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# A REMARKABLE MEDICINAL MUSHROOM: *HERICIUM ERINACEUS*

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**Abstract**

Due to the bioactive substances they contain, which promise a wide range of therapeutic effects, medicinal mushrooms have grown to be a fascinating topic. The species can be found in Europe, Asia, and North America, all of the northern hemisphere. *Hericium erinaceus* has a strong reputation as a significant medicinal mushroom, and many of its bioactive components have been turned into dietary supplements and complementary treatments. The active ingredients that produce the effects that are observed, however, frequently lack a clear relationship. There are various groups of bioactive compounds that can be produced by both the mushroom and fermented mycelia, including polysaccharides, proteins, lectins, phenols, and terpenoids. Most intriguingly, it has been discovered that two types of terpenoid chemicals, hericenones and erinacines, from cultured mycelia and fruiting bodies, respectively, induce the synthesis of nerve growth factor (NGF). In order to analyse and emphasise the scientific data pertaining to the therapeutic properties of H. erinaceus, we looked through the scientific literature.

**Keywords:** *Ziziphus jujuba*, Anti-oxidant, Anti-inflammatory, Anti-bacterial, Diclofenac.

## 1. Introduction

Food is a key factor in maintaining human health because it gives us energy and fights off diseases. Due to its benefits as both food and medicine, functional food has gained a lot of attention recently. Long used as a functional food source, mushrooms are rich in proteins, carbs, and other advantageous mycochemicals that have antioxidant and nutraceutical characteristics. The Lion's Mane (Hericium erinaceus), a common edible medicinal mushroom, has been shown to have antioxidant, anti-inflammatory, anticancer, and antibacterial properties. Because they can be used as edible mushrooms and extensively processed into extracts for therapeutic purposes, species of the genus Hericium are regarded as being commercially significant and valuable [1].

In the most recent years, *H. erinaceus* has been studied for its potential to cure depression by acting as an antidepressant. The bioactive components of several strains of H are the main topic of this review. erinaceus. The pharmacological properties of different H metabolites are the main focus. erinaceus as well as bioactive substances and their physiological characteristics. A macrofungus in the Hericiaceae family is called *Hericium erinaceus* (Bull.) Pers (Russulales, Agaricomycetes, Basidiomycota). An edible mushroom with various medical benefits is Hericium erinaceus. It is also known by a variety of other names, including bear's head mushroom, bearded hedgehog mushroom, bearded tooth fungus/mushroom, hog head mushroom, Hou Tou Gu (Chinese), lion's mane mushroom, monkey head mushroom, old man's beard mushroom, Pom Pom Mushroom, Satyr's beard fungus, white beard mushroom, and Yamabushitake (Japanese).

It has been found on dead oak, walnut, beech, maple, sycamore, and other broadleaf trees, according to reports from China, Japan, Europe, and North America. It is typically discovered on logs or stumps and has been used for a very long time in traditional Chinese medicine. the bioactive components of *H. erinaceus* includes fatty acids, terpenoids, steroids, pyranones, alkaloids, and over 80 other minor chemicals. erinaceus. purified fruit body or mycelia of H. hepatica bioactive metabolites. erinaceus possess a wide range of biological functions viz. characteristics with anti-cancer, antidiabetic, anti-diabetic, anti-hyperglycemic, anti-inflammatory, anti-microbial, antioxidant, and hypolipidemic effects. Furthermore, H. In recent years, research has focused on H. erinaceus's antidepressant-like effects for treating depressive disorders, and this review focuses on bioactive compounds of different strains of H. erinaceus. This review highlights the pharmacological activities of metabolites derived from *H. erinaceus* and their biological roles in the treatment of depressive disorders [2].

## Stimulation of nerve growth factor

The neurotrophin family includes the polypeptide known as nerve growth factor (NGF). NGF plays a role in the development and maintenance of neurons in the peripheral nervous system and is crucial for the cholinergic neurons in the central nervous system to operate (CNS). Basal forebrain cholinergic neurons need an adequate

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supply of NGF from the cortex and the hippocampus for normal operation and morphogenesis (BFCNs). Cognitive deterioration in AD is considerably exacerbated by age-dependent BFCN degradation. The NGF-boosting substances improved cognitive abilities and signs of AD. A number of H. erinaceus metabolites have demonstrated considerable CNS activity, including an improvement in cognitive function and an increase in NGF activity, and are therefore being researched for the treatment of dementia and Alzheimer's disease (AD) [3].

| Properties | Description |
|---|---|
| Induce production of nerve growth factor (NGF), preventing and treating senile dementia such as Alzheimer's | A composition comprising Phellinus baumii, *Hericium erinaceus* and Zea mays for activating and protecting brain function, and its preparation method |
| An antioxidant agent, hair suppression and skin aging | Production of *Hericium erinaceus* mycelia and fruit body with improved antioxidation activity |
| Preventing and treating hyperglycemia and cardiovascular diseases. | Traditional Chinese medicine tea for nourishing lung and reducing blood pressure |
| Preventing and treating cancer | Mixed powder of Panax notoginseng and Hericium erinaceus |

**Table 1: An illustration of a patented product containing a mushroom extract and claiming to have biological and pharmacological qualities**

Source: (Benjarong Thongbai1 et al. (2015), Hericium erinaceus, an amazing medicinal mushroom, Mycol Progress (2015) 14:91)

**Anticancer/antitumor activities**

Around 10 million people worldwide died from cancer in 2020, making it the second most common cause of death in humans. There is an urgent need to look into safe and effective medications due to lengthy treatment procedures and the significant side effects of the available anticancer medications. Mushrooms are a significant source of new metabolites with distinct structural and functional characteristics and strong cytotoxic properties. Lately, several structurally diverse bioactive metabolites from Hericium have been discovered, and their anticancer potential has been evaluated. Hericium's bioactive byproducts are also used by the pharmaceutical sector to create lead compounds for future drug development. Here, we provide a summary of how natural compounds made from H. erinaceus have an anticancer effect. The H. erinaceus extract demonstrated a number of biological actions, including an anticancer one. Since it targets the iNOS/reactive nitrogen species (RNS) and p38 mitogen-activated protein kinase (MAPK)/CCAAT enhancer-binding protein homologous protein (CHOP) pathways, erinacine A-enriched H. erinaceus mycelia has been reported to be effective against ischemic stroke [4-5].

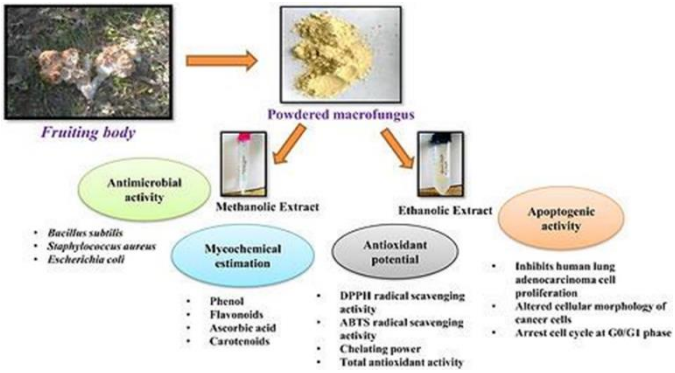


**Figure 1: Medicinal properties of Hericium erinaceus Source: (Prospecting medicinal properties of Lion's mane mushroom - Ghosh - 2021 - Journal of Food Biochemistry).**

**Anticarcinogenic effects**

An anticarcinogen is a carcinopreventive agent that reduces a carcinogen's effects on healthy cells and prevents the growth of cancer. Some of the anticarcinogenic properties of extract from H. erinaceus or bioactive from H. erinaceus are shown below. Three common procedures were used to assess the mutagenicity and genotoxicity of mycelium from H. erinaceus that had been enriched with erinacine A. (chromosomal aberration, micronuclei tests and reverse mutation). The findings demonstrated that the EAHE mycelium did not increase the number of revertant colonies in bacterial reverse mutation or cause a higher frequency of aberrations. Moreover, neither the incidence of reticulocytes per 1000 RBC nor the number of micronuclei per 1000 reticulocytes were significantly increased by EAHE mycelium. All three of these common assays indicated that EAHE mycelium was not mutagenic or genotoxic at test concentrations under typical experimental circumstances. A brand-new cerebroside called glycosphingolipid (monoglycosylceramides cerebroside E) was discovered in the fruit bodies of H. erinaceus. This has reduced the nephrotoxicity that cisplatin-induced in LLC-PK1 cells and prevented angiogenesis in HUVECs [6-7].

**Antidiabetic Activity (Alpha-glucosidase inhibitors)**

One of the fastest spreading lifestyle diseases of the twenty-first century is diabetes mellitus (DM), which has a substantial global health impact. Recent statistical research have suggested that there are currently 415 million people living with diabetes worldwide. The antidiabetic properties of chemicals identified from H. erinaceus. From the cultures of H. erinaceus, the new alkaloids erinacerins Q (73), R (74), S (75), and T (76) were purified. The IC50 values for these substances (73-76) against PTP1B were 29.1, 42.1, 28.5, and 24.9 M, respectively (the positive control, sodium vanadate, had an IC50 value of 1.2 M). With corresponding IC50 values of 12.7, 23.3, 19.5, and 20.1 M (positive control, acarbose IC50 = 273.1 M), the com-

pounds (73-76) shown inhibitory effects against a-glucosidase inhibition [8-9].

**Antioxidant potential**

By interacting with extremely reactive free radicals created during metabolism, antioxidants are the molecules that defend the cell organelles. Mushrooms are one of the top 25 natural alternatives for obtaining powerful antioxidant chemicals (Mishra et al. 2020). Here are examples of bioactive Hericium metabolites with antioxidant capabilities. In an in vitro model of FRDA (Friedreich Ataxia) using L-Buthionine Sulfoximine (L-BSO)-induced human dermal fibroblast expressing aberrant expansion of GAA triplet repeat, Lew et al. (2020) evaluated the antioxidant effects of a standardized aqueous extract of H. erinaceus. The enzyme -glutamylcysteine synthetase, which is involved in GSH synthesis, is inhibited by L-buthionine sulfoximine [10-13].

**Anti-inflammatory activity**

One of the defense mechanisms that might be disturbed by diseased situations is inflammation. It can cause multiple sclerosis, rheumatoid arthritis, psoriasis, and inflammatory bowel disorders, among other illnesses. It also has a significant impact on many complex diseases like cancer, heart disease, and AD. Antihistamines, steroids, and non-steroidal anti-inflammatory medicines are just a few of the many treatments that can be used to treat diseases that are caused by inflammation. Despite significant progress, there is still a need to treat inflammatory disorders. Hericium is known to include a variety of structurally unique bioactive metabolites that have the potential to act as a lead molecule for the development of an anti-inflammatory medication in the future. Below, we list the anti-inflammatory qualities of H. erinaceus bioactives. Inducible nitric oxide synthase (iNOS) protein expression, activation of the Nrf2/HO-1 stress-protective pathway, and inhibition of IB, p-IB (involve in the upstream NF-B signal transduction cascade) are just a few of the mechanisms that may be responsible for erinacine C (19)'s well-known antineuroinflammatory and neuroprotective effects. Lipopolysaccharide (LPS) treatment of human BV2 microglial cells resulted in reductions in levels of numerous components, including IL-6, TNF-, nitric oxide (NO), and iNOS; expression of the heme oxygenase-1 (HO-1) protein; increased nuclear transcription factor erythroid 2-related factor (Nrf2); inhibition of phosphorylation of IB (p-IB) proteins; inhibition of NF- (Keap1). Taking into account these findings, EC's mode of action entails the production of iNOS, activation of the Nrf2/HO-1 pathway, and inhibition of I-B, p-I-B [14-17].

**Anti-microbiological action**

Multidrug-resistant bacteria, such as Enterococcus faecalis and Penicillin-resistant Streptococcus pneumonia, have been found in increasing numbers during the past 20 years. Staphylococcus aureus methicillin-resistant). Many diseases brought on by multidrug resistant bacteria are difficult to diagnose and treat as a result of acquired resistance. Due to the lack of effective treatment options for fungal diseases, it is imperative to create antifungal medications that work well together to support cancer and organ/bone marrow transplant regimens. Natural compounds derived from Hericium are significant sources for developing novel metabolites that aid in modern medicine. The sections that follow discuss some advancement in the use of antimicrobials produced from Hericium [18-20].

**Herbicidal behaviour**

Herbicides are substances that kill weeds or disrupt their usual development patterns. By 2025, the size of the global herbicide market is predicted to reach $7,998.9 million in total market revenue, expanding at a CAGR of 4.8%. There have been some reports of bioactive metabolites having herbicidal effects. With ten previously reported compounds [4-(hydroxymethyl) -2 - (3-methylbut-2-en-1-yl)phenol, eulatachromene (2,2-dimethyl- 6 - hydroxymethylchromene), 6 – hydroxymethyl - 2, 2-dimethyl - chromanone, 4 – chloro – 3 , 5 - dimethoxybenzaldehyde, methyl 4 – chloro - 3, 5-dimethoxybenz erinaceus. The development of lettuce was greatly slowed down by each of these substances. At low dosages (1 and 10 nmol/paper), some of the compounds, such as, reduced the growth of hypocotyl, but at larger concentrations (100 nmol and 1 mol/paper), they showed limited action. One mol/paper of the chromans with the strongest inhibitory efficacy against hypocotyl. As the structures of were compared, it became clear that the C-6 hydroxymethyl group was crucial to this function. At 1 mol/paper, the chemical greatly stopped the growth of the root [21]. It implies that the suppression of root growth is mediated by the chromanone skeleton. The fact that compound shown a similar level of activity to compound suggests that the side chain at position C-1′ had no impact on how plants regulate their growth. The dimethoxychlorobenzene showed the highest inhibition of root growth among the dimethoxychlorobenzenes (at 1 mol/paper). This shows that the inhibitory effect is amplified by the hydroxymethyl group [22].

**Neurological Activity of Hericium erinaceus**

Neuroprotective qualities have been found in hericenones and erinacines that were isolated from H. erinaceus.In an animal model of a global ischemic stroke, Hericium erinaceus mycelia (HEM) and its isolated diterpenoid derivative, erinacine A, decreased infarction by 22% at 50 mg/kg and by 44% at 300 mg/kg. It was believed that this impact was partially mediated by its capacity to lower cytokine levels. Through a substantial delay of apoptosis, which was 20%–50% more than that reported in the control sample, a pure polysaccharide from the liquid culture broth of HEM was also discovered to possess neuroprotective potential in an in vitro setting. The same study showed HEM to be more effective than control, NGF, or brain-derived neurotrophic factor (BDNF) alone in enhancing the growth of rat adrenal nerve cells and neurite (axon or dendrite) extension. However, in a model of NG108-15 neuroblastoma cells subjected to H2O2 oxidative stress in pre-treatment and co-treatment, the aqueous

extract of H. erinaceus (as opposed to a purified polysaccharide), failed to show a protective effect. Although it is challenging to draw clinically relevant conclusions from in vitro studies, this suggests that water extracts would not have a neuroprotective effect without one particular polysaccharide being highly concentrated [23-25].

**Neurotrophic Activity and Myelination**

Human astrocytoma cells expressed NGF in a concentration-dependent manner after the addition of an ethanol extract of HEFB. Outgrowth of neurites was enhanced as well. The same researchers noticed an increase in NGF mRNA expression in the hippocampus in mice fed 5% HEFB dry powder for 7 days. An aqueous extract of HEFB boosted extracellular NGF secretion and neurite outgrowth activity, according to a different investigation. These researchers also observed a synergistic interaction between H. erinaceus aqueous extract and exogenous NGF on neurite outgrowth stimulation of neuroblastoma- glioma cells at physiologically relevant concentrations (1 μg/mL HEFB extract +10 ng/mL NGF). Myelin sheath formation in the presence of H. erinaceus extract proceeded at a higher rate and was completed by day 26, as compared to day 31 in controls. No toxic effects of the extracts were observed in this model [26-27].

**Conclusions**

H. erinaceus is notable for being a delectable food supplement as well as an edible medicinal fungus, and it has drawn a lot of interest as a possible source of several pharmaceutical characteristics. It has been in use for many decades in other eastern nations as well as for more than 1000 years in China. For the past 20 years, researchers have looked at the pharmacological effects of H. erinaceus. Several tumor cells have been significantly suppressed by polysaccharides derived from H. erinaceus fruiting bodies in both in vitro and in vivo tests (Lee et al. 2010a; Mizuno et al. 1992; Wang et al. 2001a). Mycelial cultures of H. erinaceus are presently produced on a wide scale, mostly for treating esophageal cancer, chronic gastricism, and gastric ulcers. In the two clinical trials as well as the experimental and animal studies that were presented here, no toxicity of H. erinaceus was found. Epimenorrhea, a negative outcome noted in one of the clinical trials, could not be definitively linked to the intervention. Together with the findings of previous research, the extensive historical evidence for the traditional use of lion's mane for chronic illnesses suggests H. erinaceus is safe and has significant potential as a neuroprotective and neurotrophic therapeutic agent in neurological diseases. Due to its high myconutrient content, using the entire fungus may be the most beneficial therapeutically. Additional clinical research is required to support these findings.

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