Fungal Biotec 1(2): 118–130 (2021) ISSN 2774-0323

www.fungalbiotec.org

Article

Doi 10.5943/FunBtiotec/1/2/8

Hericium: A review of the cultivation, health-enhancing applications, economic importance, industrial, and pharmaceutical applications

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Gonkhom D, Luangharn T, Raghoonundon B, Hyde KD and Thongklang N (2021) – *Hericium***:** A review of the cultivation, health-enhancing applications, economic importance, industrial, and pharmaceutical applications**.** Fungal Biotec 1(2), 118–130, Doi 10**.**5943/FunBiotec/1/2/8

Abstract

Hericium is a genus of edible mushroom with proven medicinal efficacy. The mycelium and basidiomata contain many nutrients and bioactive compounds with therapeutic uses. Recent and emerging evidence has shown that *Hericium* is helpful to various diseases with medicinal properties, such as anti-oxidant, anti-cancer, anti-diabetic, anti-hyperglycemic, hypolipidemic properties, anti-inflammatory, anti-microbial, anti-viral, and hepatoprotective. Over the past decade, many studies have been done on *Hericium* cultivation to produce enough basidiomata for culinary and medical purposes, due to its rarity in natural habitat. The purpose of this review is to provide the cultivation methods including indoor-outdoor cultivations and submerged culture methods, health-enhancing applications, economic importance, and industrial applications of *Hericium* mushroom.

Keywords – cultivation – economical – industrial applications – medicinal mushroom

Introduction

Species of *Hericium* Pers. (1794), are commonly considered as traditional food and traditional folk medicines in China (Shao et al. 2019). They are native to North America and found in the wild in East Asia countries and India (Das et al. 2011). They are rarely found in European countries but are common in Japan and North America. *Hericium* species have a variety of common names for e.g., lion's mane mushroom, hóutóugū, yamabushitake, monkey's head, Pom Pom, Bear's head, Hog's head fungus, Whitebeard, Old-man's beard, and Bearded tooth (Thongbai et al. 2015, Sangtitanu et al. 2020).

Hericium is a genus of edible and medicinal mushrooms that belongs to the family *Hericiaceae*, order *Russulales*, and class Agaricomycetes (Kirk et al. 2008, He et al. 2019). *Hericium* comprises 34 species with 66 taxon names listed in Index Fungorum (Index Fungorum 2021) and 23 species records in Notes of Genera in *Basidiomycota* (He et al. 2019). The basidiomata in this genus are white and fleshy, growing on dead trees or dried woods, the basidiomata are similar to fragile iced thorns which either hang from a branch, supporting the framework or as a tough unbranched cushion of tissue (Volk & Westmoreland 2009, Hallenberg et al. 2012, Kuo 2014). The dangling spines easily identify a mature specimen (Ouali et al. 2020). The

Submitted 12 August 2021, Accepted 20 November 2021, Published 24 December 2021
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spines are arranged by clusters or often in rows (Park et al. 2004). Identifying immature specimens can be more difficult since they tend to start as a single clump and develop their branches as they age (Mykoweb 2015). They have no caps and consist of spiny spherical to ellipsoid amyloid spores that are either smooth or covered with very fine warts (Kuo 2014). Their hyphae are gloeopleurous and filled with oil drops (Kuo 2014).

Hericium has extensively been studied for cultivation and medical purposes. Historically, the first strains of *Hericium* were cultivated in China and belonged to the species *H. erinaceus* (Suzuki & Mizuno 1997), which later became the commercial *Hericium* strain for cultivation (Sawant 2021). *Hericium* species grow slowly and inhabit the top of beech or oak trunks in pairs, in wild forests (Jiang et al. 2014). The hardwood sawdust is the most suitable substrate for *H. erinaceus* in order to attain a high yield in mushroom cultivation (Hu et al. 2008). Atila (2019) reported that a reduction in the concentrations of lignin content with low cellulose of various sawdust had a positive effect on the productivity of *Hericium*.

Most *Hericium* species have long been examined for medicinal compounds. Several bioactive compounds from *Hericium* were found to have a therapeutic potential to immune-stimulating effects (Chen et al. 2017, Sheng et al. 2017). *Hericium* is a great source for novel therapeutic compounds, and it has been found to have effects on nerves and the brain (Chong et al. 2020). Most of the neurotrophic compounds have effects on the human nerve cell, and neurogenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD) (Zhang et al. 2016, Ratto et al. 2019, Chong et al. 2020, Ryu et al. 2021). There have been many reports about the bioactive secondary metabolites, such as phenols, polyketides, terpenes (De Silva et al. 2013), polysaccharides, lipopolysaccharides, glycoproteins, pyrone, alkaloids, terpenoids, steroids, and non-ribosomal peptides (Keong et al. 2007, Chen et al. 2017).

In this review, we provide the indoor-outdoor cultivation methods, health benefits, economic significance and industrial applications of *Hericium*.

Cultivation of *Hericium*

The cultivation methods for *Hericium* differ depending on the use propose of the mushroom for e.g., for basidiomata production or for chemical investigations.

Cultivation methods for mushroom production and biomass

The adaptability of wild *Hericium* growth is not entirely clear, but it depends on the microbiological condition of the substrate surface, basic nutrition, and environmental restrictions (Bruhn et al. 2000). However, there are two methods to grow *Hericium* species including outdoor and indoor cultivation. Some *Hericium* species have been cultivated as a commercially including *H. erinaceus*, *H. abietis*, and *H. americanum* (Xiao & Chapman 1997, Hassan 2007, Sokół et al. 2015, Atila et al. 2017, Bunroj et al. 2017). Ko et al. (2005) reported that *H. americanum*, *H. coralloides*, and *H. erinaceus* fruiting bodies are usually produced on oak sawdust substrate. Additionally, sawdust substrates from various deciduous trees are also considered as the main substrate for commercial cultivation (Oei 2016).

Outdoor cultivation

The first wide scale cultivation of *Hericium* originated in China (Sokół et al. 2015). Traditional outdoor cultivation is seasonally done in the shade of a tree by making mushroom beds on unprocessed logs. The wood chips overgrown with the mycelium of *Hericium* mushroom were inoculated into dry logs or fresh tree stumps and incubated with high humidity, after which the mycelium will grow on the substrate (Ahmadi & Farsi 2017). The *Hericium* mycelia can grow on sawdust of *Acer* species (maple), *Mangifera indica* (mango), *Populus* sp. (populus), *Psidium guajava* (common guava) and *Quercus* sp. (oak) (Pathmashini et al. 2008, Stamets 2011). Several studies have recommended wood from coniferous tree species including *Pinus taeda* and *P. ponderosa* as the substrate composition for *Hericium* cultivation (Croan 2004). Outdoor production of *Hericium* produces good yield on logs of *Acer* sp. (maple), *Fagus* sp. (beech), *Quercus* sp. (oak), *Ulmus* sp. (elm), and other hardwoods (Stamets 2011, Grace & Mudge 2015). Mushroom totem inoculation method can also be used for logs or stumps outdoor cultivation using sawdust and spawn (Grace & Mudge 2015, Soderberg 2019).

Indoor cultivation

Most of the demands for *Hericium* from the commercial market are fulfilled through indoor cultivation in sawdust and wood bags (Grace & Mudge 2015). Current research is dedicated to indoor cultivation systems, largely because indoor systems are more lucrative and can be studied more efficiently (Bruhn et al. 2000).

An intensive cultivation method needs to be used in order to obtain high yields of good quality (Dai & Dong 2014). Most of the intensive cultivation for this mushroom is typically done in bottles or bags (Imtiaj & Rahman 2008). The culture substrate needs to be sterilized and it must be made from a heat-resistant material such as polypropylene (Ko et al. 2005, Sokół et al. 2015). Several reports have proved that the use of agricultural by-products as supplements increases the mycelial growth of *Hericium* (Suwanno et al. 2019 Xiao & Chapman (1997) reported conifer sawdust supplemented with wheat bran, calcium sulfate and sugar as the main substrate for the growth of H. abietis. Zhang (2000) found that the favored substrate for *H. erinaceus* mycelium growth contains mainly corncobs and cotton chaffs supplemented with wheat bran, corn meal, gypsum and sugar. Furthermore, Bunroj et al. (2017) reported para rubber sawdust supplemented with rice bran, gypsum, dolomite, yeast, leucaena leaf meal, magnesium sulphate and EM solutions (Effective Microorganism), as effective for production of *Hericium* basidiomata. Moreover, other substrates reported as beneficial for *H. americanum* mycelial growth include oak sawdust, olive press cake, and cottonseed hulls (Atila et al. 2017).

Mushroom harvesting and production

Mushroom cultivation mostly uses plastic bags with small holes so as the basidiomata are able to easily come off, thus reducing the loss of production during harvesting operations (Stamets 2011). It usually takes 33–40 days for the primordia to appear and 10 days after primordia appearance, the first flush of *Hericium* fruiting bodies can be harvested (Ko et al. 2005). Several *Hericium* cultivation experiments, the cultivation bags are capable of producing fruiting bodies for around 3–4 flush per bag (Bunroj et al. 2017). Moreover, mushroom production depends on the environmental factors including climate factors, especially temperature inducer the effect of the mushroom product (Andrew et al. 2018). *Hericium* mushrooms should be harvested when the thorns are very long, but before the tops of the fruit mass weaken and become noticeably yellow or pink (Adamant 2019). Picking mushrooms in this fashion makes the harvesting process faster. Relative humidity in the growing room should be reduced to 80% for 4–8 hours before harvesting in order to reduce surface moisture and extend shelf life (Stamets 2011).

Submerged culture: cultivation methods for the production of bioactive compounds

Submerged culturing of *Hericium* can produce bioactive secondary metabolites that might not be found in their basidiomata (Elisashvili 2012). Critical conditions for the optimization of bioactive compounds include the monitoring of nutrient consumption and respiration (Thongbai et al. 2015). Several studies have tried to ascertain the best conditions for growing and producing mushrooms so that the fungi produce higher biomass, thus increasing the availability of more essential bioactive metabolites (Lee et al. 2004). Wolters et al. (2015) reported that submerged cultivation of *H. erinaceus* is the best method to produce erinacine C. The final inoculation ratio 5:10 (v/v) at pH 7.5 of 100 mM hydroxyethyl piperazineethanesulfonic acid (HEPES), produces high biomass of erinacine C at 2.73 gram/liter.

Nevertheless, there have also been many studies showings that some important secondary metabolites are also present on basidiomata of *H. erinaceus* growing on different substrates, such as artificial media and cheap agricultural substrates (Kulisic et al. 2004, Hu et al. 2008, Malinowska et al. 2009, Cui et al. 2010, Lee et al. 2010, Zhang et al. 2012). Wittstein et al. (2016) reported the production of a bioactive compound of *H. coralloides* could be used basidiomata by homogenized mechanically and stirred with acetone then separation of biomass by filtration. With the increasing demand for bioactive compounds from this mushroom, its cultivation for fruiting bodies is much needed. At present, there are still studies being done on mycelial cultivation so as more extracts are needed to meet the needs of consumers.

Health-enhancing applications of mushrooms

Mushroom nutrient

Hericium is a good source of dietary supplements in nutritional and medical food (Fernandes et al. 2021). In general, mushrooms contain 90% of water and 10% of dry matter (Ho et al. 2020). The composition of mushrooms depends on the growing medium and cultivation conditions (Badalyan 2003). *Hericium* is a relatively good source of several nutrients including free amino acids, especially glutamic acid, and numerous volatile compounds (Friedman, 2015). In addition, *Hericium* contains sugar, fat content, and protein content in fruiting bodies (Ulziijargal & Mau 2011). The basidiomata contains various amounts of nutritional macro-micro elements as well as low amounts of potentially toxic elements (Friedman 2015, Atila 2019). The nutritional content depends not only on environment and maturation stage but also on the species (Table 1).

Table 1 Nutrient contents of basidiomata of *Hericium.*

Properties	***Hericium* species**		
	H. americanum (Atila et al. 2017)	***H. coralloides*** (Heleno et al. 2015)	***H. erinaceus*** (Stamets 2011, Heleno et al. 2015)
Ash (g/ 100g)	6.4	9.31	3.49
Carbohydrate (g/ 100g)	-	81.06	79.36
Calcium (g/ 100g)	0.026	0.0044	0.0013
Dietary fiber (%)	-	44.28	41.32
Energy (kcal/ 100 g)	-	394.67	374.79
Fat (g/ 100g)	-	2.38	1.75
Iron (g/ 100g)	4.95–7.22	0.00677	0.0203
Mannitol	-	3.86	5.63
Magnesium (g/ 100g)	0.063−0.133	0.0085	0.1230
Phosphorus (g/ 100g)	0.99–2.12	-	0.0012
Potassium (g/ 100g)	2.66–3.58	1.188	0.0044
Protein (g/ 100g)	8.5–23.7	15.4	36.4
Sodium (g/ 100g)	0.134–0.178	0.586	0.0012
Total sugar	-	10.79	23.63
Trehalose	-	0.68	0.54

In addition, *Hericium* has a high average nutritional profile (Atila et al. 2021). The health-promoting properties responsible for the mushroom's nutritional value include amino acids, proteins, carbohydrates, fatty acids, vitamins, and minerals (Friedman 2015).

Medicinal property

Hericium mushrooms have long been considered to have medicinal value. However, these mushrooms have vast prospects as a source of medicinal compounds (Elkhateeb et al. 2019). These have been investigated in vivo and in vitro model systems (Chen et al. 2019). Many bioactive substances with immunomodulatory effects have been isolated from this mushroom (Sheng et al. 2017). These include high-molecular weight compounds such as polysaccharides and low-molecular weight compounds such as polyketides (Thongbai et al. 2015). The typical bioactive compounds isolated from *Hericium* include pyrone and alkaloids, terpenoids, sterols, and nonribosomal peptides (Table 2).

Hericium is a great source of novel therapeutic compounds (Chong et al. 2020). Most of the neurotrophic compounds have positive effects on the human nerve cell and neurogenerative diseases such as Alzheimer's disease, Parkinson's disease, Prion disease, Motor neurone disease, Huntington's disease, Spinocerbellar ataxia, and Spinal muscular atrophy (Zhang et al. 2016, Ratto et al. 2019, Chong et al. 2020). Ryu et al. (2021) reported that hericerin and isohericerinol A increase and regulate the number of neurons by nerve growth factor synthesis and brain-derived neurotrophic factors, in combination with synaptophysin. hericerin and isohericerinol A can promote neuron differentiation and neuron growth, which may be useful for both preventive and therapeutic use in neurodegenerative diseases (Li et al. 2018).

Table 2 The typical bioactive compounds isolated from *Hericium.*

***Hericium* species**	**Compounds**	**References**
Hericium. coralloides	corallocins A−C; hericerin; [5-(2E)-3′,7′-dimethyl-2′,6′-octadienyl]-4-hydroxy-6-methoxy-1-isoindoline	Wittstein et al. (2016)
H. erinaceus	cyatha-3,12-diene; D-Arabinitol; erinapyrones A, B, C; erinaceolactone A, C; erinacines A, B, C, E, F, G, H, I, S, Z1; erinacerin M; erinacol; hericerin; herierin III; hericanal A; hericene A; hericenones A, B, C, D, E, F, G, H; isohericerin; isohericerinol A; methyl linoleate; orsellinaldehye; polyphenols; polysaccharides; *N*-De phenylethyl isohericerin; 11-O-acetylcyathin A3; 1-D-arabinitol-monolinoleate; 2-chloro-1,3-dimethoxy-5-methylbenzene; 4-chloro-3,5-dihydroxy-benzaldehyde; 4-[30,70-Dimethyl-20,60-octadienyl]-2-formyl-3-hydroxy-5-methyoxybenzylalcohol	Miyazawa et al. (2012) Wolters et al. (2015) Sokół et al. (2015) Chen et al. (2017) Rupcic et al. (2018) Ryu et al. (2021)
H. flagellum	erinacine Z2; erinacines A, B, C, E, F; CJ14.258	Rupcic et al. (2018)

Furthermore, the compounds have been traditionally used in China for the prevention and treatment of human diseases. The important assignment is to describe the bioactive compounds of *Hericium* and their medicinal properties. It has been demonstrated that this mushroom possesses anti-oxidant (Jiang et al. 2019), anti-cancer (Younis 2017), anti-diabetic (Wu & Xu 2015), anti-hyperglycemic (Yao et al. 2021), hypolipidemic (Liang et al. 2013), anti-inflammatory (Hetland et al. 2020), anti-microbial (Vamanu & Voica 2017), anti-viral (Liu 2019), anti-fungal (Song et al. 2020), and hepatoprotective properties (Wang et al. 2019).

Hericium as antioxidant

Miles & Chang (2004) reported that *Hericium* prevents oxidation damage to cell DNA. According to Jiang et al. (2019), the effects of anti-oxidants are diverse, which may be due to external factors such as different components by the different extraction conditions having different anti-oxidant mechanisms. Atila et al. (2018) reported that the addition of olive cakes to the sawdust substrates for *Hericium* cultivation resulted in noticeable effects of its anti-oxidant activity. Moreover, Atila et al. (2018) recommended the cottonseed husks and olive cakes with wheat bran to increase the yield of *Hericium*.

Hericium as anti-cancer

Cancer is the world's leading cause of death (Younis 2017). *Hericium* has many medicinal properties such as anti-cancer activity (Blagodatski et al. 2018). Younis (2017) reported that polar extracts from *H. erinaceus* could be a good natural anti-cancer compound source. Moreover, *Hericium* extracts (HTJ5 and HTJ5A) have anti-hepatic and are effective against liver cancer, colon cancer, and gastric cancer in vitro and tumor xenografts bearing in mice in vivo (Blagodatski et al. 2018). This compound has potential as an anti-cancer agent for the treatment of gastrointestinal cancer used alone and/or in combination with clinical chemotherapy (Li et al. 2014).

Anti-diabetic, anti-hyperglycemic and hypolipidemic properties of Hericium

Liang et al. (2013) reported that the administration of the aqueous extract of *H. erinaceus* (AEHE) in streptozotocin (STZ) induced diabetic rats, resulting in lower blood glucose levels and higher insulin levels in the blood. The AEHE treatment also reduces fat disorders (Liang et al. 2013). The AEHE of *H. erinaceus* management increased the activities of catalase, superoxide dismutase, and glutathione peroxidase, and glutathione level, and reduced malondialdehyde level in the liver tissue (Liang et al. 2013).

Hericium as anti-inflammatory agent

Hetland et al. (2020) reported that *Hericium* caused a decrease in inflammatory cytokines, oxidative stress, and changed intestinal microorganisms, thus, leading to the anti-allergic mechanism in maintaining the balance of T helper cells. *Hericium* induced anti-inflammatory mechanisms also include cytokines that cause inflammation, nerve growth that prevents the death of neurons in the ischemic brain (Lee et al. 2014), growth of beneficial intestinal microbiota protecting against inflammatory bowel disease-induced mucosa damages, and improving host immunity (Diling et al. 2017), regulating oxidative stress through signaling pathways that attenuate colitis (Ren et al. 2018).

Hericium as anti-microbial agent

The anti-microbial activity of *Hericium* is diverse due to the different species and their ability to inhabit diverse ecological niches with a variety of nutrients and physiological and biological conditions (Sheng 2017). Kim et al. (2019) reported that the anti-microbial activity of *H. erinaceus* was highly effective against *Staphylococcus aureus*, *Salmonella enteritidis*, *Vibrio parahaemolyticus*, and *Escherichia coli* at 2.5 mg/mL or above. Hence, its extract can be used as food and natural antimicrobial agent in the diet of pathogenic bacteria.

Hericium as anti-viral agent

Ellan et al. (2019) reported anti-viral activity of *H. erinaceus.* The mushrooms extract showed very prominent anti-dengue virus serotype 2 (DENV-2) activity (Ellan et al. 2019). Wang & Ng (2004) found that the low molecular weight laccase from the dried fruiting body of *H. erinaceus* showed anti-viral activity against human immunodeficiency virus (HIV) and HIV-1.

Economical importance

Since ancient times, *Hericium erinaceus* was a popular species due to its nutritional value and traditional medicinal benefits in China (Khan et al. 2013). *Hericium* has high importance and potential to improve many parts of human life (Valverde et al. 2015). In general, *Hericium* is saprobic, hence utilizing organic and agricultural wastes are recommended (Marshall & Nair 2014). *Hericium* cultivation in some countries is done on a commercial level, earning a handsome income to the growers and farmers (Scherr et al. 2004). The employment generated through cultivation and its associated allied activities is also immense (Jha 2006). Increasing the value of *Hericium* mushrooms in terms of quality products is another economic avenue (Üstün et al. 2018).

Hericium is economically important, since the mushrooms are valuable resources for agricultural, food, and medicinal applications (Park et al. 2004). Ergothioneine accumulates at higher levels in mycelia than in fruiting bodies of economically important mushroom species (Lee et al. 2009). Therefore, the mycelial medium is an effective way to increase the anti-oxidant property of economically important mushroom species (Lee et al. 2009). The search for new sources of bioactive products from *Hericium* is still being done to date (Antunes et al. 2020).

Industrial and pharmaceutical applications

The mycelia of *Hericium erinaceus* are rich in erinacines and could be potential candidates in promoting positive brain and nerve health-related activities (Li et al. 2018). Zhang et al. (2017) and Tzeng et al. (2018) reported that *H. erinaceus* powder reduced short-term memory impairment and visual recognition, and neuron generation of the hippocampus of Alzheimer's disease in a mouse model. Also, *Hericium* have been used to treat cognitive impairment in Parkinson's disease (Kuo et al. 2016, Trovato et al. 2016). In addition, Rascher et al. (2020) reported the cyathane diterpenoid erinacine C of the genus *Hericium* induces expression of the neurotrophins NGF and BDNF in glial cells, also the erinacine C promotes ETS-dependent transcription in astroglial cells, which may play a role in regulating germination and regeneration in the central nervous system.

Commercial health products made from *Hericium* are commonly used for health care and to promote learning and memory (Sokół et al. 2015). A large list of health care products that contain *H. erinaceus* extract as a medicinal ingredient has been introduced for promoting human health. There are patented health products, meal replacement powders, chewable tablets, and solids beverages containing the compounds of *H. erinaceus* that improve human health without side effects (He et al. 2017).

An only clinical study reported the intake of *Hericium* as local drugs, herbs, and in medicinal cuisine (Limanaqi et al. 2020). The pharmacological activities, including anti-allergic, anti-bacterial, anti-fungal, anti-inflammatory, anti-oxidative, anti-viral, cytotoxic, immunomodulating, antidepressive, anti-hyperlipidemic, anti-diabetic, digestive, hepatoprotective, neuroprotective, nephroprotective, osteoprotective, and hypotensive activities (Venturella et al. 2021). In attempts to assess the impact on cognitive function for clinical research, Yamabushitake was used at 750 mg/day (available as a 250 mg tablet, three-time daily for 16 weeks). The tablet contains 96% of dry powder of Yamabushitake (Mori et al. 2009). Wang et al. (2014) reported that the *Hericium* tablet was administered 3 g/day for 16 weeks and 5 g/day of fruiting bodies pulp broth were eaten. Most of them have beneficial effects on the body, especially the brain, heart and intestines. Chiu et al. (2018) reported that *Hericium* may help relieve mild symptoms of anxiety and depression and can reduce the impact of chronic illness.

Conclusion

Hericium has attracted a lot of attention as an edible mushroom, supplementary food, and potential source of medicinal compounds. It has been cultivated for more than two decades in China. Traditionally used for more than 1,000 years, *Hericium* was found to have various pharmacological effects. The significance of *Hericium* in the health and economic sector has led to various industrial applications. Studies have shown successful cultivation of *Hericium* using both indoor and outdoor cultivation methods. Moreover, submerged culture methods are capable of reducing the cost of downstream processing and increasing the bioactive compound yield. Using the research results and nutraceutical properties of *Hericium*, it is possible to develop *Hericium* based products industrially.

Acknowledgements

We appreciate the kind support given by the Research and Researchers Industries (RRI) (Grant no. PHD62I0018/2562) and Thailand Science Research and Innovation (TSRI) grant "Macro fungi diversity research from the Lancang-Mekong Watershed and surrounding areas" (Grant no. DBG6280009).

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