FOOD AS MEDICINE:

LION'S MANE MUSHROOM HERICIUM ERINACEUS

Ву

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A slide presentation for HealthCare Provider Seminar Jan 2019







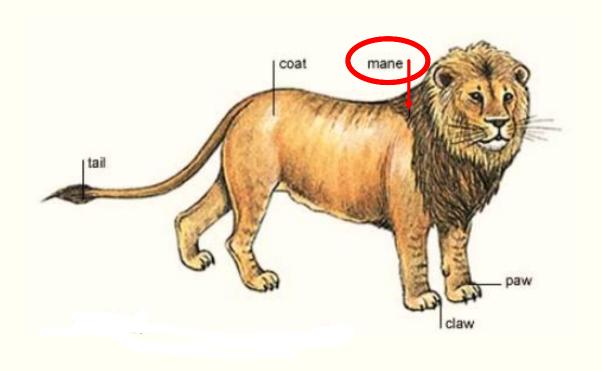


Lecture outline

- What is a lion's mane mushroom?
- Stats, cultivation, scientific classification
- Anatomy, life cycle
- Nutrients and bioactive compounds
- Health benefits
- Pharmacological effects, interactions, toxicity
- Clinical studies
- Summary

What is a Lion's Mane Mushroom

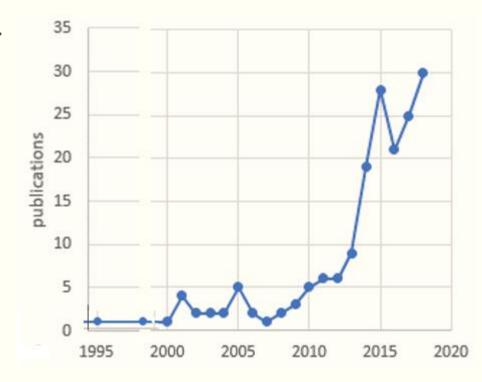
(Hericium erinaceus)

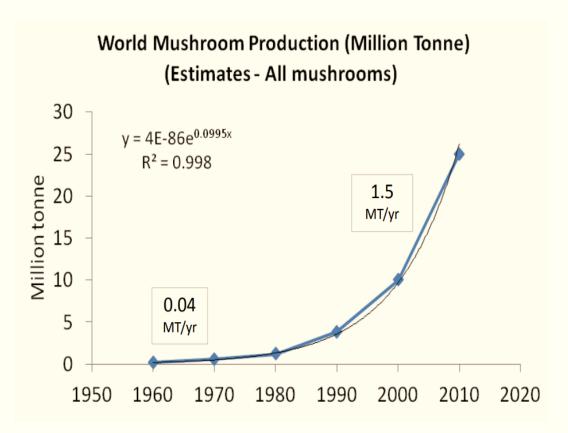


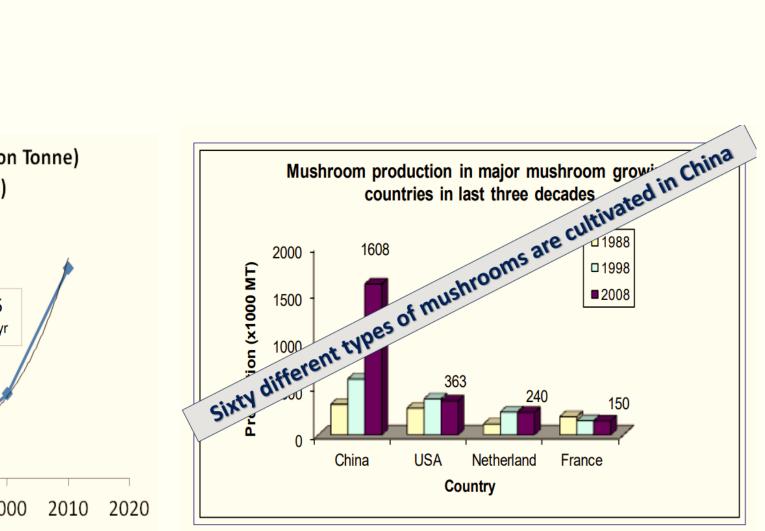


Advances in the scientific study of lion's mane mushroom: number of publication in PubMed from 2000 to 2018

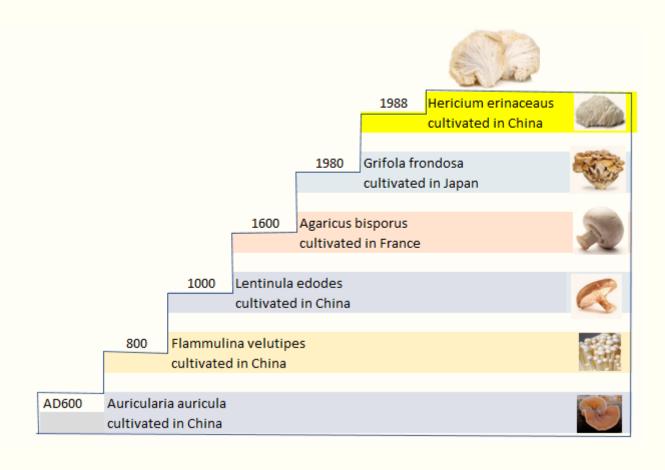
- Scientific studies on lion's mane began In 2000.
- Major areas of interest are:
 - Immune system: Immune-modulation
 - Nervous system: Nerve growth factor
 - Neuro-regeneration
 - Neuroprotection
 - Cognition
 - Nerve injury
 - Cardiovascular system:
 - Blood pressure
 - Lipids and cholesterol
 - Neoplasm: anti-cancer







Cultivation of Lion's mane (*Hericium erinaceus*) mushroom





Scientific classification of Lion's Mane (*Hericium erinaceus*)

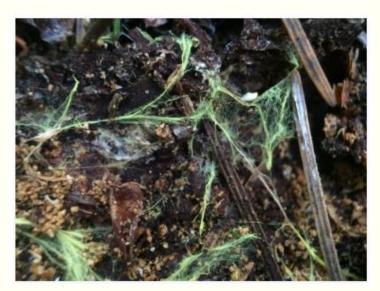
Kingdom	Fungi
Division	Basidomycota
Class	Agaricomycetes
Order	Russulales
Family	Hericeae
Genus	Hericium
Species	H. eirnaceus



Anatomy of a typical mushroom vs lion's mane mushroom



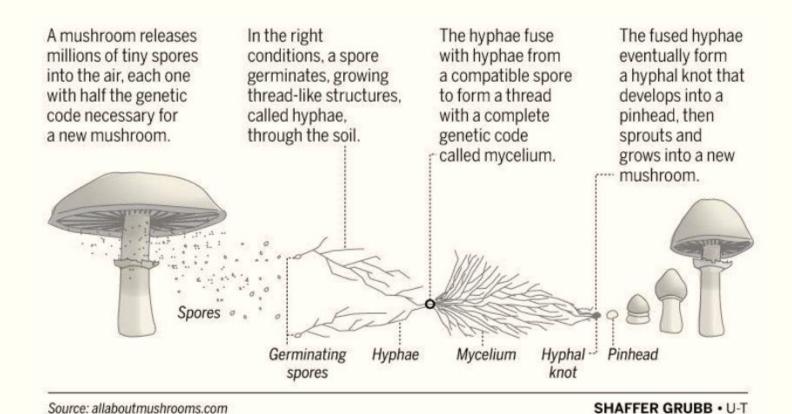
Mycelium of a mushroom



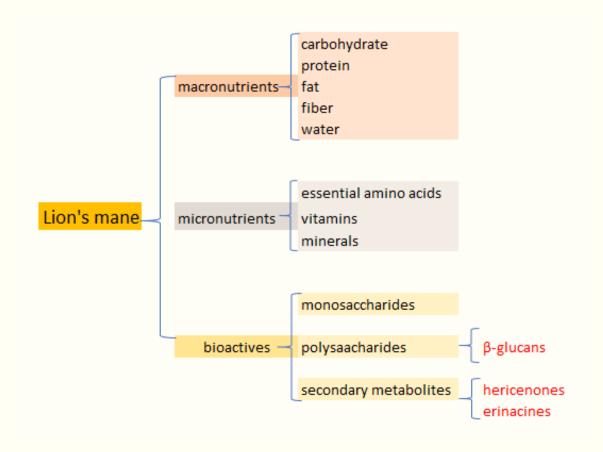




Life cycle of a mushroom

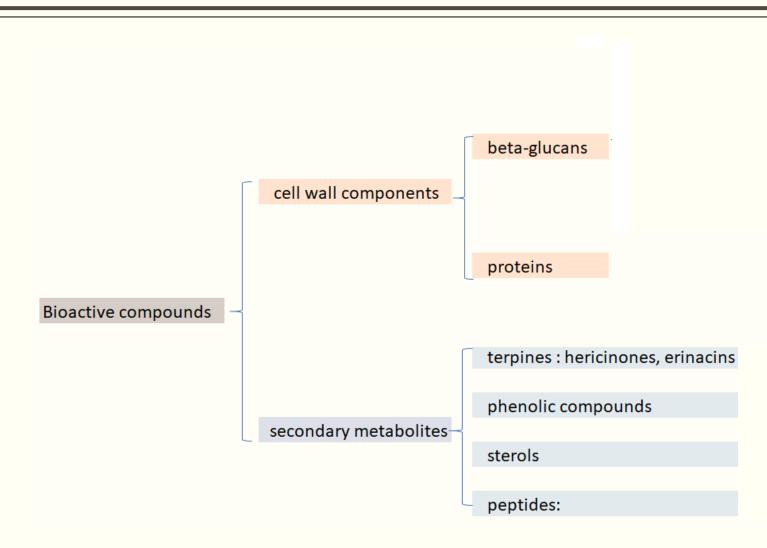


Nutrient composition of Lion's mane (*Hericium erinaceus*)



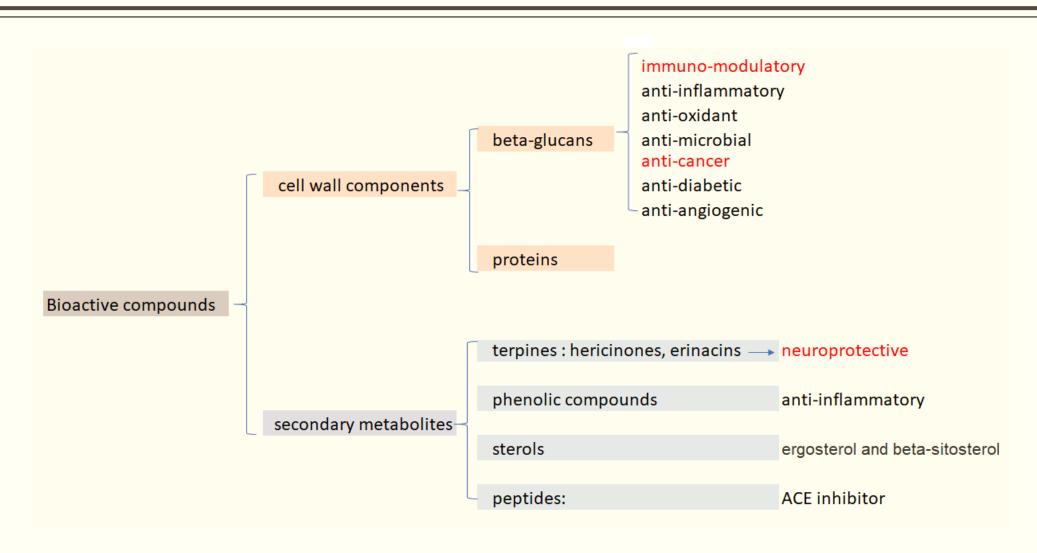


Bioactive compounds of Lion's Mane (*Hericium erinaceus*)



Bioactive compounds & functions of

Lion's Mane (*Hericium erinaceus*)

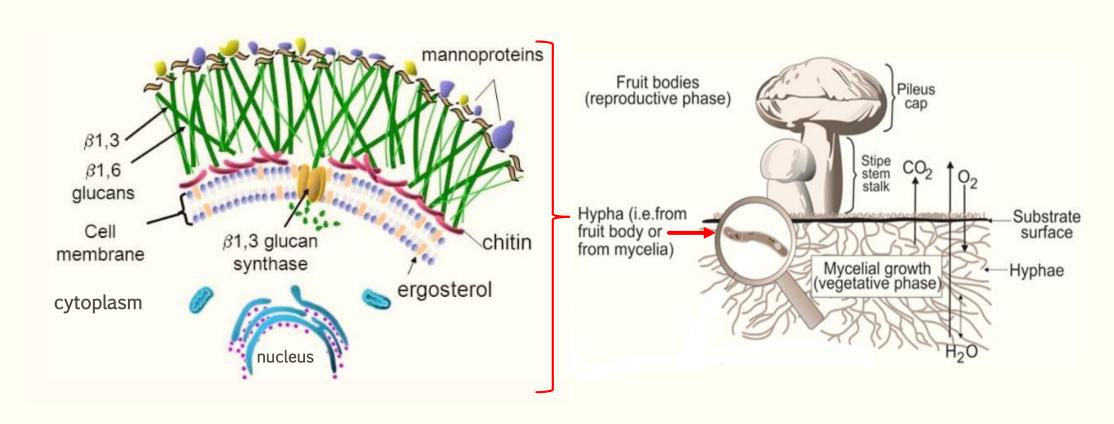


What is a polysaccharide?

 A long chain of carbohydrate consisting of a number of sugar molecules bonded together, e.g. starch, cellulose or glycogen.

■ The polysaccharide from lion's mane mushroom (hericium mane) is called beta-glucan.

Location of \(\beta \)-glucans in mushroom cell wall



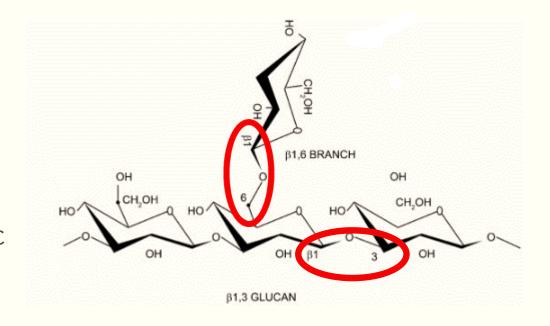
What is a beta-glucan?

Beta (β) refers to the orientation of the linkage bond.

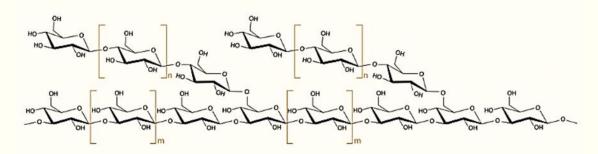
 Glucan molecule is a polysaccharide of D-glucose monomers, linked by glycosidic bonds.

What is a Beta-1, 3 and Beta-1,6 Glucan?

- Beta refers to the structural configuration of the molecule.
- Glucan refers to a polysaccharide of D-glucose monomers, linked by glycosidic bonds
- The number 1,3 and 1,6 refers to the glycosidic linkage and bonding of the glucose molecule



What is the main function of \$\beta\$-glucan



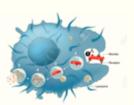
Beta-1, 3 and Beta-1,6 Glucan

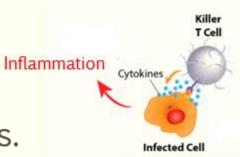
- Immune System Booster or
- Biological Response Modifier

Effects of \(\beta \)-glucans on the Immune System

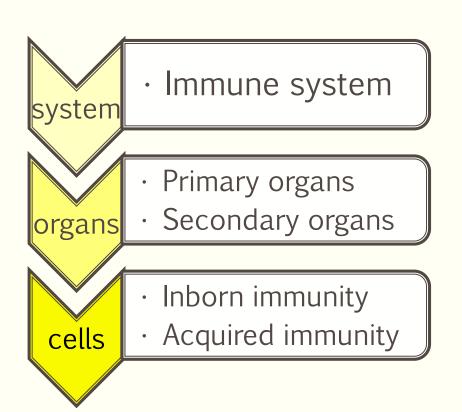
- Removal of dead cells by phagocytosis.
- Destruction of cancer cells by lysis.
- Generation and release of cytokines.
- Communication with immune cells.
- Protection from fungi, bacteria and virus.

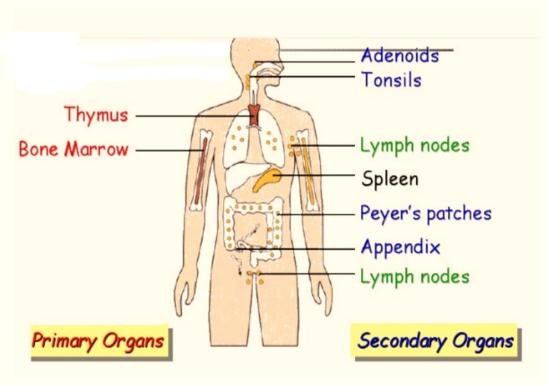
Phagocytosis





What is the Immune System?



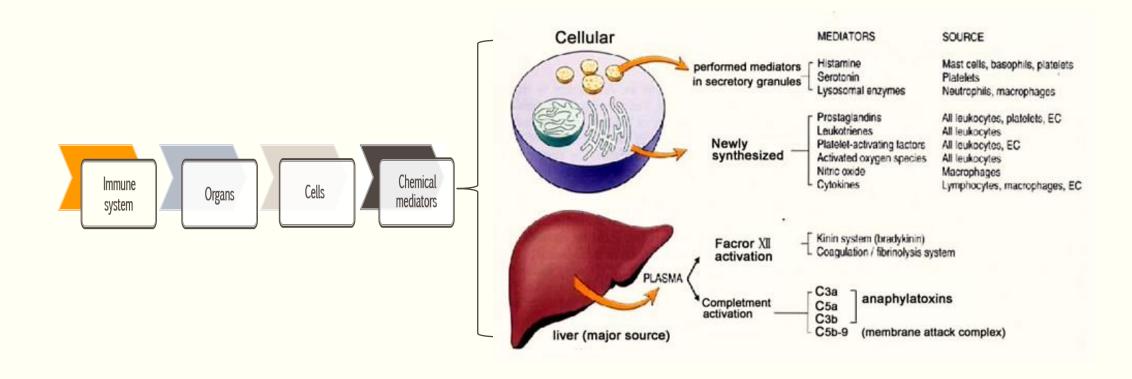


Components of the immune system



The components of the immune system:

Cell derived and plasma derived chemical mediators

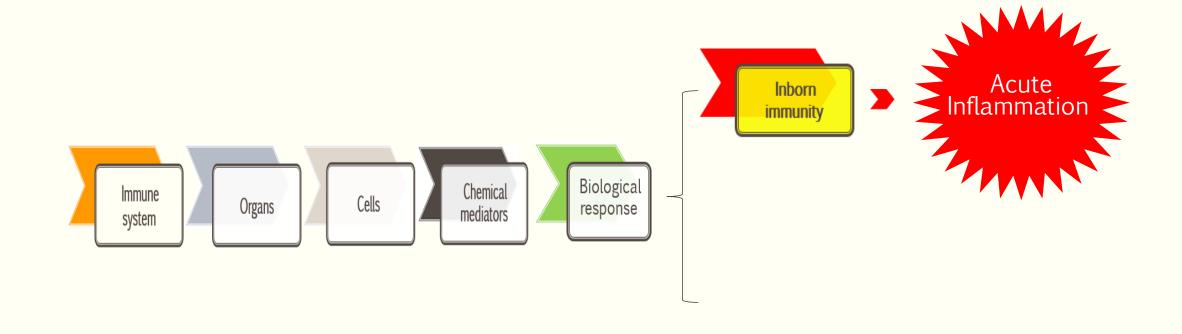


Components of the immune system

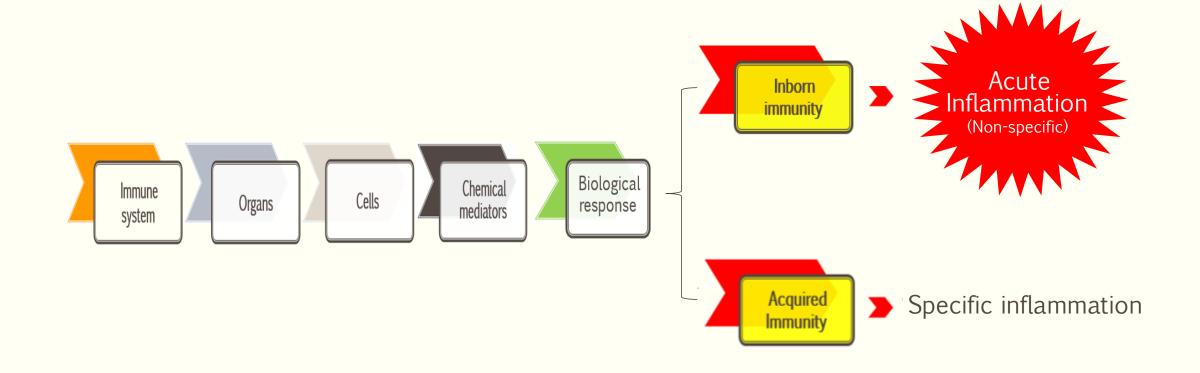


Functions of the immune system:

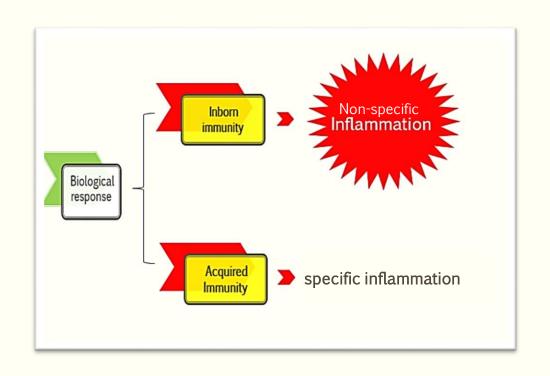
Biologic response

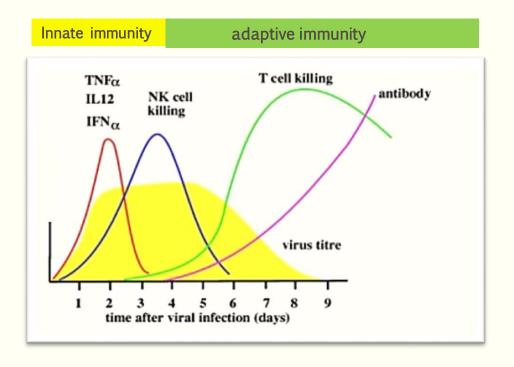


Functions of the immune system



Timeline in evolution of Inborn (innate) and Acquired (adaptive) immunity





β-glucans: immuno-modulatory actions of lion's mane mushrooms

Lion's mane mushrooms strengthen the immune system by enhancing the

• actions of white blood cells: • Neutrophils

Macrophages

NK cells

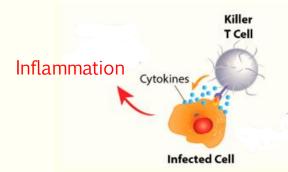
Phagocytosis



Lysis

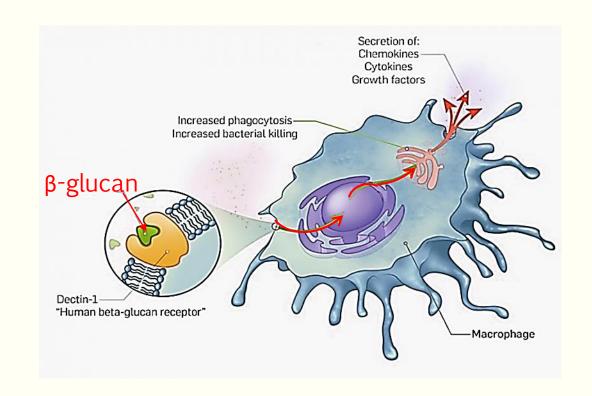


- and reducing the release of inflammatory cytokines e.g.
 - TNF-α
 - iL-1\$

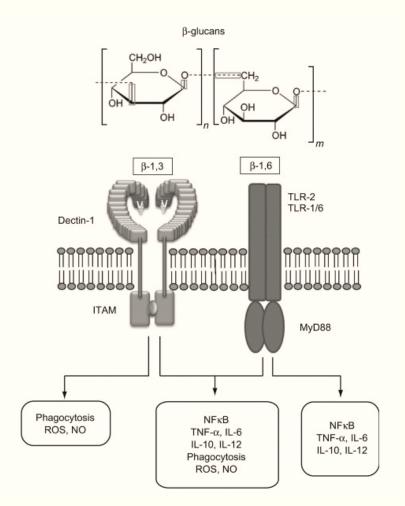


The human beta-glucan receptor is widely expressed in immune cells

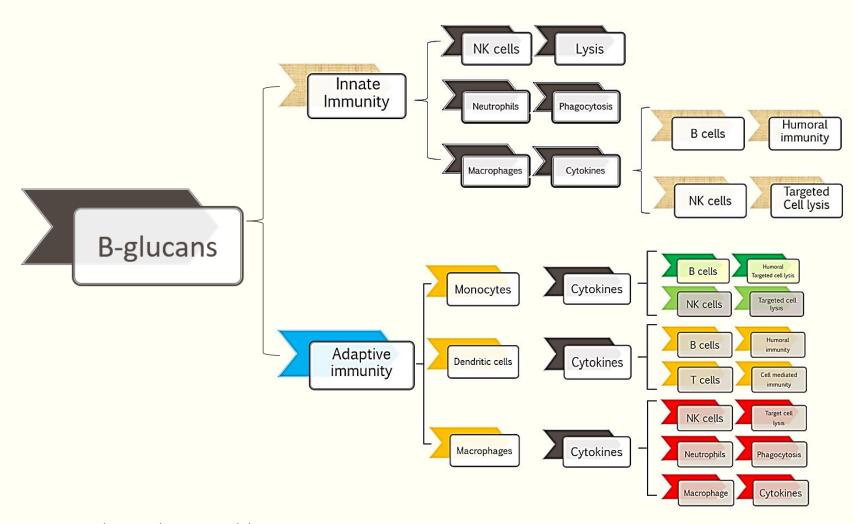
- Monocyte
- Macrophage
- Dendritic cells
- Neutrophils
- Eosinophils
- B cells
- Subpopulation T cells



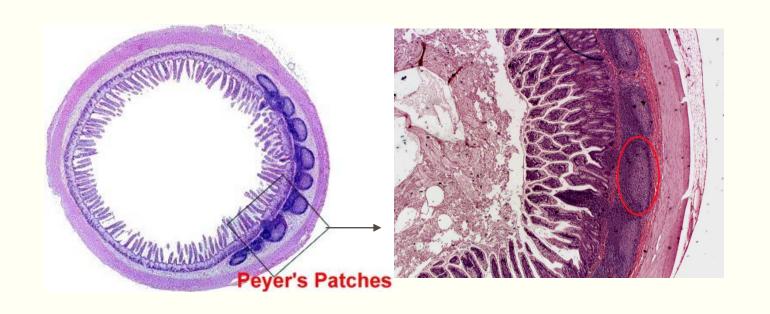
Conceptual model for the interaction between β -glucans and receptors of the innate immune system (macrophages) Interaction between Dectin-1 and toll-like receptors (TLRs) results in synergistic effects. ROS, reactive oxygen species.

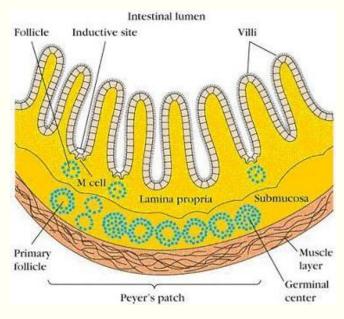


Cellular and hormonal effects of β -Glucans on the immune system

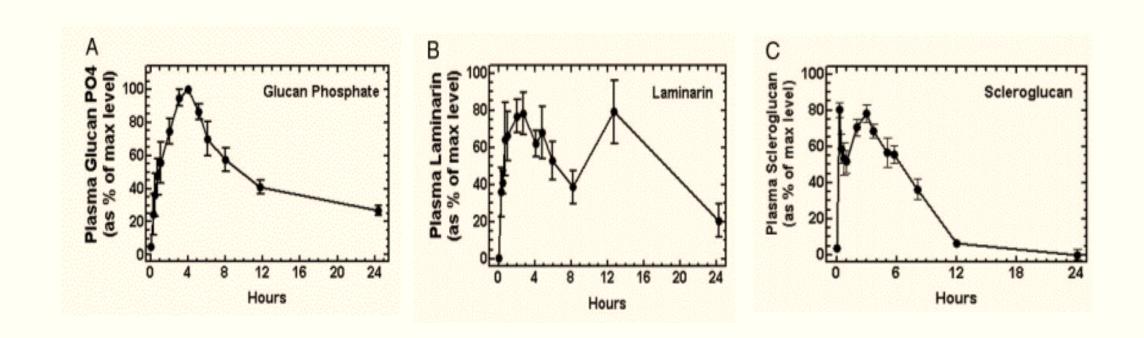


Absorption of soluble \beta-glucans in the intestine

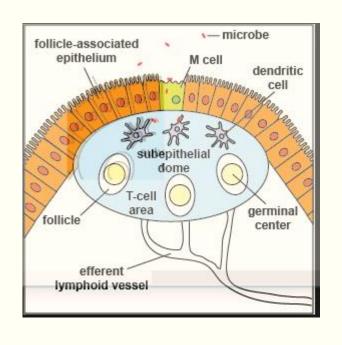


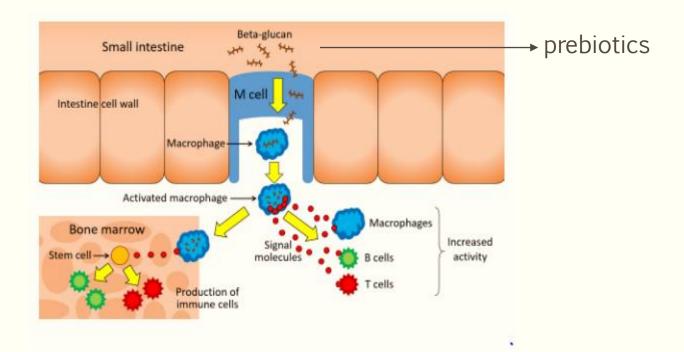


Oral delivery and absorption of single dose of soluble glucans in intestinal tract of rats



Uptake of Beta 1,3/1,6 Glucan in the intestinal tract

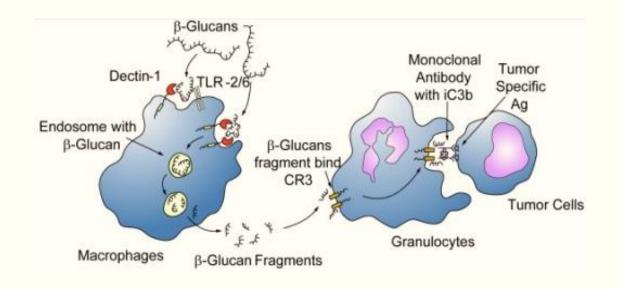




https://www.action-inter.net/beta-1316-glucan-and-the-immune-system.html

The uptake and fate of insoluble β -glucan in immune cells

insuluble β –glucans in small intestine macrophage bone marrow mononuclear phagocytes conversion of insoluble βglucan to soluble fragments circulating Immune cells: granulosytes, monocytes anti-inflammation anti-cancer



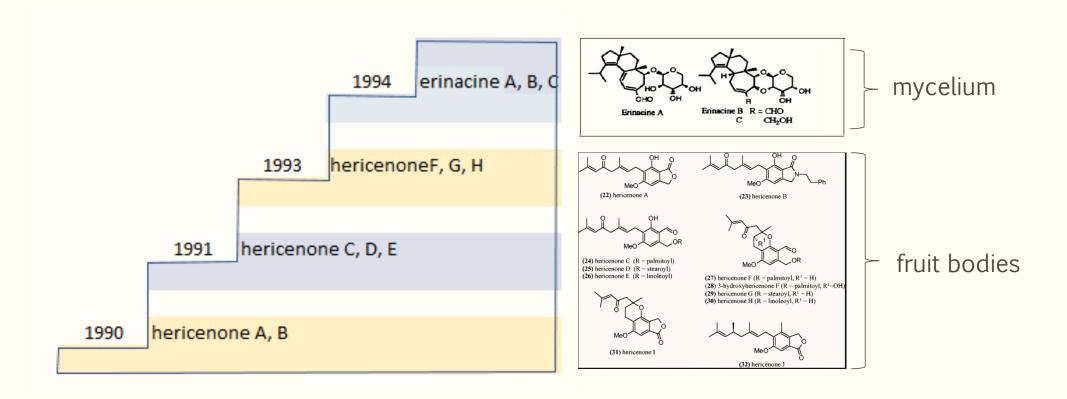
Bioavailability of \$\beta\$-glucans

- Bioavailability of \(\mathcal{B}\)-glucans has not been clearly established.
- Intravenously administered (1,3)-β-glucans have similar half-lives
- 70% of (1,3)-β-glucans are deposited in the liver and spleen
- Glucan derived from Grifola frondosa is reported to have a $T_{1/2}$ of 6.4 h following systemic administration in normal mice.
- In rabbits, intravenous administration of a 92-kDa radio labelled (1,3)- β -glucan isolated from Candida albicans showed a distribution $T_{1/2}$ of less than 5 min.
- Most of the radio labelled (1,3)-β-glucan (>97%) was associated with cell-free plasma, while radioactivity associated with blood cells was initially found in platelets and later (2 h) distributed to polymorphonuclear leukocytes and red blood cells.

What are hericenones and erinacines in lion's mane (*Hericium erinaceus*)?

- They are terpenoid compounds derived from lion's mane mushroom.
- Hericenones are derived from the fruiting bodies of the mushroom.
 They are volatile, and numbered from 1 to 17.
- Erinacines are derived from the mycelium of the mushroom. They are non-volatile and numbered from 18 to 39.
- The molecular weight of hericenones vary from 300 to 600 g/mol.
- The molecular weight of erinacines vary from 400 to 500 g/mol.
- Hericenones number 3, 4, 5, 8 are nerve growth factor stimulators.
- Erinacines number 18, 19, 20, 33, 34, 35, 36 are nerve growth factor stimulators.

Milestones in the discovery of hericenones and erinacines from fruiting bodies and mycelium of lion's mane mushroom



Number of hericenones from fruiting body of lion's mane mushroom

	name	Number	NGF synthesis stimulators
	hericenones	1-8	3, 4, 5, 8
	hericenes	9-12	
Fruit body —	erinacerin	13-14	
	3-hydroxyhericenone	15	
	hericenones	16-17	



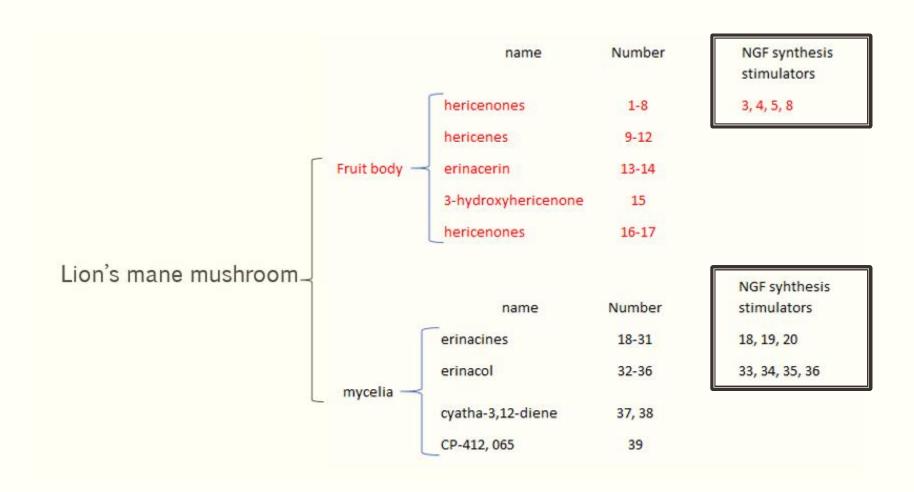


Number of erinacines from mycelia of lion's mane mushroom

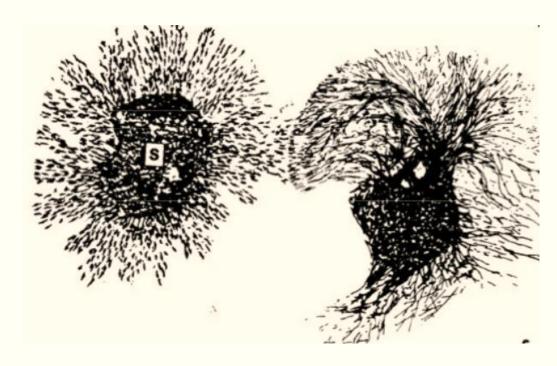
	name	Number	NGF synthesis stimulators
mycelia —	erinacines	18-31	18, 19, 20
	erinacol	32-36	33, 34, 35, 36
	cyatha-3,12-diene	37, 38	
	CP-412, 065	39	



Number of NGF (nerve growth factor) stimulators in lion's mane mushroom



Discovery of Nerve Growth Factor during 1950s



mouse tumor cells

sensory ganglion

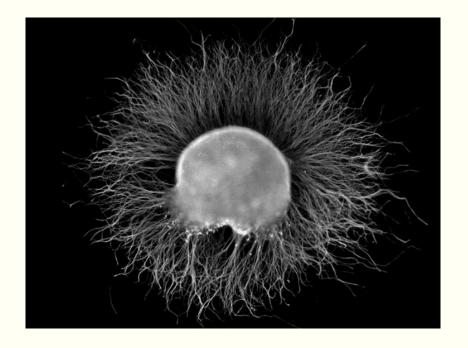


Nobel laureate 1986
Rita Levi-Montalcini in 2009, at her 100th birthday party.

What is a Nerve Growth Factor (NGF)?

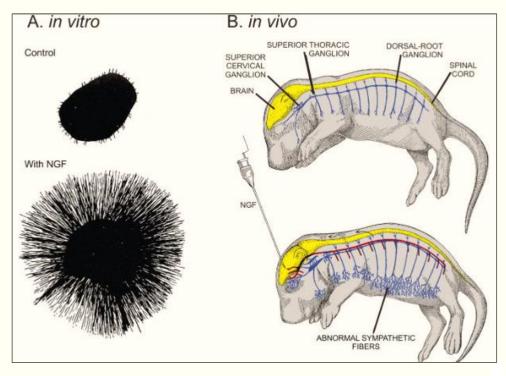
- Protein
- 118 amino acids
- Molecular weight 26,959 Da

neuron
leukocytes: mast cells, eosinophils
bone marrow stromal cells
thymus
salivary gland
oral keratinocytes
endothelial cells
fibroblasts



http://nootropicgeek.com/lions-mane-mushroom-review/

Nerve growth factor (NGF) promotes neurite outgrowth in vitro and axon outgrowth in vivo

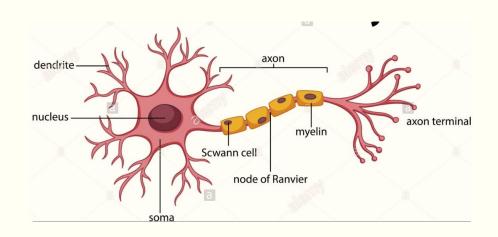


chick dorsal root ganglia

rat sympathetic nerve fibers

What are the functions of Nerve Growth factor (NGF)

- Growth of neurons
- Development of neurons
- Differentiation of neurons
- Survival of neurons
- Formation of myelin sheath in sensory neurons
- Neurotrophic modulation of synaptic transmission
- Function as immune-modulator in inflammation
- Function as nootropics
- NGF synthesis declines with age



Comparison of Hericenones, Erinacines and Beta-glucans in lion's mane

Hericenone and erinacine

- Hericenones are from fruiting bodies of lion's mane
- Erinacines are from mycelium of lion's mane
- Both are water soluble
- Molecular weight of hericenone A: 330.38 g/mol
 - hericenone C: 570.811 g/mol
 - Hericenone F: 570.811 g/m
- Molecular weight of erinacine E: 432.557
- Erinacines A, B and C are strong nerve growth factor (NGF) synthesis stimulators

Beta-glucans

- β-glucans are from cell wall of lion's mane
- Lion's mane β-glucans are insoluble in water
- Molecular weights range 35-650 K daltons
- Uptake in intestine by macrophages
- Stimulate innate and adaptive immunity:
- May act as prebiotic

Effects of bioactive compounds from *hericium erinaceus* in vitro and in vivo

In vitro

- inhibit LDL oxidation
- inhibit HMG Co-A reductase
- anti-inflammatory
- neuronal survival
- neurotrophic
- induce apoptosis

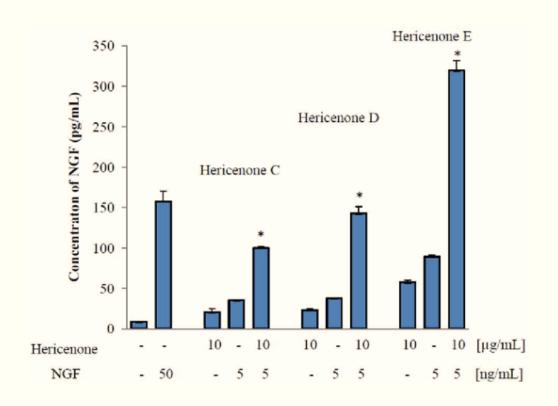
Animals

- anti-gastric ulcer
- anti-ulcerative colitis
- anti-hyperlipidemic
- anti-fatigue
- restore nerve injury
- anti-cancer
- anti-metastasis

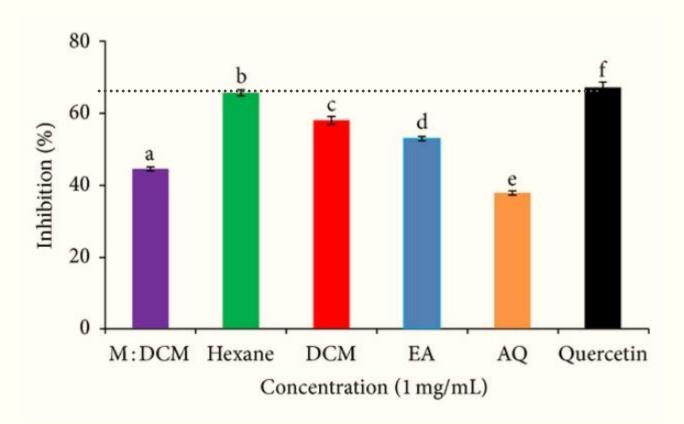
Human

- improve cognitive function
- improve depression and anxiety

Effects of hericenone C, D, and E on the stimulation of NGF secretion by neurite-bearing PC12 cells in the presence or absence of NGF

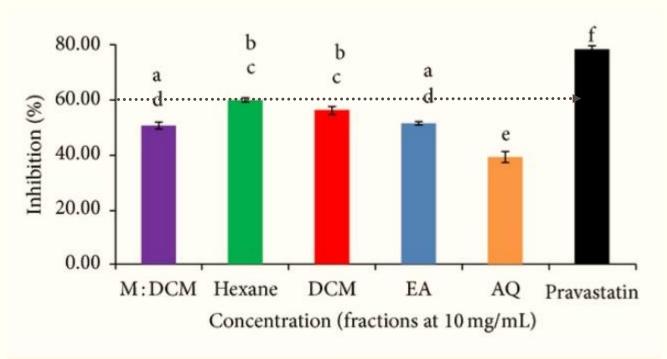


Effect of *H. erinaceus* solvent-solvent fractions on inhibiting the oxidation of human LDL molecules (2014)



methanol: dichloromethane (M:DCM), hexane (HEX), dichloromethane (DCM), ethyl acetate (EA), and aqueous residue (AQ).

Effect of *H. erinaceus* solvent-solvent fractions on inhibiting the activity of HMG Co-A reductase (2014)



methanol: dichloromethane (M:DCM), hexane (HEX), dichloromethane (DCM), ethyl acetate (EA), and aqueous residue (AQ).

Anti-Inflammatory Effects of Ethanol Extract of Lion's Mane Medicinal Mushroom, Hericium erinaceus (Agaricomycetes), in Mice with Ulcerative Colitis. 2016

Abstract

This study investigated the anti-inflammatory activity of ethanol extracts of Hericium erinaceus in the inflammatory bowel disease (IBD) model. Twenty

C57BL/6 reduced myeloperoxidase accumulation in colon tissues, attenuated histological administra change in the neutrophils and lymphocyte infiltration, and protected the mucosal prove body weight epithelium. and colon

lammation. Orally EEE markedly hocyte infiltration, matory mediators

malondialdehyde, and

reduced E suppressed the production of inflammatory mediators: tumor necrosis factor- α , and proted interleukin (IL)-1β, and IL-6 in colon tissues including 1

superoxide dismutase in serum to suppress the oxidative stress. These results suggest that HEEE can be applied as a protective agent in the treatment of IBDs.

Anti-Gastric Ulcer Activity of Polysaccharide Fraction Isolated from Mycelium Culture of Lion's Mane Medicinal Mushroom, *Hericium erinaceus* (Higher Basidiomycetes). 2015

Abstract

Hericium erinaceus is a culinary-medicinal mushroom that is used in traditional medicine, in folk medicine, and as medicinal cuisine in Asian countries such as China, Japan, and Korea. H. erinaceus exhibits various pharmacological properties, such as anti-cancer, immunomodulation, anti-dementia,

extract,

polysaccharide fraction can significantly decrease the ulcerated area compared with the control group

ve principle in the ent, with anti-gastric using an ethanol-

induced ulcer model in mice and with an 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay using MC cell lines. The results suggest that the polysaccharide fraction can significantly decrease the ulcerated area compared with the control group and the effect is fairly dose dependent, irrespective of animal or cell experiments. These results indicate that the polysaccharide fraction is the active component of the H. erinaceus mycelium culture, which protects against gastric ulcers.

https://www.ncbi.nlm.nih.gov/pubmed/26853960

Neurotrophic properties of the Lion's mane medicinal mushroom, *Hericium erinaceus* from Malaysia. 2013

Abstract

Neurotrophic factors are important in promoting the growth and differentiation of neurons. Nerve growth factor (NGF) is essential for the maintenance of the basal forebrain cholinergic system. Hericenones and erinacines isolated from the medicinal mushroom Hericium erinaceus can induce NGF synthesis in nerve cells. In this study, we evaluated the synergistic interaction between H. erinaceus aqueous extract and exogenous NGF on the

aqueous extract of H. erinaceus contained neuroactive compounds which induced NGF-synthesis and promoted neurite outgrowth

compounds that induced the secretion of extracellular NGF in NG108-15 cells, thereby promoting neurite outgrowth activity. However, the H. erinaceus extract failed to protect NG108-15 cells subjected to oxidative stress when applied in pre-treatment and co-treatment modes. In conclusion, the aqueous extract of H. erinaceus contained neuroactive compounds which induced NGF-synthesis and promoted neurite outgrowth in NG108-15 cells. The extract also enhanced the neurite outgrowth stimulation activity of NGF when applied in combination. The aqueous preparation of H. erinaceus had neurotrophic but not neuroprotective activities.

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Neuroregenerative potential of lion's mane mushroom, *Hericium erinaceus* in the treatment of peripheral nerve injury (2012)

Abstract

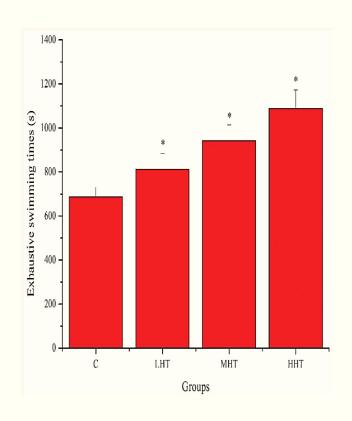
We present a model case study of the activity of aqueous extract of Hericium erinaceus fresh fruit bodies in promoting functional recovery following crush injury to the peroneal nerve in adult female Sprague-Dawley rats. The aim was to explore the possible use of this mushroom in nerve repair. The activities of aqueous extract were compared to activities exhibited by mecobalamin (vitamin B12), which has been widely used in the treatment of

Regeneration of axons and reinnervation of motor endplates/neuromuscular junction in extensor digitorum longus muscle of rats in treated groups developed better than in the negative control group

neurotrophin-promoted cell survival, while MAPK cascade is involved in mediating neurite outgrowth. Immediate early gene expression was also involved in the cascade of events leading to regeneration. Local axonal protein synthetic machinery was also enhanced in the distal segments of crushed nerves in treated groups. Therefore, daily oral administration of H. erinaceus could promote the regeneration of injured rat peroneal nerve in the early stage of recovery.

https://www.ncbi.nlm.nih.gov/pubmed/23510212

Effects of polysaccharide extracts from lion's mane mushroom (*Hericium erinaceus*) in swimming times of rats (2014)



Effects of Hericium erinaceus on exhaustive swimming times. Values are expressed as the means \pm SD. *P<0.05, compared with the C group.

- C, control;
- LHT, low-dose HEP-treated group;
- MHT, moderate-dose HEP-treated group;
- HHT, high-dose HEP-treated group.

https://www.spandidos-publications.com/10.3892/etm.2014.2139

Hericium erinaceus (Lion's Mane) mushroom extracts inhibit metastasis of cancer cells to the lung in CT-26 colon cancer-transplanted mice. (2013)

Abstract

This study investigated the antimetastatic activity of four Hericium erinaceus edible mushroom extracts using CT-26 murine colon carcinoma cells as an indicator of inhibition of cell migration to the lung. Hot water (HWE) and microwaved 50% ethanol (MWE) extracts of H. erinaceus strongly elicited

cancer cell death thro expression of matrix another extracellular extracellular signal-re reduced phosphoryla HWE and MWE redu

Hot water (HWE) and microwaved 50% ethanol (MWE) extracts of H. erinaceus reduced the formation of tumor nodules in the lung by about 50% and 55%, respectively,

VE and MWE reduced the sminogen activator (u-PA), and MWE down-regulated (K) phosphorylations. The Dietary administration of creases in lung weight

caused by cancer celi metastasis. These results demonstrate the ellectiveness of hive and livive as beneficial antimetastatic agents, targeting their upstream signaling molecules for mediating the expression of the ECM-degrading proteinases. Acidic and alkaline extracts were not bioactive. Bioactivity seems to be related to composition. H. erinaceus edible mushrooms have the potential to serve as a health-promoting functional food.

High molecular weight of polysaccharides from *Hericium erinaceus* against amyloid beta-induced neurotoxicity (2016)

Abstract

BACKGROUND: Hericium erinaceus (HE) is a well-known mushroom in traditional Chinese food and medicine. HE extracts from the fruiting body and mycelia not only exhibit immunomodulatory, antimutagenic and antitumor activity but also have neuroprotective properties. Here, we purified HE polysaccharides (HEPS), composed of two high molecular weight polysaccharides (1.7 × 10(5) Da and 1.1 × 10(5) Da), and evaluated their protective

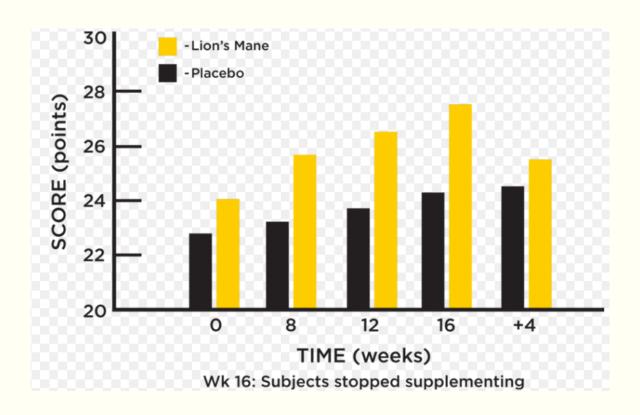
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HEPS exhibit antioxidant and neuroprotective effects on Aβ-induced neurotoxicity in neurons.

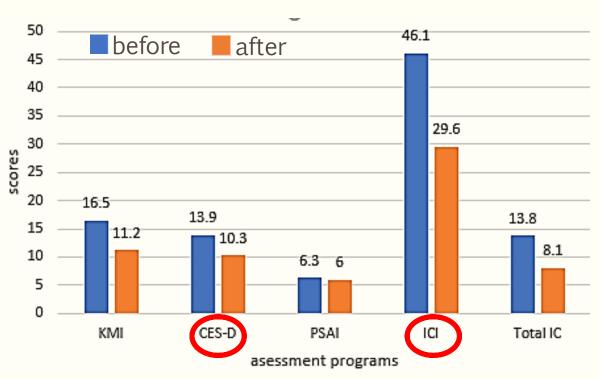
RESULT: Our results showed that 250 μ g/ml HEPS was harmless and promoted cell viability with 1.2 μ M A β treatment. We observed that the free radical scavenging rate exceeded 90 % when the concentration of HEPS was higher than 1 mg/mL in cells. The HEPS decreased the production of ROS from 80 to 58 % in a dose-dependent manner. Cell pretreatment with 250 μ g/mL HEPS significantly reduced A β -induced high MMPs from 74 to 51 % and 94 to 62 % at 24 and 48 h, respectively. Finally, 250 μ g/mL of HEPS prevented A β -induced cell shrinkage and nuclear degradation of PC12 cells.

CONCLUSION: Our results demonstrate that HEPS exhibit antioxidant and neuroprotective effects on Aβ-induced neurotoxicity in neurons.

Improving effects of the mushroom Yamabushitake (*Hericium erinaceus*) on mild cognitive impairment: a double-blind placebo-controlled clinical trial based on the Revised Hasegawa Dementia Scale (HDS-R).



Effects of maitake mushroom (Hericium erinaceus) on depression and anxiety among 30 subjects in a 4-week double blind placebo control trial (2010).



- •KMI: Kupperman Menopausal Index
- •CES-D: Center for Epidemiologic Studies Depression
- •PSQI: Pittsburgh Sleep Quality Index,
- •ICI: Indefinite Complaints Index

Side effects, interactions, dosage

- No adverse reaction has been reported on the use of lion's mane as a food.
- No adverse reaction has been reported on the use of lion's mane supplements.
- No information is available on the interaction of lion's mane with drugs.
- There is not enough scientific information to recommend the appropriate dosage.

Lion's mane mushroom: commercial products

Products

- Raw lion's mane
- Powder
- Extract
- Capsules
- Dietary supplement

Advertised health benefits

- Immune function
- Anxiety and depression
- Cognitive health
- Digestive health
- High cholesterol
- Diabetes
- Wound healing
- Cancer

Examples of lion's mane mushroom extracts

elixir

Supplement Facts

Serving Size: 1 mL (~45 drops) Servings Per Container: 30

Amount Per Serving

Proprietary Blend

1 mL †

Fresh Lion's Mane (*Hericium erinaceus*) mycelium extract ‡

Dried Lion's Mane (*Hericium erinaceus*) fruitbody extract ‡

†Daily value not established ‡Certified Organic

Other ingredients: water, alcohol ‡ (alcohol content: 30–40%), myceliated brown rice ‡

capsule

Supplement Facts

Serving Size: 1000mg Servings Per Jar: 30 Amount Per Serving 9

%DV**

Lion's Mane Mushroom 1000mg

*No Daily Value Established **Based on 2,000 Calorie Diet

Suggested Use: As a dietary supplement, take 1000mg once daily.

Warning: Keep out of reach of children. Do not take this or any other supplement if under the age of 18, pregnant or nursing a baby, or if you have any known or suspected medical conditions, and/or taking prescription drug(s) or OTC medication(s).

Storage: Store in a cool and dry place. Keep away from direct sunlight and heat. Manufactured for Nootropics Depot 8380 S. Kyrene Rd. Ste. 110 Tempe, AZ 85284 Support@NootropicsDepot.com

Mixture of extracts

Supplement Facts

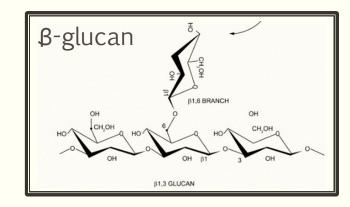
Serving Size: 1000mg / 2 Capsules • Servings Per Container: 45

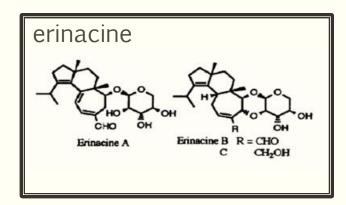
Other ingredients: Tapioca (Plantcap® vegetable capsule)

**All ingredients are Certified Organic. † Daily Value not established

Buyers beware (*caveat emptor*) in buying dietary supplements

- Nootropics are smart or cognitive enhancers.
- Beta-glucans are not nootropics.
- Beta-glucans are biological response modifiers.
- Some hericenones and erinacines are nootropics.
- The pharmacological properties of beta-glucans, hericenones and erinacines in lion's mane mushroom have yet to be defined.





Some delicious lion's mane mushroom cuisine



Lion's Mane Mushrooms and Garlic - E ...



Sparta Lion's Mane Mushroom Salad



Pan-Fried Lion-Mane Mushr...



Poached Lion's Mane Mushroom



Mane and Oyster Mushroom Pasta Recipe ...



Stir fry Lion's Mane Mushroom - Pict...

Summary

- Lion's mane mushroom is scientifically known as Hericium erinaceus.
- Investigations of Its health benefits began in the year 2000.
- Besides macro and micronutrients, beneficial bioactive compounds have been analyzed and studied.
- The bioactive compounds consist of polysaccharides and secondary metabolites
- β -glucans in polysaccharides are immuno-modulatory and anti-cancer.
- The important metabolites are hericenones and erinacines. Several of them are strong stimulators of nerve growth factor (NGF) synthesis.
- Lion's mane mushroom is a safe and delicious mushroom. No adverse reactions have been reported.

ANY QUESTION?

Please contact

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