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File: ■ Lion's Mane (*Hericium erinaceus*, Hericiaceae) ■ Neurodegenerative Disease

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RE: Lion's Mane Mushroom May Have Protective Effects Against Neurodegenerative Disease by Mitigating Inflammatory Pathways

Contato AG, Conte-Junior CA. Lion's mane mushroom (*Hericium erinaceus*): A neuroprotective fungus with antioxidant, anti-inflammatory, and antimicrobial potential—a narrative review. *Nutrients*. April 2025;17(8):1307. doi: 10.3390/nu1781307.

Chronic inflammation and oxidative stress are the precursors to many underlying diseases, such as cardiovascular diseases, diabetes, neurodegenerative diseases, and cancer. Current pharmacological treatment includes synthetic drugs; however, many of these have unwanted side effects and long-term health risks. Mushrooms have a rich history as functional food and medicine owing to their nutritional and chemical profile. Lion's mane (*Hericium erinaceus*, Hericiaceae) has been shown to enhance cognitive function, improve memory and concentration, and protect against neurodegenerative diseases. Additionally, lion's mane has been used to support gastrointestinal health. The purpose of this narrative review is to explore the bioactive components of lion's mane with special attention to their neuroprotective properties and mechanisms of action.

A keyword search was performed through March 2025, using PubMed, Scopus, Science Direct, Web of Science, and Google Scholar. Articles published in English, online reports, and electronic books were included that studied lion's mane in combination with at least one of the keywords, such as anti-inflammatory, bioavailability, and blood-brain barrier. Also included were articles that studied the habitat, cultivation, and characteristics of lion's mane.

Lion's mane is a saprotrophic and weak parasitic fungus. It grows on dead or dying hardwood trees in temperate forests in North America, Europe, and Asia. Lion's mane tends to grow higher up in the tree, complicating harvest. Due to its popularity, lion's mane is commercially cultivated to produce higher yields, year-round availability, and improved quality. Commercial cultivation includes log cultivation, sawdust blocks, and liquid fermentation. Log cultivation produces a low yield with a growth time between six and 12 months. Sawdust produces a high yield over six to eight weeks, and liquid fermentation has a very high yield in just five to 10 days. Studies show that the chemical make-up of lion's mane is affected by the cultivation and fungal development stage. Lion's mane is administered in many forms, including capsules, tablets, powder, liquid extract, functional beverages, and protein bars. Supercritical fluid extraction has been

shown to improve efficiency in isolating specific compounds while preserving bioavailability.

Lion's mane is comprised of polysaccharides, terpenoids, phenolic compounds, and bioactive proteins. These contribute to its antioxidant, anti-inflammatory, and neuroprotective activities. β -glucans are among the most studied compounds of lion's mane. Research shows these compounds have immunomodulatory, antimicrobial, and antitumor effects. β -glucans activate macrophages, natural killer cells, and T lymphocytes.

Hericenones and erinacines are terpenoids in lion's mane attributed to its neurogenerative and neuroprotective properties. Studies show these compounds stimulated nerve growth factor, which makes them particularly important for Alzheimer's and Parkinson's diseases. Hericenones and erinacines have also been shown to modulate key inflammatory pathways, including nuclear factor kappa B (NF- κ B) and cyclooxygenase-2, to reduce chronic systemic inflammation and neuroinflammation. Mitigating these pathways has also demonstrated a beneficial effect on autoimmune disorders. Specifically, erinacines and hericenones inhibit phosphorylation of inhibitor of NF- κ B, which prevents NF- κ B activation, reducing the inflammatory process.

Additionally, lion's mane contains ergothioneine. Recent studies show this compound has potent antioxidant properties shown to neutralize reactive oxygen species and reduce oxidative stress in neuronal cells. Ergothioneine has been shown to have distinct bioavailability over other dietary antioxidants.

Most studies are in vitro or animal studies; however, several clinical trials evaluating the efficacy of lion's mane cognitive function and gastrointestinal health were presented. A randomized, double-blind, placebo-controlled trial evaluated cognitive function in Japanese men and women aged 50–80 years who were diagnosed with mild cognitive impairment. Treatment included lion's mane extract over 16 weeks compared to a placebo. Significant improvements were observed in the treatment group compared to the placebo; however, those improvements declined after discontinuing use of the supplement. Another clinical trial evaluated patients diagnosed with early-stage Alzheimer's disease. Findings showed that regular consumption of lion's mane improved memory recall and reduced neuropsychiatric symptoms. Details of this study were not provided.

A retrospective multicenter study included patients diagnosed with mild-to-moderate ulcerative colitis. Lion's mane in conjunction with 5-aminosalicylic acid (5-ASA) was shown to significantly improve remission rates compared to 5-ASA alone. Fecal calprotectin levels decreased significantly in both groups but was significantly greater in the treatment group compared to the control. A small-scale study showed that lion's mane reduced stress levels and improved mood regulation. Details of this study were not provided.

Lastly, lion's mane was shown to protect against gram-positive bacteria with a lesser effect against gram-negative bacteria. The antimicrobial activity varied between studies depending on the bioactive compound and target microorganism. It was shown that lion's mane has inhibitory properties rather than bactericidal. It was also shown to enhance the efficacy of existing antibiotics, providing a synergistic effect.

The authors conclude that preclinical and in vitro studies show neuroprotective, antimicrobial, and immunomodulatory properties of isolated compounds in lion's mane. However, large scale, human studies are needed to confirm preclinical and in vitro

studies, determine dosage, long-term safety, and potential drug interactions of lion's mane. Finally, further studies are needed to determine standardization in extraction methods and bioactive composition.

The authors declare no conflicts of interest

—*Samaara Robbins*

Referenced article can be accessed at <https://www.mdpi.com/2072-6643/17/8/1307>.

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