COMMENT
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Hericium erinaceus: the enchanting medicinal-culinary mushroom of East Asian tradition

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Hericium mushrooms, a type of fungi imbued with mystical connotations in traditional East Asian diet and medicine, hold a prestigious position as the foremost among the "eight treasures of the mountain" in China, earning them the moniker "mountain delicacies and marine flavors." As traditional medicinal fungi, *Hericium* mushrooms are renowned for their brain-boosting and cognitive-enhancing properties. *Hericium erinaceus* (*H. erinaceus*) is the leading variety of *Hericium* mushrooms and has been cultivated on a large scale. In addition, some new species such as the *Hericium coralloides*, *Hericium alpestre*, and *Hericium rajendrae* have been progressively discovered and documented [1, 2]. The recent pursuit of health and nutrition has propelled this nutrient-rich and bioactive mushroom into the limelight. This article explores the traditional uses of *Hericium* mushrooms, the chemical structures and biological activities of their secondary metabolites, as well as the pivotal role of omics technologies in this field (Figure 1).

H. erinaceus has been a traditional mushroom in East Asia since ancient times and has a rich culinary and medicinal history. In Korea, it is called Norugungdengi and is mainly eaten as an edible mushroom. In Japan, it is known as Yamabushitake and is valued for its neuroprotective effects on the central nervous system. In China, *H. erinaceus* is known as houtougu (monkey head mushroom) because of its lion's mane-like fruiting body, and has been used as a food and medicine for hundreds of years, with a traceable history dating as far back as the Sui Dynasty. The *Miscellaneous Records of Unusual Objects in Linhai Soil* written in the Sui Dynasty recorded people's love for *H. erinaceus* soup, and the Tang Dynasty book *Dietary Therapy Materia Medica* recorded the nutritional value of *H. erinaceus*. The *Yinshan Zhengyao* of the Yuan Dynasty and the *Compendium of Materia Medica* of the Ming Dynasty recorded of the Ming Dynasty recorded the medicinal value of *H. erinaceus* in detail. The *National Compendium of Chinese Herbal Medicines*, published in 1975, and the *New Materia Medica*, published in 1999, both recorded in detail the medicinal efficacy of *H. erinaceus* as a traditional Chinese medicine. Currently, seven China Food and Drug Administration-approved traditional proprietary Chinese medicines made from the fruiting bodies and mycelial extracts of the *H. erinaceus* are in circulation in China [3].

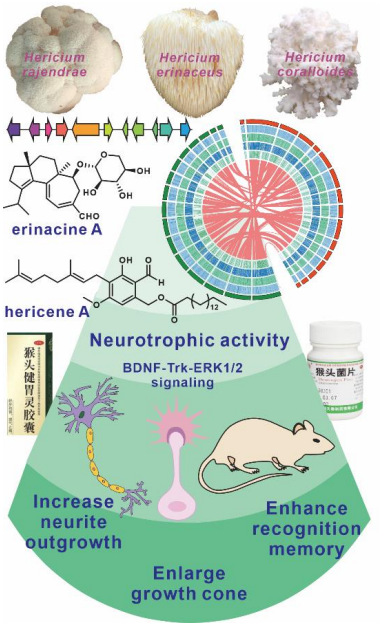

Figure 1 Traditional use, chemical composition, biological activity and genome of *Hericium* mushrooms. BDNF, brain-derived neurotrophic factor.

Modern natural product investigations have identified over 200 natural compounds from *Hericium* mushrooms [4], with the erinacine diterpenes [5] and hericenones polyketide-meroterpenoids being the main constituents of their metabolites. The diterpene skeleton of erinacine, cyathane, is a diterpene molecular skeleton found in several mushrooms [6]. Hericenones, on the other hand, are meroterpenes composed of orsellinic acid and isoprenoid, geranyl or farnesyl moieties. The orsellinic acid scaffold is produced in a variety of mushrooms [7]. *Hericium* secondary metabolites, primarily erinacines and hericenones, exhibit a range of biological activities and pharmacological effects. Their anti-neurodegenerative disease activity is particularly notable, with a focus on neurotrophic, neuroprotective, and anti-inflammatory aspects. A group of compounds known as erinacines and hericenones has become a hot topic in neuroscience research. These compounds have been found to protect neurons from damage by promoting the synthesis of nerve growth factor, offering a new perspective for the treatment of Alzheimer's disease. Relevant animal experiments suggest that they have potential therapeutic effects on neurodegenerative diseases such as Alzheimer's disease by activating signaling pathways like TrkA/Erk1/2 [8]. Hypoglycaemic activity is another characteristic medicinal property of *Hericium* mushrooms as a traditional medicinal fungus, and the monomer compounds found to have α-glucosidase inhibitory activity part of hericenones [9] may be the molecular basis of the hypoglycaemic activity of *Hericium* mushrooms. Another pharmacological activity of *Hericium* mushrooms that must be mentioned as an herbal medicine is stomachic and digestive stimulant, which is the main medicinal effect of several proprietary Chinese medicines. The discovery of molecules that inhibit *Helicobacter pylori* provided the theoretical basis for this effect of *H. erinaceus* [10].

Technological advancements, especially high-throughput sequencing and metabolomics analysis, have significantly advanced *Hericium* research. These technologies enable rapid identification and quantification of metabolites in the mushroom, revealing the complexity and diversity of its metabolome. Genomic studies of *Hericium* mushrooms provide new clues for understanding its intricate biosynthetic pathways. Through genomic analysis of *H. rajendrae*, researchers discovered the *hra* gene cluster responsible for erinacine synthesis [1], revealing its biosynthetic pathway and offering the possibility of producing these active compounds through synthetic biology methods. Whole genome sequencing of *H. erinaceus* identified its microsatellite signature, which provides essential information for the development of molecular markers for horticultural traits [11]. Another whole genome sequencing of *H. erinaceus* provides new insights into the biosynthesis of polysaccharides in *H. erinaceus* [12].

Research on *Hericium* mushrooms is not only scientifically significant but also hold potential industrial applications. For instance,

its fruiting bodies have been developed into health foods and pharmaceuticals, with its neuroprotective and anti-inflammatory activities offering new hope for treating various diseases. However, the artificial cultivation and large-scale production of *Hericium* mushrooms still face challenges, including optimization of growth media, control of growth conditions, and the extraction and purification of products. Addressing these issues requires interdisciplinary collaboration, combining knowledge from fields such as biology, chemical engineering, and molecular biology. Future research will continue to explore the secondary metabolites of *Hericium* mushrooms, especially those yet undiscovered, and their potential in treating neurodegenerative diseases and other illnesses. Moreover, the development of synthetic biology and gene-editing technologies will provide new avenues for the customized production of *Hericium* mushrooms active compounds. With these technologies, scientists hope to develop more effective and healthier *Hericium* mushrooms foods in the near future, thereby improving human health and quality of life.

References

1. Wei J, Cheng M, Zhu J, et al. Comparative Genomic Analysis and Metabolic Potential Profiling of a Novel Culinary-Medicinal Mushroom, *Hericium rajendrae* (Basidiomycota). *J Fungi.* 2023;9(10):1018. Available at: http://doi.org/10.3390/jof9101018
2. Cesaroni V, Brusoni M, Cusaro CM, et al. Phylogenetic Comparison between Italian and Worldwide *Hericium* Species (Agaricomycetes). *Int J Med Mushrooms.* 2019;21(10):943–954. Available at: http://doi.org/10.1615/IntJMedMushrooms.2019032561
3. Tan Y-F, Mo J-S, Wang Y-K, et al. The ethnopharmacology, phytochemistry and pharmacology of the genus *Hericium*. *J Ethnopharmacol.* 2024;319:117353. Available at: http://doi.org/10.1016/j.jep.2023.117353
4. Qi J, Wu J, Kang S-j, et al. The chemical structures, biosynthesis, and biological activities of secondary metabolites from the culinary-medicinal mushrooms of the genus *Hericium*: A review. *Chin J Nat Med*. 2024;22:1–24. Available at: https://doi.org/10.1016/S1875-5364(24)60590-X
5. Wei J, Li J, Feng X, et al. Unprecedented Neoverrucosane and Cyathane Diterpenoids with Anti-Neuroinflammatory Activity from Cultures of the Culinary-Medicinal Mushroom *Hericium erinaceus*. *Molecules.* 2023;28(17):6380. Available at: http://doi.org/10.3390/molecules28176380
6. Qi J, Gao Y-Q, Kang S, Liu C, Gao J-M. Secondary Metabolites of Bird's Nest Fungi: Chemical Structures and Biological Activities. *J Agric Food Chem.* 2023;71(17):6513–6524. Available at: http://doi.org/10.1021/acs.jafc.3c00904
7. Han H, Yu C, Qi J, et al. High-efficient production of mushroom polyketide compounds in a platform host *Aspergillus oryzae*. *Microb Cell Fact.* 2023;22(1):60. Available at: http://doi.org/10.1186/s12934-023-02071-9
8. Mitchell DJ, Blasier KR, Jeffery ED, et al. Trk Activation of the ERK1/2 Kinase Pathway Stimulates Intermediate Chain Phosphorylation and Recruits Cytoplasmic Dynein to Signaling Endosomes for Retrograde Axonal Transport. *J Neurosci.* 2012;32(44):15495–15510. Available at: http://doi.org/10.1523/jneurosci.5599-11.2012
9. Lee SK, Ryu SH, Turk A, et al. Characterization of α-glucosidase inhibitory constituents of the fruiting body of lion's mane mushroom (*Hericium erinaceus*). *J Ethnopharmacol.* 2020;262(15):113197. Available at: http://doi.org/10.1016/j.jep.2020.113197
10. Zhang Z, Liu R-N, Tang Q-J, Zhang J-S, Yang Y, Shang X-D. A new diterpene from the fungal mycelia of *Hericium erinaceus*. *Phytochem Lett.* 2015;11:151–156. Available at: http://doi.org/10.1016/j.phytol.2014.12.011
11. Gong W, Wang Y, Xie C, Zhou Y, Zhu Z, Peng Y. Whole genome sequence of an edible and medicinal mushroom, *Hericium erinaceus* (Basidiomycota, Fungi). *Genomics.* 2020;112(3):2393–2399. Available at: http://doi.org/10.1016/j.ygeno.2020.01.011
12. Gong M, Zhang H, Wu D, et al. Key metabolism pathways and regulatory mechanisms of high polysaccharide yielding in *Hericium erinaceus*. *BMC Genomics.* 2021;22(1):160. Available at: http://doi.org/10.1186/s12864-021-07480-x

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

H. Erinaceus, *Hericium erinaceus.*

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