AARM
Association for the Advancement of Restorative Medicine

Hericium erinaceus

Lion's mane

Alternative names

Sheep's head, Bear's head, Bearded tooth carpophore, Yamabushitake.

Indications

Neuroprotection, neurotrophic activity, cognitive function, neurodegenerative diseases, ischemic stroke

Mechanism of Action

Exact mechanisms of action are still being elucidated, but several biologically active metabolites have been isolated from Lion's mane mushroom (*Hericium erinaceus*) that hold promise for nerve and brain health. Of particular interest are hericenones and erinacines, which are believed to occur only in *Hericium* spp. Hericenones are isolated from Lion's mane fruiting bodies, and erinacines are isolated from the mycelium.[1,2,3] Both hericenones and erinacines are low molecular weight compounds that potentially cross the blood–brain barrier.[4]

Hericenones
Hericenones A, B, C, D, E, F, G, and H are aromatic compounds isolated from the fruiting bodies of Lion's mane mushroom. Hericenones have shown a strong stimulatory effect on the biosynthesis of nerve growth factor (NGF) *in vitro*. In the presence of hericenones C, D, E, and H at 33 µg/mL, mouse astroglial cells secreted 23.5±1.0, 10.8±0.8, 13.9±2.1, and 45.1±1.1 pg/mL NGF, respectively, into the culture medium.[5,6,7] The degree of bioactivity for hericenone D was almost as high as epinephrine,[8] a powerful inducer of NGF in its own right. However, in a bioassay using mouse astroglial cell, the volume of NGF secreted into the medium in the presence of erinacines was greater than with hericenones.[4]

Erinacines
Erinacines are cyathin diterpenoids that appear to stimulate the synthesis of NGF. To date, 15 erinacines (erinacines A–K and P–S) have been identified.[3] Several erinacines show neuroprotective activity. For example, erinacines A, B, C, E, F, H, and I are strong inducers of NGF synthesis both *in vitro* and *in vivo*.[9,10,11,12] In addition, erinacines have been found to decrease amyloid-β plaque deposition,[13] increase expression of insulin-degrading enzyme (erinacines A and S),[14] and mitigate neuropathic pain (erinacine E).[15,16,17]

Evidence-Based Research

Neurotrophic activity and myelination
An ethanol extract of Lion's mane fruiting body improved NGF gene expression in human astrocytoma cells, in a concentration-dependent manner. Neurite outgrowth was also improved.[18] In the presence of

a Lion's mane extract, cultivated cerebellar cells underwent myelination earlier and at a greater rate than controls. Growth of nerve and glial cells was observed to be normal, with intact cell structure that looked similar to cells observed *in vivo*.[19] Mice fed dry powder of 5% Lion's mane fruiting body for seven days, showed an increase in the level of NGF mRNA expression in the hippocampus.[20] Another *in vitro* study showed that Lion's mane mycelia were more effective than control, NGF, or brain-derived neurotrophic factor (BDNF) alone in enhancing the growth of rat neurite extensions.[8]

Neuroprotection

The neuroprotective effect of erinacine A-enriched *H. erinaceus* mycelia was evaluated in a neurotoxin-induced model of Parkinson's disease. Results showed that dopaminergic lesions and oxidative stress in the stratum and substantia nigra were significantly improved after pretreatment with 3 mg/kg erinacine A-enriched *H. erinaceus* mycelia for 25 days.[21] Erinacine A also increased NGF and catecholamine levels in the locus coeruleus and hippocampus of rats when administered at doses of 8 mg/kg body weight.[22] In a rodent model of transient focal cerebral ischemia, pretreatment with 3 mg/g erinacine A-enriched *H. erinaceus* mycelia orally for 5 days decreased infarction by 22% at 50 mg/kg and 44% at 300 mg/kg. This effect was thought to be partially mediated by reducing cytokine levels.[23]

In another study, immunohistochemistry for neuronal nuclei (NeuN) showed significantly more neurons after brain injuries in rats treated with erinacine A-enriched *H. erinaceus* mycelia.[24]

Cognitive function

Oral supplementation with Lion's mane induced a statistically significant improvement in spatial short-term and visual recognition memory in wild-type mice.[25] In another study using a mouse model of Alzheimer's disease, oral administration of Lion's mane fruiting body increased hippocampal expression of NGF mRNA, and prevented the impairment of short-term, spatial, and visual recognition memory observed in non-treated mice.[26] Another study of 5-month-old transgenic mice in a rodent model of Alzheimer's disease found that oral administration of Lion's mane mycelia containing 19 mg/g erinacine for 30 days diminished cerebral amyloid β plaque burden; prevented recruitment and activation of plaque-associated microglia and astrocytes; augmented expression of insulin-degrading enzyme; increased the ratio of NGF-to-NGF precursor (proNGF); and increased proliferation of both neuronal progenitors and the number of new neurons in the dentate gyrus region. In addition, mice treated with *H. erinaceus* mycelia recovered behavioral deficits after 81 days of administration.[27]

Clinical Trials

In a double-blind placebo-controlled study of 50-80-year-old Japanese men and women (*n*=30) diagnosed with mild cognitive impairment, oral intake of 250 mg tablets containing 96% of Lion's mane dry powder three times a day for 16 weeks was associated with marked improvement in cognitive function, as measured by the revised Hasegawa Dementia Scale (HDS-R), when compared with controls. Scores on the HDS-R decreased, however, by 4 weeks after cessation of the intervention.[28]

In another small randomized clinical study (*n*=30), post-menopausal women who consumed 2 g/day of Lion's mane fruiting bodies baked into cookies for 4 weeks showed a reduction in anxiety and depression symptoms compared with controls. The Indefinite Complaints Index categories for Palpitation and Incentive showed a statistically significant improvement in treated subjects versus controls. The categories of Irritating, Anxious, and Concentration also indicated a trend in the direction of improvement in this population.[29]

Safety in Pregnancy and Breastfeeding

To date, there has been no concerted investigation into the use of Lion's mane mushroom in pregnancy and lactation. Erinacine-enriched Lion's mane mycelium showed no evidence of teratogenicity in Sprague-Dawley rats in doses up to 2625 mg/kg.[30]

General Safety

Experimental studies suggest that Lion's mane mycelium is safe, with no evident adverse effects. In rats, the acute oral LD_{50} of Lion's mane mycelia enriched with its bioactive compounds was found to be higher than 5 g/kg,[31] suggesting the mycelium is reasonably safe with regards to overdose. Repeated daily doses of up to 3 g/kg of Lion's mane mycelium enriched with its bioactive compounds have also been used in rats with no adverse effects.[32] Furthermore, Lion's mane 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.[33] No adverse clinical or biochemical events were reported in the clinical trial of subjects with mild cognitive impairment.[28] In a study of post-menopausal women,[29] one subject reported epimenorrhea, but its association with Lion's mane supplementation was inconclusive. Allergies and sensitivities to mushrooms are not unusual.

Dosage

The dose of Lion's mane dried fruiting body recommended for increasing NGF production is 3–5 g per day. A dose of 250 mg of 96% Lion's mane dry powder three times a day for 16 weeks was associated with significant improvement on a dementia rating scale in subjects with mild cognitive impairment.[28] Four weeks of 2.0 g/day of Lion's mane fruiting bodies baked into cookies was associated with improvement in symptoms of anxiety and depression in post-menopausal women.[29] It is best to supplement with preparations of Lion's mane that use a combination of aqueous and alcohol extraction, to ensure the whole spectrum of contents is present.[30]

Traditional Uses

Lion's mane mushroom is a culinary and medicinal fungus common to North America and Asia. Its fruiting bodies and mycelia have been used for centuries in traditional Chinese medicine for their anti-inflammatory and immune-supporting effects. A medication known as Wei Le Xin Chong Ji is available commercially in China to treat ulcers, inflammation, and alimentary tract neoplasm. Medicinally, Lion's mane has been administered as tablets made from dried and powdered fruiting bodies. Lion's mane is also known for its effects on the central nervous system. It is used for insomnia, vacuity (weakness), and hypodynamia, which are characteristic symptoms of Qi deficiency in Traditional Chinese Medicine.

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