

Reviews

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Hericium erinaceus: an edible mushroom with medicinal values

Abstract

Mushrooms are considered as nutritionally functional foods and source of physiologically beneficial medicines. *Hericium erinaceus*, also known as Lion's Mane Mushroom or Hedgehog Mushroom, is an edible fungus, which has a long history of usage in traditional Chinese medicine. This mushroom is rich in some physiologically important components, especially β -glucan polysaccharides, which are responsible for anti-cancer, immuno-modulating, hypolipidemic, antioxidant and neuro-protective activities of this mushroom. *H. erinaceus* has also been reported to have anti-microbial, anti-hypertensive, anti-diabetic, wound healing properties among other therapeutic potentials. This review article has overviewed the recent advances in the research and study on *H. erinaceus* and discussed the potential health beneficial activities of this mushroom, with the recognition of bioactive compounds responsible for these medicinal properties.

Keywords: anti-cancer, anti-lipidemic, Hedgehog Mushroom, immuno-modulation, neuro-protection

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1 Introduction

There is a renaissance of interest in natural remedies in many parts of the world at present days. A large number

of investigators believe that natural products or traditional medicines (or alternative medicines) are the promising source of new therapeutics. Natural products are the chemical compounds or substances produced by living organisms, found in nature that usually have pharmacological or biological activities. Natural products are vastly used in pharmaceutical drug discovery and drug design. Many of the natural compounds are important in the treatment of life-threatening conditions. The preventive and therapeutic effects of copious natural products against life-threatening diseases have been well documented [1]. Medicines from the natural sources are usually thought to have fewer side effects. From the ancient times, mushrooms have been recognized as nutritionally functional foods and source of physiologically beneficial medicines. Mushrooms are the manifestation of the common saying, "Medicines and foods have a common origin." Several species of mushrooms under the genus of *Pleurotus*, *Ganoderma*, *Cordyceps*, *Lentinus*, *Herichium* and *Grifola* have been reported widely to have anti-cancer, anti-diabetic, anti-hypertensive, anti-microbial, cardio-protective, hepato-protective and other health beneficial roles [2–8].

Hericium erinaceus is an edible mushroom with medicinal values, which is also known as Lion's Mane Mushroom or Hedgehog Mushroom. This mushroom belongs to the class of Agaricomycetes under the phylum basidiomycota. Figure 1 represents the photograph of *H. erinaceus* fruit bodies (Photography: David Work). In Chinese and Japanese, this mushroom is called "hóu tóu gū" and "yamabushitake," respectively [9]. This mushroom is mostly found in East Asian countries and has a long history of usage in traditional Chinese medicine [10]. Numerous studies have been reported the potential medicinal values or health beneficial activities of this mushroom, like anti-cancer, anti-hypertensive, hypolipidemic, neuronal disease protecting activities, etc. However, most of the information about this mushroom is scattered. We have explored the scientific databases like Pubmed, SCOPUS and Google Scholar, and in this review, we summarized the recent advances in information on the

health beneficial properties of *H. erinaceus* mushroom, which may contribute to further research on medicinal or therapeutic roles of this mushroom. The bioactive chemical compounds of this mushroom have also been discussed here.



Figure 1 Photograph of fruit bodies of *H. erinaceus* (Photography credit: David Work. This photograph is used with kind permission of photographer. Available in <http://fiddlehead.smugmug.com/Fungi/Mushroom-Photos>).

2 Medicinal values of *H. erinaceus*

Several scientific studies have documented the medicinal or health beneficial effects of fruit bodies and mycelium of *H. erinaceus* mushroom and their chemical extracts.

2.1 Anti-cancerous and immuno-modulating activities

It has been demonstrated by several studies over the last 2–3 decades that *H. erinaceus* mushroom possesses anti-cancer activities. Immuno-modulation is one of the major mechanisms of anti-cancer activities of *H. erinaceus*. Wang *et al.* [11] studied anti-tumor and immuno-modulation activity of the polysaccharides extracted from the culture broth of *H. erinaceus* and *H. laciniatum* in mice with imprinting control regions (ICRs). Their results revealed that both polysaccharides had significant anti-artificial pulmonary metastatic tumor effects.

Additionally, the polysaccharide from *H. erinaceus* was more effective than that from *H. laciniatum*. They also reported that the polysaccharides enhanced the increase of T cells and macrophages. The number of CD4+ cells and macrophages were significantly higher in the test group than in the control group. Liu *et al.* [12] reported the anti-tumor activity and immunity regulating effects of the polysaccharides of *H. erinaceus* and *Lentinus edodes* on the mice burdened with sarcoma 180 (S-180). In a study by Lee *et al.* [13], the crude water-soluble polysaccharide of *H. erinaceus* up-regulated some functional immuno-modulating events mediated by activated macrophages, such as production of nitric oxide (NO) and expression of cytokines (IL-1 β and TNF- β), which might be responsible for the anti-cancerous properties of this mushroom. Lee and Hong [14] suggested the potential of this mushroom against hepatocellular carcinoma cell line HepG2. They have demonstrated that the crude water-soluble polysaccharide from this mushroom acts as an enhancer to sensitize doxorubicin (Dox)-mediated apoptotic signaling, and this sensitization can be achieved by reducing c-FLIP expression via c-Jun N-terminal kinase (JNK) activation and enhancing intracellular Dox accumulation via the inhibition of nuclear factor (NF)- κ B activity in HepG2 cells.

In a study by Kim *et al.* [15], the intra-peritoneal injections of hot water extract and microwaving (in 50% ethanol/water) extract of *H. erinaceus* for 2 weeks reduced the tumor weights by 38 and 41%, respectively, in Balb/c mice intracutaneously transplanted on the backs with CT-26 colon cancer cells. These extracts increased the cytolytic activity of splenic natural killer (NK) cells, restored NO production and phagocytosis in peritoneal macrophages to 95–98% of normal levels, and increased the release of pro-inflammatory cytokines TNF- α , interleukin-1 β , and interleukin-6 from macrophages. The extracts also reduced the cyclooxygenase 2 and 5-lipoxygenase expression, which down-regulated the VEGF expression, resulting in inhibition of neo-angiogenesis inside the tumors. The potency of these extracts against U937 human monocytic leukemia cells has also been evaluated by Kim *et al.* [16]. The aqueous and aqueous/ethanolic extract of *H. erinaceus* showed the suppression of cell proliferation and induced mitochondria-mediated caspase-3 and caspase-9 activation in U937 cells. However, the ethanol extract of *H. erinaceus* showed no significant effect on cellular proliferation, as well as cell cycle and apoptosis in CH72 murine skin carcinoma cells [17]. Also, in another experiment, Choi *et al.* [18] found no significant effect of methanol extract from *H. erinaceus* on the proliferation of vascular smooth muscle. The immuno-modulating activity of *H. erinaceus* was studied on macrophage cell

line RAW 264.7 by Kim *et al.* [19]. They tested the ethanol extract of *H. erinaceus* on RAW 264.7 and suggested that the chloroform fraction of the ethanol extract of *H. erinaceus* may provide an anti-inflammatory effect by attenuating the generation of excessive NO, prostaglandin E2 and reactive oxygen species and by suppressing the expression of pro-inflammatory genes through the inhibition of NF- κ B p65 subunit, phosphorylation of I- κ B, extracellular signal-regulated kinase, and JNK in a dose-dependent manner [19].

2.2 Cardio-vascular complications protecting activities

H. erinaceus possesses significant beneficial properties against cardiovascular complications. Mushrooms have a long history to be used as nutraceuticals against the dysregulation of lipid metabolism related to cardiovascular diseases. The hypolipidemic effect of an exo-biopolymer produced from a submerged mycelial culture of *H. erinaceus* was investigated by Yang *et al.* [9] in dietary-induced hyperlipidemic rats. They found that the hypolipidemic effects were proportionally increased with the increasing concentration of the exo-biopolymer by oral administration. The exo-biopolymer, at the dose of 200 mg/kg body weight, reduced the plasma total cholesterol by 32.9%, LDL cholesterol by 45.4%, triglyceride by 34.3%, phospholipid by 18.9%, atherogenic index by 58.7% and hepatic HMG-CoA reductase activity by 20.2%, and it increased the plasma HDL cholesterol level by 31.1% as compared to the control group. The ethanol extract of *H. erinaceus* improved the lipid metabolism in C57BL/6J mice fed a high-fat diet, and these effects were mediated by the modulation of lipid metabolic gene expression, at least in part via activation of PPAR- α [10]. Inhibitors of platelet aggregation are preventive or therapeutic agents of various vascular diseases, including myocardial infarction and stroke, as platelet aggregation in the blood vessel causes thrombosis. Mori *et al.* [20] found that the ethanol extract of *H. erinaceus* potently inhibited platelet aggregation induced by collagen. They identified hericenone B as the active compound against platelet aggregation in human and rabbit platelets.

2.3 Neuro-protective activities

Neurotrophic factors are essential for the maintenance and organization of neurons functionally. Therefore, neurotrophic factor-like substances or their inducers are

expected to be applied for the treatment of neurodegenerative diseases. Mori *et al.* [21] reported that the ethanol extract of *H. erinaceus* promoted nerve growth factor mRNA expression in a concentration-dependent manner via the activation of the JNK pathway. *H. erinaceus* has been suggested by Mori *et al.* [22] also to be useful in the prevention or treatment of dementia and cognitive dysfunction, as they found that dietary administration of *H. erinaceus* powder prevented the impairments of spatial short-term and visual recognition memory induced by amyloid β (25–35) peptide in male ICR mice. Nagano *et al.* [23] investigated the clinical effects of *H. erinaceus* on menopause, depression, sleep quality and indefinite complaints and suggested that intake of this mushroom can reduce the depression and anxiety in female subjects. In another clinical study, a double-blind, parallel-group, placebo-controlled trial was performed by Mori *et al.* [24] on 50- to 80-year-old Japanese men and women with mild cognitive impairment. Oral administration of *H. erinaceus* powder showed significantly increased scores on the cognitive function scale with no adverse effect in laboratory tests. Wong *et al.* [25] investigated the possible use of aqueous extract of *H. erinaceus* fruiting bodies in the treatment of axonometric peroneal nerve injury in adult female Sprague–Dawley rats by daily oral administration, and the data suggested that the extract could promote the regeneration of injured rat peroneal nerve in the early stage of recovery.

Myelin sheaths wrap neuronal axons and provide support, protection, feeding and isolation of the neurons, and an injury of myelin structure leads to the impairment and severe illness of the nerve system. In an *in vitro* study by Kolotushkina *et al.* [26], the extract of *H. erinaceus* promoted the normal development of cultivated cerebellar cells and demonstrated a regulatory effect on the process of myelin genesis process.

2.4 Antioxidant activities

Oxidative stresses have been implicated in several degenerative processes, diseases and syndromes, including cancer, cardiovascular complications, neurodegenerative diseases and a wide variety of age-related disorders [27, 28]. For this, food supplements or natural medicines which have antioxidant activities are of special interests. The antioxidant index, as well as free radical scavenging activity, lipid peroxidation inhibitory activities of hot water extract of *H. erinaceus* has been reported by Abdullah *et al.* [29]. Wong *et al.* [30] found that the

mycelium extract of *H. erinaceus* is rich in phenolic content and has potential ferric reducing antioxidant power. The fresh fruit body extract was also found to have the potent 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity. And, oven-dried fruit body extract was excellent in reducing the extent of carotene bleaching. They have also reported that the total phenolic content and total antioxidant activity in the oven-dried fruit body extract was higher compared to the freeze-dried or fresh fruit body extract. This may be due to the generation and accumulation of Maillard's reaction products, which are known to have antioxidant properties [30]. In a recent study by Han *et al.* [31], *H. erinaceus* polysaccharides showed significant antioxidant activity against ischemia reperfusion induced renal oxidative injury damage in experimental animals. In that study, pre-administration of mushroom polysaccharide decreased lipid peroxidation level and increased antioxidant enzyme activities in mice [31]. The antioxidant activity of the endo-polysaccharides from *H. erinaceus* mycelium has also been documented [32].

2.5 Other therapeutic activities

Nearly three decades ago, the effectiveness of *H. erinaceus* therapy on chronic atrophic gastritis had been reported by Xu *et al.* [33] in a double-blind study. The effects of methanol extract from *H. erinaceus* were tested on CCl₄-induced hepatic damage in rats by Choi *et al.* [18], who reported that the extract has strong protective effect on hepatic damage. Abdulla *et al.* [34] reported the wound healing property of this mushroom. In their study, wounds dressed with the aqueous extract of *H. erinaceus* fruit bodies enhanced the acceleration of wound healing enclosure in experimentally wounded male Sprague-Dawley rats. Inhibitors of angiotensin I-converting enzyme (ACE) are being used to reduce blood pressure and lower the risk of hypertension complications. Abdullah *et al.* [29] reported that the hot water extract of *H. erinaceus*, along with some other edible and medicinal mushrooms, showed ACE inhibitory activity *in vitro*. The endo-polysaccharide fractions of the *H. erinaceus* mycelium grown on tofu (a Chinese food made by beans) showed potent hepatoprotective effect *in vivo* [32]. Wong *et al.* [30] reported the anti-microbial activities of *H. erinaceus*. They found that the fresh fruit body extract inhibited the growth of several bacteria, such as *Bacillus cereus*, *B. subtilis*, *Enterococcus faecalis*, *Salmonella* sp., *Shigella* sp. and *Plesiomonas shigelloides*; however, no antifungal activity was found by their study. Wang *et al.*

[35] reported the hypoglycemic activity of *H. erinaceus*, which suggested this mushroom as an anti-diabetic therapeutic agent too. They concentrated the methanol extract of *H. erinaceus* to remove solvent yielding a residue (named as HEM) and added to the diet of streptozotocin-induced diabetic rats. In that study, they have found that the rats fed with HEM had significantly lower elevation rates of blood glucose level than those not fed with HEM.

3 Bioactive components of *H. erinaceus*

Different bioactive polysaccharides are supposed to be the major effective components of mushrooms, which are responsible for their medicinal properties (Table 1). Most of the medicinal properties of *H. erinaceus* discussed above have been recognized by the activities of its polysaccharide fraction. Like many other edible or medicinal mushrooms, most of the therapeutic polysaccharides found in *H. erinaceus*, are β -glucans [13, 16]. Lee *et al.* [13] identified the immuno-modulatory and anti-tumorous compound of *H. erinaceus* as a low-molecular-mass polysaccharide with a laminarin-like triple helix conformation of a β -1,3-branched- β -1,6-glucan by using the Fourier transform infrared spectroscopy, and gas chromatography-mass spectrometry (GC-MS) technology. A new heteropolysaccharide (HEP1) with a (1 \rightarrow 6)-linked α -D-galactopyranosyl backbone with branches that are composed of rhamnose and glucose was isolated from the fruit bodies of *H. erinaceus*, by Jia *et al.* [36]. Another novel hetero-polysaccharide, HEPF3, was isolated by Zhang *et al.* [37] from the fruit bodies of *H. erinaceus*, which is composed of fucose and galactose. Compositional analysis, methylation analysis, together with ¹H and ¹³C NMR spectroscopy established that HEPF3 consists of a branched penta-saccharide repeating unit.

Four crystalline and one liquid bioactive compounds were isolated by Qian *et al.* [38] from the solid cultured extract of *H. erinaceus*. Their chemical structures were determined as 6-methyl-2,5-dihydroxymethyl- γ -pyranone, 2-hydroxymethyl-5- α -hydroxy-ethyl- γ -pyranone, 4-chloro-3,5-dimethoxybenzoic-O-arabitol ester, 4-chloro-3,5-dimethoxybenzoic methylester and 4-chloro-3,5-dimethoxybenzoic acid. In addition, a mixture of palmitic and stearic acid, a mixture of behenic acid and tetracosanic acid and a mixture of 5- α -ergostan-3-one, 5- α -stigmasten-22-en-3-one and 5- α -stigmastan-3-one were also been isolated by Qian *et al.* [38]. Hericenone B,

Table 1 The health beneficial bio-active components of *H. erinaceus* mushroom.

Compounds	Beneficial bio-activities
β -Glucans (polysaccharides) (e.g. β -1,3-branched-beta-1,6-glucan with laminarin-like triple helix conformation)	Anti-cancerous, immuno-modulatory, neuro-protective and anti-oxidant
HEP1 [a hetero-polysaccharide, with (1 \rightarrow 6)-linked α -D-galactopyranosyl backbone]	Anti-cancerous and immuno-modulatory
HEPF3 (a hetero-polysaccharide, with a branched penta-saccharide repeating unit)	Anti-cancerous and immuno-modulatory
Endo-polysaccharides	Hepato-protective and anti-oxidant
Other polysaccharides: 6-methyl-2,5-dihydroxymethyl- γ -pyranone; 2-hydroxymethyl-5- α -hydroxy-ethyl- γ -pyranone; 4-chloro-3,5-dimethoxybenzoic-O-arabitol ester; 4-chloro-3,5-dimethoxybenzoic methyl ester and 4-chloro-3,5-dimethoxybenzoic acid	Wide spectrum health beneficial effects, including anti-cancerous and immuno-modulatory activities
Lipid compounds: palmitic and stearic acid mixture; behenic acid and tetracosanic acid mixture; 5- α -ergostan-3-one; 5- α -stigmasten-22-en-3-one and 5- α -stigmastan-3-one	Wide spectrum health beneficial effects
Hericenone B (phenolic compound)	Anti-platelet aggregation (protection of myocardial infarction, stroke, etc.)

a phenolic compound, was isolated from the ethanol extract of *H. erinaceus* and identified as the potential anti-platelet aggregating agent by Mori *et al.* [20].

4 Concluding remarks

Mushrooms are the good example of medicinal foods or food supplements. From the ancient times, mushrooms have been recognized as important food items because of their taste, flavor, high nutritional values and several medicinal properties. *H. erinaceus* is a delicious mushroom with potential medicinal importance. This

mushroom is mainly consumed in East Asian countries, and most of the research works have been performed in China, Japan and Korea. This study suggests its worldwide research, cultivation and consumption. Daily consumption of this mushroom may keep people away from several life-threatening disorders. However, the worldwide scientific study on *H. erinaceus* is not common. More basic clinical studies are recommended as further research to establish its therapeutic potential against life-threatening human disorders.

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