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A REVIEW ON HERICIUM ERINACEUS: NATURE'S MEDICINAL RESERVOIR

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ABSTRACT

Mushrooms are rapidly becoming recognized as a promising source of novel proteins. Hericium erinaceus is one of the widely used edible mushrooms around the world, primarily in Asian countries. H. erinaceus is used in traditional medicines, and mushroom-based foods. 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, immunomodulating, hypolipidemic, anti-oxidant and neuroprotective activities of this mushroom. Hericium erinaceus (H. erinaceus) has also been reported to have anti-microbial, anti-hypertensive, anti-diabetic, wound healing properties among other therapeutic potentials. These stunning properties along with the absence of toxicity render these biopolymers ideal compounds for developing novel functional foods or nutraceuticals with the increase in consumers' consciousness and demand for healthy food. Large scale production and industrial application of some fungal proteins prove their biotechnological potential and establish higher fungi as a valuable, although relatively unexplored, source of unique proteins. 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: Hericium erinaceus, anti-cancer, Hericiaceae, Lion's mane mushroom, anti-diabetic, Hericenones.

INTRODUCTION

Traditional systems of medicine continue to be widely practiced on many accounts. Population rises, inadequate supply of drugs, prohibitive cost of treatments, side effects of several synthetic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments[1, 2].

Ancient, traditional, and modern cultures around the world have known about the nutritive and medicinal properties of mushrooms for centuries. As early as 450 BCE, the Greek physician Hippocrates identified mushrooms as potent anti-inflammatory agents, useful for cauterizing wounds.

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Ancient, traditional, and modern cultures around the world have known about the nutritive and medicinal properties of mushrooms for centuries. As early as 450 BCE, the Greek physician Hippocrates identified mushrooms as potent anti-inflammatory agents, useful for cauterizing wounds. In the East, reverence for fungi is evident in the Chinese description of ling zhi (Ganoderma lucidum), as the "spirit plant," believed to provide longevity and spiritual potency. Modern medicine has been slower to catch on to the immense potential of fungi. Despite Fleming's 1929 discovery of penicillin, and the subsequent implementation of the fungi-chemical as a blockbuster pharmaceutical in the 1940s, it is only in the last few decades that medical science has looked beyond the anti-microbial and cholesterol-lowering properties of fungi for other potential applications[3-5].

Medicinal mushrooms have become a compelling topic because the bioactive compounds they contain promise a plethora of therapeutic properties. Hericium erinaceus commonly known as "Houtou" or "Shishigashira" in China and "Yamabushitake" in Japan, has commonly been prescribed in Traditional Chinese Medicine (TCM), because its consumption has been shown to be beneficial to human health. The species is found throughout the northern hemisphere in Europe, Asia, and North America. Hericium erinaceus has been firmly established as an important medicinal mushroom and its numerous bioactive compounds have been developed into food supplements and alternative

medicines. However, the correspondence of the active components that cause the observed effects is often not clear [6,7].

Edible mushrooms are one of the acceptable functional foods for human and are being used for several hundred years. Mushrooms are known for its texture, flavour, and health-promoting property. Especially, mushrooms are a rich source of all essential amino acids that are required by the human beings. They are considered as a healthy food because of its enriched protein and dietary fiber content with low calories and fat. Thus far, more than two thousand mushrooms species have been reported. Edible mushrooms have been screened and studied for several medicinal properties like anti-cancer and anti-microbial activities. Moreover, mushrooms were used as alternative food-based medicines. Among all culinary mushrooms, Hericium erinaceus (most commonly known as lion's mane) has been widely reported to have therapeutic activities related to the promotion of nerve and brain health[8-11].

Fig 1: Hericium erinaceus

Distribution

Hericium erinaceus (also called lion's mane mushroom, monkey head mushroom, bearded tooth mushroom, satyr's beard, bearded hedgehog mushroom, pom pom mushroom, or bearded tooth fungus) is an edible and medicinal mushroom belonging to the tooth fungus group. Although H. erinaceus is native to Europe. European countries due to poor germination and establishment. This specific genus fruits between August and December in the United Kingdom, and will continue to produce spores until as late as February in the following year12.

Table 1: Scientific classification

Kingdom	Fungi
Division	Basidiomycota
Class	Agaricomycetes
Order	Russulales
Family	Hericiaceae
Genus	**Hericium**
Species	**H. erinaceus**
Binominal Name	**Hericium erinaceus (Bull.) Persoon**

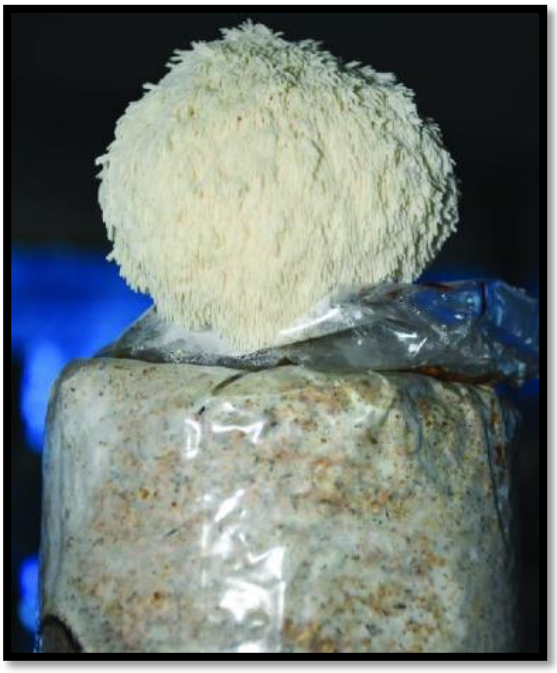

Fig 2: Hericium erinaceus (Top-fruiting body and bottom-mycelium)

Traditional uses

Hericium erinaceus (Lion's mane, Yamabushitake, or bearded tooth carpophore) grows on old or dead broadleaf trees, and is used as both food and medicine in parts of Asia. The fruiting body is called hóu tóu gū (monkey head mushroom) in Chinese and Yamabushitake (mountain monk mushroom) in Japanese. In Chinese and Japanese medical systems, it has traditionally been used to fortify the spleen, nourish the gut, and also as an anti-cancer drug. Lion's mane is said to be nutritive to the five internal organs (liver, lung, spleen, heart and kidney), and promotes good digestion, general vigor, and strength. It is also recommended for gastric and duodenal ulcers, as well as chronic gastritis (in prepared tablet form). The mushroom is also known for its effects on the central nervous system, and is used for insomnia, vacuity (weakness), and hypodynamia, which are characteristic symptoms of Qi deficiency in Traditional Chinese Medicine (TCM) [13,14].

Chemistry[15-21]

The bioactive metabolites of H. erinaceus are polysaccharides, sterols and terpenoids.

Polysaccharides:

Fungal polysaccharides are found mainly in cell walls, and are present in large quantities in both fruiting bodies and cultured mycelium. Hericium erinaceus fruiting bodies (HEFB) contain immunoactive β-glucan polysaccharides, as well as α-glucans and glucan-protein complexes. A total of more than 35 H. erinaceus polysaccharides (HEP) have been extracted to date from cultured, wild-growing, or fermentative mycelia and fresh/dried fruiting bodies. Of these β-glucans represent the main polysaccharides. HEP are composed of xylose (7.8%), ribose (2.7%), glucose (68.4%), arabinose (11.3%), galactose (2.5%), and mannose (5.2%). Four different polysaccharides isolated

from the H. erinaceus sporocarp show anti-tumor activity: xylans, glucoxylans, heteroxyloglucans, and galactoxyloglucans. Chemical analysis shows that the total content of HEP found in fruiting bodies is higher than that in mycelium.

Terpenoids:

Terpenoids are a class of naturally occurring hydrocarbons that consist of terpenes attached to an oxygen containing group. Terpenoids make up over 60% of products in the natural world. A variety of diterpenes and sesquiterpenes are found in the fruiting body and fermenting mycelium of H. erinaceus.

Of particular pharmacological interest are two classes of terpenoid compounds thus far known to occur only in Hericium spp.: hericenones, a group of aromatic compounds isolated from the fruiting body; and erinacines, a group of cyathane-type diterpenoids found in the mycelium. Both groups of substances easily cross the blood-brain barrier (BBB), and have been found to have neurotrophic and in some cases neuroprotective effects.

Sterols:

Ten erinarols, described as erinarol A–J, five ergostane-type sterol fatty acid esters, and ten ergostane-type sterols have been identified in the fruiting body of *H. erinaceus.*

Erinacines in the mycelium of H. erinaceum[22-24]

Erinacines are groups of cyathin diterpenoids that show biological activities. To date, 15 erinacines (Erinacines A - K and P - S) have been identified.

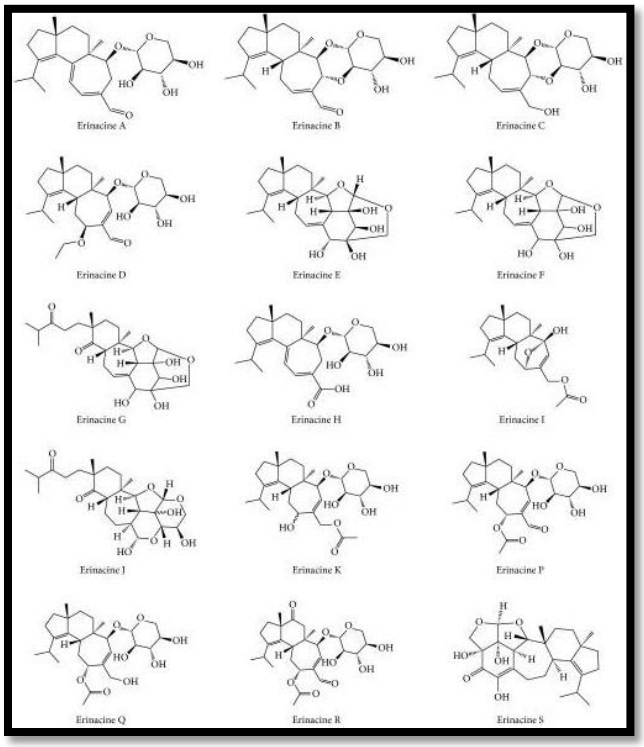

Fig 3: Structures of Erinacines

Hericenones in the fruiting body of H. erinaceum[25-28]

Hericenones are aromatic compounds isolated from the fruiting body of H. erinaceus. Hericenones A to H was identified. And hericenes A-C and hericerin were isolated from the mushroom H. erinaceus.

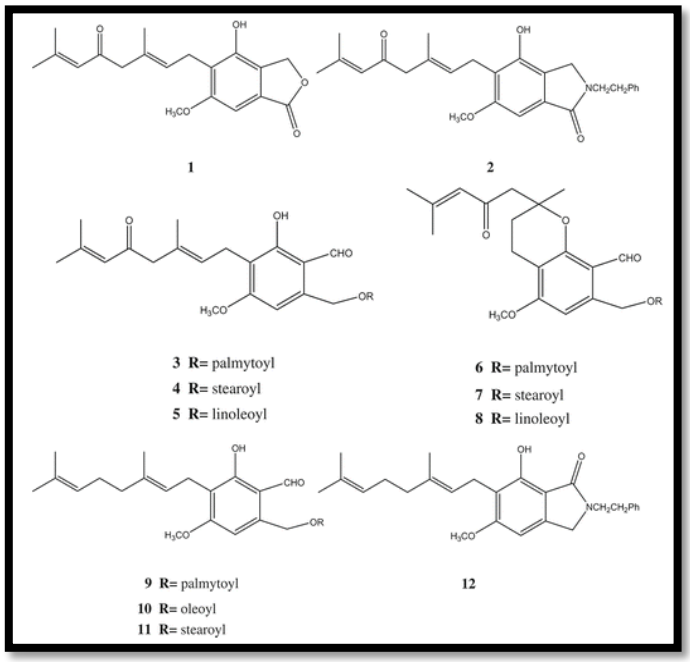

Fig 4: Structures of Hericenones A (1), B (2), C (3), D (4), E (5), F (6), G (7), H (8), hericenes A–C (9–11), hericerin (12)

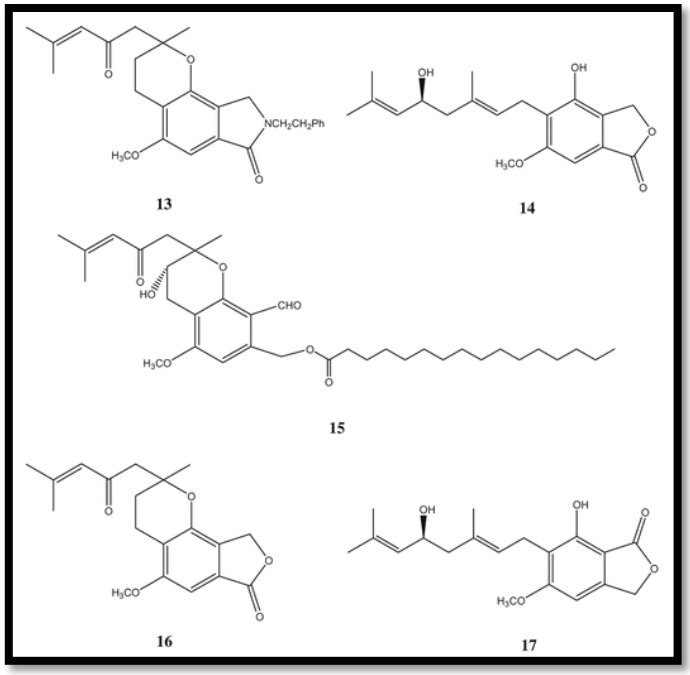

Fig 5: Structures of Erinacerin A (13), B (14), 3-Hydroxyhericenone F (15), hericenone I (16), hericenone J (17)

Novel compounds

Many novel bioactive compounds of H. erinaceus are being actively discovered. Other than hericenones and erinacines, several newly identified compounds isolated from the fruiting body of H. erinaceus, including ergosterol peroxide, cerevisterol and 3, 5, 9-trihydroxyergosta 7, 22-dien 6-one.

Hericium erinaceus is a mushroom belonging to the family Hericiaceae and has been known as Chinese medicine or food in China and Japan without harmful effects. H. erinaceus grows on old or dead broadleaf trees and has been used as a medicine for treatment of gastricism in traditional Chinese medicine for more than 1000 years. Recently, the chemical constituents of H. erinaceus have been investigated for its interesting and significant bioactivities. Hericenones and erinacines were isolated from the fruiting body and mycelium of H. erinaceus, respectively.

Ethnopharmacological uses

Herbal medicine can be cost effective complementary and alternative medicine for the treatment of different diseases. Mushrooms are functional foods with high nutritional values and are great sources of novel therapeutic compounds.

Table 2: Ethnopharmacological value

S. No.	Pharmacological activity	Reference
1	Anti-depressant activity	29
2	Neuroprotective activity	30
3	Anti-parkinson's effect	31,32
4	Immunomodulatory activity	33
5	Anti-tumour activity	34,35
6	Anti-Helicobacter pylori effect	36
7	Anti-oxidant activity	37
8	Anti-gastric ulcer activity	38
9	Anti-inflammatory effect	39,40
10	Anti-hyperglycemic and anti-hyperlipidemic activities	41
11	Anti-diabetic activity	42
12	Wound healing activity	43
13	Neuroprotective activity	44
14	Hemagglutinating activity	45

Hericium erinaceus, an ideal culinary-medicinal mushroom, has become a well-established candidate in promoting positive brain and nerve health-related activities by inducing the nerve growth factor from its bioactive ingredient. The evidence so far has shown that H. erinaceus mycelium enriched with its active compounds is capable of delaying neuronal cell death in rats with neurodegenerative diseases, such as ischemic stroke, Parkinson's disease, Alzheimer's disease, and depression. Moreover, results have indicated that administration of H. erinaceus mycelia enriched with its active compounds can promote functional recovery and enhance nerve regeneration in rats with neuropathic pain or presbycusis.

Hericenones and erinacines are two natural products isolated from the fruiting body and mycelium of H. erinaceus, respectively, and most compounds exhibit the activity of promoting NGF synthesis. Hericenones and erinacines are low-molecular weight compounds that easily cross the blood brain barrier. In a bioassay using mouse astroglial cell, the amounts of NGF secreted into the medium in the presence of erinacines were greater than for hericenones. The pre-clinical and clinical studies have demonstrated that H. erinaceus significantly ameliorates depressive disorder through monoaminergic modulation, neurogenic/neurotrophic, and anti-inflammatory pathways, indicating the potential role of H. erinaceus as complementary and alternative medicine for the treatment of depression [17,46,47].

Toxicity studies

To date, all experimental studies have suggested that H. erinaceus mycelium is safe and devoid of adverse effects. In an animal study, the acute oral LD50 of H. erinaceus mycelia enriched with its active compounds was found to be higher than 5 g/kg in rats, indicating that the mycelium is reasonably safe in cases of overdose. Repeated daily doses of H. erinaceus mycelium enriched with its active compounds up to 3 g/kg have also been used without any adverse effects in rats. Moreover, H. erinaceus mycelium was found not to be mutagenic in the bacterial reverse mutation test (Ames test), in vitro chromosome aberration test, and in-vivo erythrocyte micronucleus test, with and without metabolic activation. Further investigations also showed that erinacine-enriched H. erinaceus mycelium was not teratogenic in Sprague-Dawley rats with doses up to 2625 mg/kg. In a well-designed clinical trial, erinacine-enriched H. erinaceus mycelia demonstrated significant clinical efficacy and had good safety and tolerability in 36 patients with Alzheimer's disease [48-50].

Reported adverse effects

No adverse clinical or biochemical events were reported in the clinical trial of subjects with mild cognitive impairment. In the study of menopausal women, one subject reported epimenorrhea (18 days menorrhea/month). However, whether or not supplementation with H. erinaceus was the cause of the epimenorrhea is inconclusive[51,52]. Allergies and sensitivities to mushrooms are not unusual. One case report describes a 63 yr old male who suffered acute respiratory failure and lymphocytosis in his lungs. The report suggests he had used an extract of dry H. erinaceus (with no further description given) daily for 4 months in commonly available doses, and the connection between the two was considered to be probable. In another case report, a 53-year-old male exposed to Hericium erinaceus fruiting bodies (HEFB) occupationally, developed chronic dermatitis on his hands, with painful fissures within 1 month of exposure. The dermatitis spread to his forearms, face, and legs, at which point he ceased exposure to the HEFB and his symptoms resolved. His patch tests were negative for the European standard series, and positive for HEFB. Sensitization was confirmed by a highly positive Repeated Open Application Test (ROAT) with an aqueous emulsion of HEFB. Interestingly, patch and prick tests were negative for other culinary mushrooms suggesting a lack of cross-sensitivity[15].

CONCLUSION

The culinary medicinal mushroom Hericium erinaceus is widely consumed in Asian countries, but apparently not in the United States, for its nutritional and health benefits. To stimulate broader interest in the reported beneficial properties, this overview surveys and consolidates the widely scattered

literature on the chemistry (isolation and structural characterization of polysaccharides and secondary metabolites such as erinacines, hericerins, hericenones, resorcinols, steroids, and mono and di-terpenes), the nutritional composition and the exceptional nutritional and health-promoting aspects of Hericium erinaceus. The reported health-promoting properties of the mushroom fruit bodies, mycelia, and bioactive pure compounds include anti-biotic, anti-carcinogenic, anti-diabetic, anti-fatigue, anti-hypertensive, anti-hyperlipidemic, anti-senescence, cardioprotective, hepatoprotective, nephroprotective, neuroprotective, and improvement of anxiety, cognitive function, and depression, as well as anti-inflammatory, anti-oxidative, and immunostimulating properties in cells, animals and humans. The collated information and suggestion for further research might facilitate and guide further studies to optimize the use of the whole mushrooms and bioactive compounds to help prevent or treat animal and human diseases.

Mushrooms produce many bioactive proteins, including FIPs, ribosome-inactivating proteins, lectins, ribonucleases, anti-bacterial/anti-fungal proteins, laccases, and other proteins. Although increasing reports are available on the isolation, purification, and functions of mushroom proteins, the mechanisms of their actions (e.g., immunomodulation, anti-proliferation, anti-virus, anti-microbes, etc.) are still poorly understood. Therefore, novel technologies should be promising in this aspect, and the relationship between structure and bioactivity should be considered. We provided up-to-date information on this mushroom, including its taxonomy and a summary of bioactive compounds that appear related to the therapeutic potential of H. erinaceus. Its rich micronutrients composition suggests that using the whole fungus may be most advantageous clinically. More clinical studies are needed to corroborate these conclusions.

Author contributions

All authors contributed to data collection, drafting or revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Conflict of interest

All authors declare that there is no conflict of interests regarding publication of this paper.

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Ethical approval

Not required.

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