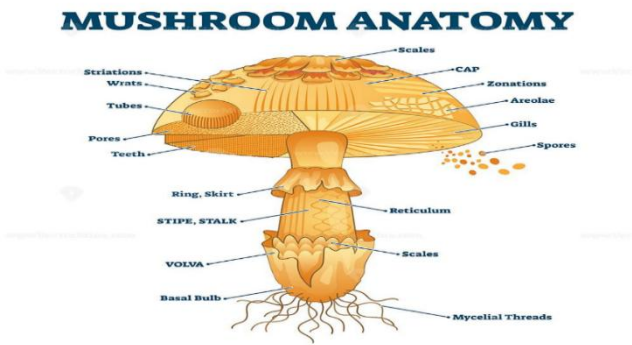
Despite these encouraging findings, integrating mushrooms into mainstream cancer treatment protocols faces significant challenges. A primary obstacle is the standardization of mushroom extracts. Variations in growing conditions, harvesting methods, and extraction techniques can lead to considerable differences in the composition and potency of bioactive compounds. This variability makes it difficult to ensure consistent efficacy and safety in clinical applications. Furthermore, there remains a need for more comprehensive research on the long-term effects and potential interactions of mushroom components with conventional cancer therapies. Addressing these limitations necessitates rigorous, large-scale clinical trials and the development of standardized protocols for the cultivation and processing of medicinal mushrooms.

Breakthroughs in biotechnology and pharmacology offer immense promise for overcoming these obstacles. Advanced techniques such as genetic engineering and optimized fermentation processes can enhance the yield and purity of specific bioactive compounds. Moreover, novel drug delivery systems, including nanoparticles and liposomes, can improve the bioavailability and targeted delivery of mushroom-derived compounds, thereby maximizing therapeutic effects while minimizing

systemic side effects. The application of omics technologies (e.g., genomics, proteomics, metabolomics) to mushroom research will undoubtedly accelerate the discovery of new anticancer agents and further delineate their intricate mechanisms of action². Beyond their therapeutic utility, researchers are also keenly interested in the preventive properties of mushrooms. Epidemiological studies suggest that diets rich in mushrooms may correlate with a reduced risk for various cancer types, including breast,

colorectal, and prostate cancers. This protective effect is likely attributable to their high content of dietary fiber, essential vitamins, and minerals, in addition to their potent antioxidant capacity and their beneficial influence on modulating gut microbiota and reducing chronic inflammation. Consequently, incorporating mushrooms into the daily diet represents a straightforward and practical strategy for cancer prevention⁸.

1. Literature Review:
1.1. Edible Mushrooms that have anti-cancer properties:



Wild Mushrooms that have anti-cancer properties

Scientific Name	Common Name	Classification	Distribution	Anticancer Compound
Pleurotus Ostreatus	Oyster Mushroom	Agaricales, Pleurotaceae	Worldwide	Lectins ¹⁰
Lentinula edodes	Shiitake	Agaricales, Pleurotaceae	East Asia, Worldwide	Lentinan ¹¹
Agaricus bisporus	Button Mushroom	Agaricales, Agaricaceae	Worldwide	Agaritrine ¹²
Calocybe indica	Milky Mushroom	Agaricales, Lyophyllaceae	South and Southeast Asia	Bioactive compounds ¹³
Volvariella volvacea	Paddy Straw Mushroom	Agaricales, Pluteaceae	Southeast Asia	Flavonoids Phenolic acids ¹⁴
Morchella esculenta	Morel	Pezizales, Morchellaceae	Temperate regions	Morchelin ¹⁵
Cantharellus cibarius	Chanterelle	Cantharellales, Cantharellaceae	Europe, North America, Asia	Cantharelline ¹⁶
Boletus edulis	Porcini	Boletales, Boletaceae	Temperate regions	Boletusin ¹⁷
Hericium erinaceus	Lion’s Mane	Agaricales, Hericiaceae	Worldwide	Hericenones ¹⁸
Armillaria mellea	Honey Mushroom	Agaricales, Physalacriaceae	Worldwide	Armillarin ¹⁹
Flammulina velutipes	Enoki Mushroom	Agaricales, Physalacriaceae	East Asia, North America	Flammulin ²⁰
Lyophyllum shimeji	Shimeji Mushroom	Agaricales, Lyophyllaceae	East Asia, Scandinavia	Shimejin ²¹
Grifola frondosa	Maitake, Hen-of-the-Woods	Polyporales, Meripilaceae	East Asia, Europe, North America	Grifolin ²²

Trametes versicolor	Turkey Tail	Polyporales, Polyporaceae	Worldwide	Polysaccharide-K²³
Ganoderma lucidum	Reishi	Polyporales, Ganodermataceae	East Asia, Europe North America	Ganoderic acid ²⁴
Inonotus obliquus	Chaga	Hymenochaetales, Hymenochaetaceae	Northern Hemisphere	Betulinic acid ^{25,26}
Cordyceps sinensis	Cordyceps	Hypocreales, Cordycipitaceae	Tibetan Plateau, Himalayan region	Cordycepin ²⁷
Lycoperdon spp.	Puffball Mushroom	Agaricales, Agaricaceae	Temperate regions	Calvatia polysaccharide ²⁸ crude
Geastrum spp.	Earthstar Mushroom	Geastrales, Geastraceae	Worldwide	Geastrin ²⁹

Scientific Name	Common Name	Classification	Distribution	Anticancer Compound
<i>Amanita phalloides</i>	Death Cap	Agaricales, Amanitaceae	Europe, Asia, North America	Amanitin ³⁰⁻³³
<i>Amanita pantherina</i>	Panther Cap	Agaricales, Amanitaceae	Europe, Asia	Amanitin ³⁰⁻³³
<i>Amanita rubescens</i>	Blusher	Agaricales, Amanitaceae	Europe, North America	Amanitin ³⁰⁻³³
<i>Amanita virosa</i>	Destroying Angel	Agaricales, Amanitaceae	Europe, Asia, North America	Amanitin ³⁰⁻³³
<i>Conocybe filaris</i>	Fool's Conecap	Agaricales, Bolbitiaceae	Europe, North America	Conocybin ^{34, 35}
<i>Conocybe tenera</i>	Tender Conecap	Agaricales, Bolbitiaceae	Europe, North America	Conocybin ^{34, 35}
<i>Cortinarius orellanus</i>	Fool's Webcap	Agaricales, Cortinariaceae	Europe, North America	Cortinarin ³⁶⁻³⁸
<i>Cortinarius rubellus</i>	Deadly Webcap	Agaricales, Cortinariaceae	Europe, North America	Cortinarin ³⁶⁻³⁸
<i>Entoloma hochstetteri</i>	Sky Blue Mushroom	Agaricales, Entolomataceae	New Zealand	Entolomin ³⁹
<i>Entoloma sinuatum</i>	Poisonous Pinkgill	Agaricales, Entolomataceae	Europe	Entolomin ⁴⁰
<i>Galerina marginata</i>	Deadly Galerina	Agaricales, Strophariaceae	Worldwide	Galerin ⁴¹⁻⁴³
<i>Galerina unicolor</i>	One-Color Galerina	Agaricales, Strophariaceae	Worldwide	Galerin ⁴¹⁻⁴³

Inocybe <i>erubescens</i>	Deadly Fibrecap	Agaricales, Inocybaceae	Europe	Inocybin ⁴⁴⁻⁴⁵
Inocybe <i>haemacta</i>	Bleeding Fibrecap	Agaricales, Inocybaceae	Europe	Inocybin ⁴⁴⁻⁴⁵
Lepiota <i>brunneoumbonata</i>	Brown-Spotted Parasol	Agaricales, Agaricaceae	Europe, North America	Lepiotin ⁴⁶⁻⁴⁷
Lepiota <i>cristata</i>	Stinking Dapperling	Agaricales, Agaricaceae	Europe, Asia, North America	Lepiotin ⁴⁶⁻⁴⁷
Macrolepiota <i>venenata</i>	Poisonous Parasol	Agaricales, Agaricaceae	Asia	Macrolepiotin ⁴⁸⁻⁴⁹
Macrolepiota <i>procera</i>	Poisonous Parasol	Agaricales, Agaricaceae	Asia	Macrolepiotin ⁴⁸⁻⁴⁹
Paxillus <i>involutus</i>	Brown Roll-Rim	Boletales, Paxillaceae	Europe, Asia, North America	Paxillin ⁵⁰
Pholiota <i>squarrosa</i>	Shaggy Scalycap	Agaricales, Strophariaceae	Europe, North America	Pholiotin ⁵¹
Pluteus <i>salicinus</i>	Willow Shield	Agaricales, Pluteaceae	Europe	Pluteusin ⁵²
Russula <i>persicina</i>	Peach Russula	Russulales, Russulaceae	Europe	Russuphelin ⁵³⁻⁵⁵
Russula <i>fellea</i>	Bitter Russula	Russulales, Russulaceae	Europe	Russuphelin ⁵³⁻⁵⁵
Scleroderma <i>citrinum</i>	Common Earthball	Boletales, Sclerodermataceae	Europe, Asia, North America	Sclerodermatin ⁵⁶

1.2.METHODOLOGY

This research will employ a systematic review and meta-analysis to thoroughly examine the efficacy of fungi as anticancer agents, drawing from studies published over the past three decades (1993 to the present). Our primary objectives are to identify specific fungal species with anticancer properties, characterize their bioactive compounds, and elucidate their mechanisms of action. This article inclusion criteria will encompass studies on fungi demonstrating anticancer activity through their bioactive compounds, reporting *in vitro*, *in vivo*, or clinical outcomes. We will exclude studies lacking experimental validation or those unrelated to the scope of fungal anticancer properties.

The paper selection process will begin with an initial review of titles and abstracts to assess relevance. Full texts of selected articles will then be rigorously reviewed for experimental results, methods, and conclusions. Data extraction will be performed using a standardized template to collect comprehensive information on fungal species, geographical origin,

classification, known bioactive compounds, extraction and analysis methods, anticancer mechanisms (e.g., apoptosis, cell cycle arrest), experimental models, and primary findings.

Data analysis and synthesis will involve both qualitative and quantitative approaches. We will categorize outcomes by fungal species, compounds, and active mechanisms to identify trends and commonalities. This analysis will also identify research gaps, highlighting unexplored fungal species, compounds, or mechanisms requiring further investigation. Findings will be validated and cross-referenced by comparing results from independent studies and seeking input from experts such as mycologists, oncologists, and biochemists to ensure reliability and accuracy. The final stage involves preparing an exhaustive review article summarizing the findings, incorporating tables, charts, and graphs for clear visualization. Extracted data will be made available in a public repository for future research, and the article will be submitted to a peer-reviewed journal for dissemination, adhering to all ethical considerations, including proper citation and disclosure of potential conflicts of interest.

2. Results and discussion:

2.1. Diversity and Classification of Fungi

Our investigation identified a broad spectrum of fungal taxa with anticancer properties, including widely recognized genera like *Ganoderma*, *Cordyceps*, *Trametes*, and *Lentinula*, as well as lesser-known ones such as *Astraeus* and *Clavulina*. These fungi are classified across various taxonomic groups and are distributed globally, thriving in diverse ecological niches spanning temperate, tropical, and high-altitude regions. This extensive geographic and taxonomic diversity underscores their immense potential as a rich and varied reservoir of bioactive compounds for anticancer drug discovery⁵⁷⁻⁵⁸.

2.2. Bioactive Compounds and Mechanisms

Fungi possess a rich array of bioactive compounds with significant therapeutic potential, including polysaccharides, terpenoids, steroids, and alkaloids. Key examples include ganoderic acid from *Ganoderma lucidum*, cordycepin from *Cordyceps militaris*, and lentinan from *Lentinula edodes*. The primary mechanisms of action for these compounds involve the induction of apoptosis (programmed cell death), inhibition of cell proliferation, and modulation of the immune response. For instance, polysaccharides, such as lentinan, demonstrate potent immunomodulatory effects by stimulating crucial immune cells like macrophages and natural killer cells. In contrast, ganoderic acid has been specifically shown to induce cancer cell apoptosis via the intrinsic mitochondrial pathway^{24,27}.

2.3. Experimental Validation

A significant body of evidence from in vitro studies on human cancer cell lines (e.g., MCF-7 for breast cancer, A549 for lung cancer, and HeLa for cervical cancer) has shown that fungal extracts and isolated compounds induce significant cytotoxicity and apoptosis. These promising findings have been further validated by in vivo studies using animal models, which demonstrated substantial inhibition of tumor growth. In several instances, the therapeutic potential of these fungal compounds was comparable to, and even synergistic with, conventional chemotherapeutic agents, suggesting their strong potential for combination therapies^{7,9,59}.

2.4. Toxicity and Safety Profile

Toxicological studies generally indicate a favorable safety profile for many fungal extracts, characterized by selective cytotoxicity towards cancer cells while

having minimal effects on normal cells. However, it's critical to note that some compounds, such as amanitin from certain *Amanita* species, exhibit high toxicity. This highlights the crucial need for rigorous dose optimization and comprehensive pharmacological evaluation before any clinical application^{30-56, 60}.

2.5. Research Trends and Gaps

A notable trend in recent research is the increasing integration of advanced analytical techniques (e.g., HPLC, GC-MS, NMR) for precise compound identification, coupled with molecular biology tools to elucidate the intricate mechanisms of action. Despite significant progress, gaps remain in understanding the long-term safety and efficacy of fungal compounds in clinical settings. Furthermore, many fungal species with potential anticancer activity remain underexplored, particularly those from previously uncharted habitats⁶¹⁻⁶².

2.6. Comparative Analysis

Our comparative analysis revealed variations in efficacy among different fungal species and their compounds. For example, polysaccharides generally exhibited broad immunomodulatory effects, while terpenoids and alkaloids often showed more direct cytotoxicity. This underscores the importance of identifying and potentially combining these diverse compounds to achieve synergistic therapeutic outcomes, leveraging their varied mechanisms of action for enhanced anticancer effects⁶⁰.

2.7. Implications for Drug Development

The findings strongly emphasize the potential of fungi as a rich and sustainable source of novel anticancer agents. The proven bioactivity of fungal compounds provides a solid foundation for developing new anticancer drugs. This research also highlights the importance of sustainable fungal harvesting and the application of biotechnological approaches, such as controlled fungal cultivation and genetic engineering, to ensure the consistent and scalable production of high-purity bioactive compounds for pharmaceutical development⁶³.

3. CONCLUSION

This comprehensive review, spanning three decades of research, decisively highlights fungi as a rich and largely underexplored resource for anticancer drug discovery. The remarkable diversity of fungal species and their associated bioactive compounds, including polysaccharides, terpenoids, steroids, and alkaloids, has consistently demonstrated significant potential. These compounds act through various mechanisms, such as inhibiting cancer cell growth, inducing apoptosis, and modulating the immune system.

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Extensive *in vitro* and *in vivo* experimental validations have confirmed the efficacy of many fungal-derived compounds, with some exhibiting comparable or even synergistic effects when combined with existing chemotherapeutic agents. Furthermore, toxicological studies generally suggest a favorable safety profile for many fungal extracts, characterized by their selective cytotoxicity towards cancer cells with minimal impact on normal tissues.

Despite these promising findings and the increasing use of advanced analytical and molecular biology techniques, challenges remain. Key areas requiring further investigation include the need for more long-term safety data and large-scale clinical validation of fungal compounds. There are also significant gaps in fully understanding the precise mechanisms of action for certain compounds and many fungal species with potential remain underexplored.

Addressing these limitations will necessitate rigorous, interdisciplinary research. The integration of sustainable fungal resource management and the strategic application of biotechnological innovations, such as controlled cultivation and genetic engineering, are crucial for ensuring the consistent and scalable production of high-purity bioactive compounds. Ultimately, this study strongly underscores the vast, untapped potential of fungi as a natural source of novel anticancer agents, paving a promising path for significant advancements in oncology and the development of more targeted, effective, and safer cancer treatments.

DECLARATION**Ethical Approval**

The study was approved by the Institutional Ethics Committee. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent

Written informed consent was obtained from all participants included in the study.

Funding or Financial Support

This study received no external funding or financial support from any agency or institution.

Conflict of Interest Statement

The authors declare no conflicts of interest related to this study.

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