BRAIN FUNGI & NOOTROPIC MUSHROOMS

Potent mushroom medicines for brain health, focus, happiness & longevity

Dr. Lindsay Chimileski

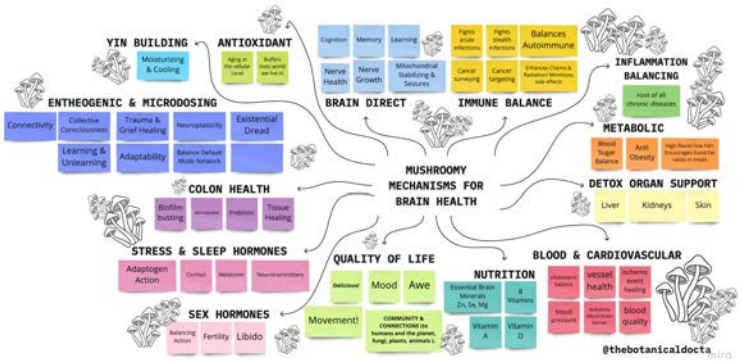
Mushroom Medicine Lindsay Chimileski ND Lac RH

no·o·trop·ic
/ˌnōəˈträpik/

1. **(of a drug) used to enhance memory or other cognitive functions.**
2. **Nootropics (/noʊ.əˈtroʊpɪks/ *noh-ə-TROHP-iks*, or /noʊ.əˈtrɒpɪks/ *noh-ə-TROP-iks*[1]) (colloquial: smart drugs and cognitive enhancers) are drugs, supplements, and other substances that are claimed to improve cognitive function, particularly executive functions, attention, memory, creativity, or motivation, in healthy individuals.**

Wikipedia

Mushroom Medicine with Lindsay Chimileski ND LAC RH



All of our medicinal mushrooms are going to touch on these mechanisms—due to shared basic polysaccharides, antioxidants, minerals, triterpenoids and vitamins.

Of course there are some nuances to it and specific indications but in general they ALL will help brain health.

Mushroomy Mechanisms for Brain Health

- **High in antioxidants and minerals**
- **Immune regulation: beta-glucans,**
  - **Antibody Antibody opsonization**
  - **Anti-viral & Stealth pathogen targeting**
  - **(often a part of the pathology)**
  - **Auto-immune degeneration like MS**
- **Cholesterol balance & Cardiovascular health**
- **Blood flow, prevention & treatment of Ischemic events**
- **Blood Sugar balance/Insulin/Metabolic Balance**
- **Neuronal tissue affinity & can cross and stabilize the blood brain barrier**
- **Cancer surveillance and adjunctive/direct and recovery of chemo/radiation treatments**
- **Gut health/healing, balanced flora, prebiotic, biofilm bust**
- **Liver health**
- **Detox& Metal chelating: liver, kidneys, lungs skin**
- **Buffering toxic burden, i.e. cigarette smoke, pollution**

- **Building blocks of essential nutrients for neurons & neurotransmitters**
  - **Serotonin, Betacarotenes, Vitamin D2**
- **Healthy & youthful skin**
- **Yin building and moisturizing to the system**
- **Stimulating, ADHD**
- **Seizure Formulas**
- **Mitochondrial support**
- **Brain longevity, cognitive function, memory, learning**
- **Hormones balancing**
- **Adaptogenic, Stress balance**
- **Supports physical recovery, endurance and stamina**
- **Quality of life & Mental health, Nervines**
  - **Tastes delicious**
  - **Fun to hunt in the woods! and make weird mushroom friends & community**
- **Entheogenic & Psychedelic**
- **AWE!**

Mushroom Medicine with Lindsay Chimileski ND LAC RH

This is why everyone is so jazzed up about medicinal mushrooms

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Nutritional Powerhouse

Mushroom Medicine as food

Generalized Benefits of Medicinal Mushrooms
mostly via the b-glucans and antioxidants which are present in all

- **Heart disease-** balancing lipids, inflammation and oxidation
- **Immune** system balance
- **Acute or chronic, prevention, palliative or targeted immune and cancer therapies**
- **Liver support**- detoxification support, tissue healing, antiviral (hepatitis), can help the burden of many medications on the liver
- **Digestive health** & healing inflamed digestive tissues
- **Skin health-** yin/moisture building, antioxidant, detoxication/liver/digestion
- Many have **anti-diabetic, anti-obesity and blood sugar** balancing actions too

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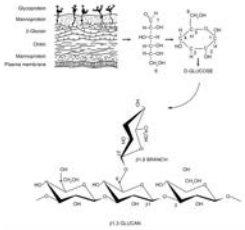
Cook Your Mushrooms!



Heat, water, salt, fat etc all help to break down the chitin, to exposes active molecules

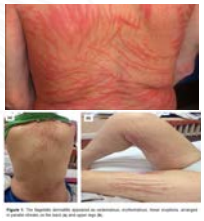
ALWAYS *cook your mushrooms for better absorption of active constituents and nutrients.*

Tastes better too! Uncooked more likely to have issues with contamination and some causes dermatitis, i.e.

But if the health and taste benefits of cooked aren't enough for you…

Shiitake flagellate Dermatitis

- **Rare skin eruption**
- **Resembles whiplash marks**
- **Occurs after consumption of raw shiitake**
- **Reaction to lentinan, a thermolabil polysaccharide which decomposes upon heating**
- **Linearly arranged erythematous, pruritic papules on trunk, limbs**
- **Usually self-limited, resolving within 10 days of onset.**



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J Am Coll Nutr. 2015;34(6):478-87. doi: 10.1080/07315724.2014.950391. Epub 2015 Apr 11.

Consuming Lentinula edodes (Shiitake) Mushrooms Daily Improves Human Immunity: A Randomized Dietary Intervention in Healthy Young Adults.

Dai X[1], Stanilka JM[1], Rowe CA[1], Esteves EA[2], Nieves C Jr[1], Spaiser SJ[1], Christman MC[2], Langkamp-Henken B[1], Percival SS[1].

Author information

Abstract

BACKGROUND: Mushrooms are widely cited for their medicinal qualities, yet very few human intervention studies have been done using contemporary guidelines.

OBJECTIVE: The aim of this study was to determine whether consumption of whole, dried Lentinula edodes (shiitake) mushrooms could improve human immune function. Primary objectives were to ascertain whether L. edodes consumption would improve γδ-T cell proliferation and activation responses, quantify a dose response, and elicit cytokine secretion patterns. Secondary objectives included determining changes in natural killer T (NK-T) cell proliferation and activation, secretory immunoglobulin A (sIgA) in saliva, and C-reactive protein (CRP) in serum.

DESIGN: Fifty-two healthy males and females, aged 21-41 years, participated in a 4-week parallel group study, consuming either 5 or 10 g of mushrooms daily. Each subject had blood drawn before and after 4 weeks of daily L. edodes consumption. Saliva and serum were also collected. Peripheral blood mononuclear cells were cultured in autologous serum for 24 hours or 6 days, stained, and examined by flow cytometry.

RESULTS: Eating L. edodes for 4 weeks resulted in increased ex vivo proliferation of γδ-T (60% more, $p < 0.0001$) and NK-T (2-fold more, $p < 0.0001$) cells. Both cell types also demonstrated a greater ability to express activation receptors, suggesting that consuming mushrooms improved cell effector function. The increase in sIgA implied improved gut immunity. The reduction in CRP suggested lower inflammation. The pattern of cytokines secreted before and after mushroom consumption was significantly different; consumption resulted in increased interleukin (IL)-4, IL-10, tumor necrosis factor (TNF)-α, and IL-1α levels, a decreased macrophage inflammatory protein-1α/chemokine C-C ligand 3 (MIP-1α/CCL3) level, and no change to IL-6, IL-1β, MIP-1β, IL-17 and interferon (IFN)-γ levels.

CONCLUSIONS: Regular L. edodes consumption resulted in improved immunity, as seen by improved cell proliferation and activation and increased sIgA production. The changes observed in cytokine and serum CRP levels suggest that these improvements occurred under conditions that were less inflammatory than those that existed before consumption.

TRIAL REGISTRATION: ClinicalTrials.gov NCT01398176.

= 5-10 grams of shiitakes daily to improve immune health

52 healthy adults
5 or 10 g of mushrooms daily for 4 weeks.
= improved immune cell counts
Reduced CRP, inflammation

Versus some 500 mg raw cap of myceliated oats

28 g

Fresh Mushrooms
~ 90% water

141 g

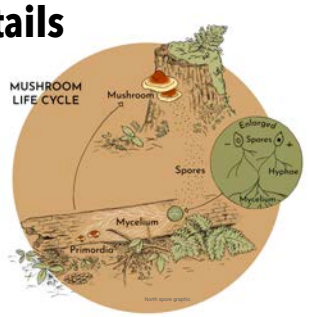
Mushroom medicine

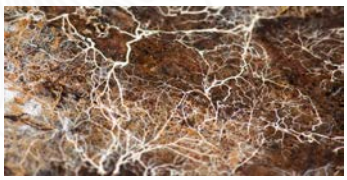
Lindsay Chimileski ND Lac RH

Mushroom Medicine Details

Variables that influence the outcomes

- ***What part of the mushroom is it?***
- ***What life stage?***
- ***Fruiting Body or Mycelium?***
- ***If mycelium, what kind…***





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Fruiting Body:

What has always classically been used: the ethnobotany, TCM and traditional use/ foundation we build on.
Most research research is on the fruiting bodies; more now on mycelium
Active, "full spectrum" More active constituents- beta-glucans, antioxidants, triterpenes, minerals (phosphorus, copper, zinc, potassium); vitamins (C, D, beta-carotene, Bs). * one known *exception* is erinacine A in lions mane mycelium [hericenones C &D in fruiting body]

Mycelium:

Typically grown on grain, oats, corn etc
Less investment, faster & easier grow in masses, faster turnover.
Typically less active compounds- up to 50% less beta-glucans than fruiting bodies ***50-80% starch from the growing substrate–***
I think of it as a fermented food such as tempeh- still has nutritional value but not as much of the strong medicinal actions
Pure mycelium extracts grown in liquid fermentation tanks to get mycelium without growth substrate
Potential for different beneficial components, enzymes higher etc, we just do not know all those constituents yet. ***More and more research is being done. Likely a great medicines too, but different. Use combos if anything.***

Mycelial growth of P. djamor on different spawning materials, namely (A) sweet sorghum, (B) rice grain, and (C) corn grits after 10 days after incubation.

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Choosing Potent Mushroom Medicines

the need to knows

FRUITING BODIES
- More active beta glucans
- What has always been traditionally used
- Mycelium can be 50-80% grains

EXTRACTED POWDER > Raw
- Raw powders use hot water extraction at least - make tea, soup etc due to chitin

DOUBLE EXTRACTION "best" in simple terms to get both alcohol and water soluble constituents
- BETA GLUCANS- hot water soluble
- TRITERPENOIDS- alcohol

DOSE- Whole mushroom/powder doses range from 2 to 16 to 50 grams in divided daily doses. At least 6g in most for therapeutic Chinese Pharmacopoeia Doses

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CONSTITUENTS WE CARE ABOUT

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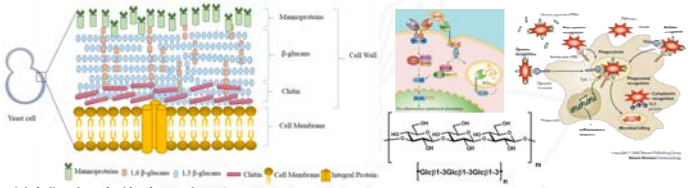
Constituents we care about Beta-glucans



Triple helix polysaccharides (beta-D glucans)

- **Natural sources such as mushrooms, yeast, algae, cereal grains and bacteria.**
- **All fungi and yeasts have triple helix polysaccharides (beta-D glucans) in their cell walls, contributing to structural support**
- **Glucose polymer-chain core or repeating d-glucose polymers bonded at carbon 1 of the saccharide ring to the carbon 3 or 6 of the next (beta 1-3, beta 1-6)**
- **Not all beta-glucans are equally effective at triggering an appropriate immune response:** Depends on the core chain length, complexity of branching, molecular structure, degrees of branching and solubility, differences in molecular weight and solution conformation, and methods of production, extraction and purification. It is suggested the more complex, the more active immunomodulatory and anti-cancer effects.
- **Most medicinal mushrooms have β-1,3;1,6-glucans** (bacteria often 1,4)

–> Heat breaks down chitin, exposes active molecules = *cook your mushrooms to get the medicine!*

–> Large molecular weight fungal compounds bind to gut receptors to initiate complex immune activation via dectin, toll-like receptors and others. Evidence suggests that the activity of these polysaccharides is dependent on their size, with high molecular weight (100 000-200 000) fractions being most active, while fractions from the same source with molecular weights of 500-10 000 show no activity. The fact that there are polysaccharides with different chemical structures, but all of which have immunomodulating activity, suggests that the immune response is in part non-specific, determined by size rather than by chemical structure.

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Universal Benefits of Medicinal Mushrooms

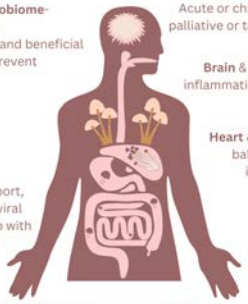
ALL MUSHROOMS HAVE B-GLUCANS AND ANTIOXIDANTS, WHICH ARE BENEFICIAL FOR

Digestive health & healing: inflamed digestive tissues.

Balancing action on intestinal **microbiome**- helps promote bifidobacteria and beneficial bacteria and prevent infections.

High in **Fiber**

Liver support: **detoxification** support, tissue healing, antiviral (hepatitis), can help with medication burden



Immune system balance: Acute or chronic, prevention, palliative or targeted therapies

Brain & nerve health: inflammation, oxidation

Heart & **Circulation**: balancing lipids, inflammation, oxidation

Skin health: yin/moisture building, **antioxidant** rich, detoxication via liver, flora and lymph to improve skin

Metabolic: anti-diabetic, anti-obesity and blood sugar balancing actions

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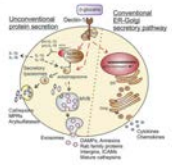
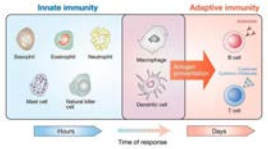
FUNGI CONSTITUENTS WE CARE ABOUT

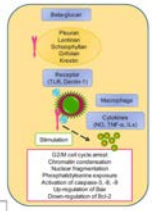
BETA GLUCANS



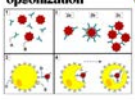
Dectin-1 pathway activates robust autophagy-dependent unconventional protein secretion in human macrophages.

The global innate immune response activated by b-glucans in human macrophages.





Antibody opsonization



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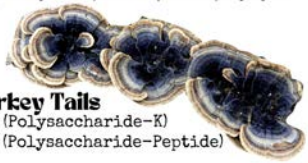
FUNGI CONSTITUENTS WE CARE ABOUT

BETA GLUCANS

Proteoglycans/ polysaccharide-peptides, protein polysaccharides or glycoproteins = a beta-glucan with a particular protein

As a rule, these protein-linked glucans have greater immunopotentiation activity than the corresponding free glucans



Turkey Tails
PSK (Polysaccharide-K)
PSP (Polysaccharide-Peptide)

Japanese trials since 1970

- PSK significantly extended survival at five years or beyond in cancers of the stomach, colon-rectum, esophagus, nasopharynx, and lung (non-small cell types), and in a HLA B40-positive breast cancer subset.
- PSP was subjected to Phase II and Phase III trials in China. **In double-blind trials, PSP significantly extended five-year survival in esophageal cancer. PSP significantly improved quality of life, provided substantial pain relief, and enhanced immune status in 70-97 percent of patients with cancers of the stomach, esophagus, lung, ovary, and cervix.**
- **PSK and PSP boosted immune cell production, ameliorated chemotherapy symptoms, and enhanced tumor infiltration by dendritic and cytotoxic T-cells.** Their extremely high tolerability, proven benefits to survival and quality of life, and compatibility with chemotherapy and radiation therapy makes them well suited for cancer management regimens.

Reishi
fungal immunomodulatory proteins FIM
active ganoderma polysaccharides peptide GPP

Shiitake
Lentinan erodes mycelia LEM

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PROTEOGLUCANS

protein-bound β-glucans

Maitake D-Fraction

Unique D-Fraction is a standardized form of protein-bound β-glucans (proteoglucan)

While most mushroom-derived β-glucans have a 1,3 main chain with 1,6 branches only, β-glucans found in D-Fraction have a unique and complex structure, containing both a 1,6 main chain having a greater degree of 1,3 branches, and a 1,3 main chain having 1,6 branches

STUDY: TNBC cells to investigate if D-Fraction is able to attenuate their aggressive phenotype.

Findings:

- D-Fraction decreases MDA-MB-231 cell viability through apoptosis induction and reduces their metastatic potential.
- D-Fraction increases cell-cell adhesion by increasing E-cadherin protein levels and β-catenin membrane localization, and increases cell-substrate adhesion.
- D-Fraction also decreases cell motility by affecting actin cytoskeleton rearrangements, and proteolytic activity of MMP-2 and MMP-9.
- Furthermore, D-Fraction decreases the invasive capacity of MDA-MB-231 cells.
- In concordance, D-Fraction retards tumor growth and reduces lung metastases in a xenograft model.
- Altogether, these results suggest the potential therapeutic role of D-Fraction in aggressive TNBC.

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SESQUITERPENES

Class of terpenes that consist of three isoprene unit
(one isoprene unit has 5 carbons with hydrogens attached to it)

- Found in Hops, Cedarwood, Sandalwood, Myrrh, Patchouli, Ginger , Clary Sage (and many more).
- Aromatic, volatile but not as much as monoterpenes (most essential oils)
- Slow oxidizing, higher boiling points.
- **In nature, sesquiterpene lactones play an important role in plant defense, as antibacterials, antivirals, antifungals, insecticides and by reducing the herbivores' appetites for such plants and mushrooms.**
- **Anti-inflammatory, Antispasmodic**
- **Antimicrobial**
- **Calming & Soothing to nervous system**
- **Cytotoxic and anticancer activity.**

Humulene

Bioactive sesquiterpenes produced by fungi: are they useful for humans as well?

Abstract

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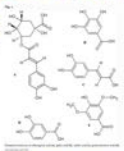
FUNGI CONSTITUENTS WE CARE ABOUT

POLYPHENOLS & PIGMENTS

Phenolic derivatives, carotenoids, lycopene all exhibit antioxidant activity.

Examples of phenolic acids present in mushroom species are: chlorogenic, gallic, caffeic, protocatechuic, and syringic acid, norbadione A, 4-hydroxybenzoic, ferulic, *p*-coumaric, protocatechuic, trans-cinnamic, and vanillic acid (2,5-dihydroxybenzoic acid



***p*-Hydroxybenzoic, gallic and protocatechuic acids=** antioxidant, antibacterial, antiviral, antifungal, anti-inflammatory and gastric secretion-stimulatory actions, documented by in vitro and in vivo studies

protocatechuic acid= immunomodulating, spasmolytic, cardioprotectant, anticoagulant and chemopreventive properties. A strong positive correlation was observed between antioxidant activity of mushrooms and the amount of phenolic compounds

β-carotene, the other examples of carotenoids are lycopene, lutein, zeaxanthin, cryptoxanthin, and phytoene
These compounds are usually red or orange in color but can also be colorless. Importantly, they usually do not degrade during cooking or baking

Culinary–medicinal mushrooms: a review of organic compounds and bioelements with antioxidant activity

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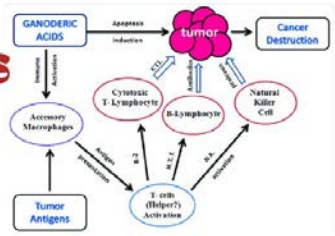
Triterpenes & Triterpenoids



Adaptogenic actions
Hormonal
Bitter
Anti-tumor
5-alpha reductase activity
Hepatoprotective

RIESHI
Ganoderic Acids

Anti-neoplastic
Cancer fighting
Immunostimulating activity

CHAGA
Inotodiol
Trametonolic acid
Betulinic acid

CONSTITUENTS WE CARE ABOUT
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FUNGI CONSTITUENTS WE CARE ABOUT

INDOLE COMPOUNDS

Melatonin & Melanin Precursors
is found in selected mushrooms such as Chaga, *L. deliciosus* and *B. edulis*
There is a large discrepancy in melatonin levels, depending not only on the species, but also on environmental conditions and levels of UV.

Serotonin precursor L-tryptophan
The highest amount of -tryptophan was found also in *C. cibarius* fruiting bodies but it varies in all fruiting bodies. Good source of this for vegetarians.

Serotonin 5HTP analogues Psilocin and Psilocybin
the hallucinogenic indolealkylamines IAAs are analogues of 5-hydroxytryptamine (5-HT or serotonin)

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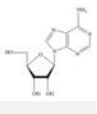
FUNGI CONSTITUENTS WE CARE ABOUT

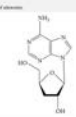
INDOLE COMPOUNDS

One of the four building bloods to DNA and RNA
Provides energy to drive many processes in living cells
ATP Adenosine triphosphate
AMP Adenosine monophosphate cAMP
Can help with irregular heart rhythms

Adenosine
Cordycepin
Adenosine analogue with the absence of oxygen in the 3' position of its ribose entity

Many intracellular targets, including nucleic acid, apoptosis, and cell cycle
Cordycepin can participate in various molecular processes in cells because of its similarity with adenosine
Cordycepin has a neuroprotective effect in the ischemic brain, which is due to the inhibition of inflammation and increase of antioxidants activity related to lesion pathogenesis
Cordycepin showed the obvious analgesic effect
Induce steroidogenesis





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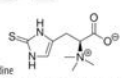
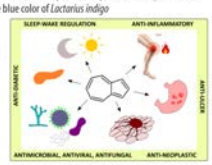
ANTIOXIDANTS

Ergothioneine



- a nonprotein amino acid, is a derivative of histidine
- Cells with less are more prone to the effects of oxidative damage, including lipid peroxidation and defects in the oxidation of DNA or protein
- In the human body, ergothioneine occurs in the highest concentration in the erythrocytes, kidneys, liver, eyes, and semen
- Antioxidant effect of ergothioneine is believed to be associated with the stimulation of glutathione formation as well as the effect on the signal transduction pathways taking place in the cells, including NF-kB

Azulenes
Azulenes, belonging to the class of terpenoids, also exhibit antioxidant activity is a blue dye which is responsible for the blue color of *Lactarius indigo*



Antioxidant minerals
Selenium, Zinc, Manganese, Magnesium , Copper

Culinary–medicinal mushrooms: a review of organic compounds and bioelements with antioxidant activity

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FUNGI CONSTITUENTS WE CARE ABOUT

VITAMIN D

Vitamin D precursor ergosterol

which ultraviolet B converts to ergocalciferol D2

- Mushrooms skin (like mammals) create vitamin D when exposed to sunlight.
- Mushrooms are rich in the vitamin D precursor ergosterol, which ultraviolet B converts to ergocalciferol D2 [Mammal epidermis has *cholecalciferol*, which ultraviolet light converts to *D3*.]
- Our system can convert both D vitamins into 25-hydroxyvitamin D, and then into the active form of 1,25-dihydroxyvitamin D in our kidneys.
- Putting your mushrooms in the vitamin d, even long after they have been cut will boost their vitamin D levels. This is best done for no more the 6 hours (10-4) of sunlight for 2days. After that UV destruction interfere with this process and benefit. Gills up!

Photobiology of vitamin D in mushrooms and its bioavailability in humans

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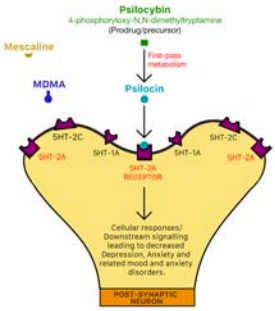
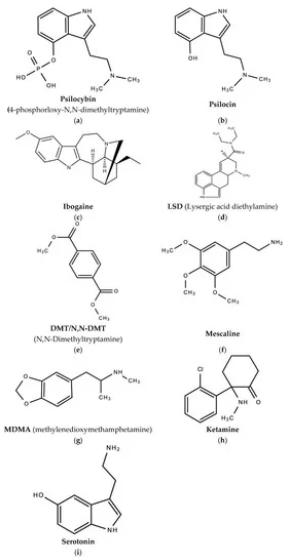
Constituents we care about

Psilocybin

- Psilocybin and psilocin, indolealkylamines, are structurally similar
- To the neurotransmitter serotonin (5-hydroxytryptamine or 5-HT).
- Psilocin mainly interacts with 5-HT1A, 5-HT2A and 5-HT2C receptor subtypes: a mixed receptor agonist.
- Unlike MDMA, Psilocybe do not just flood the brain with serotonin. They target a specific subtype of serotonin receptor–the 5-HT2A receptor- to which they bind directly, thereby activating it/
- The 5-HT2A receptor is known to play a key role in regulating mood, anxiety, schizophrenia, trauma processing, PTSD, joy, creativity and consciousness





Lindsay Chimileski ND LAc RH

Constituents we care about

Mushroom Neurologically Bio-Active Compounds

MANY fungi show the ability to induce neurite growth:

Sarcodon spp/ pheasant back

Cyanthus spp./Birdnest fungi

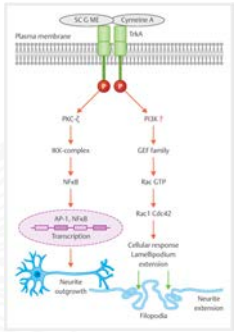


Fig. 3 Proposed model on the underlying mechanism of action of **cyrneine A** (**1**) and scabromine G methyl ester (**14**) and induced neurite outgrowth.

Treatment of cyrneine A (1)-induced neuronal differentiation through the formation of lamellipodia and filopodia at the growth cones as a result of actin polymerization via the Rac1-dependent pathway. Cyrneine A (**1**) treatment may have enhanced the level of PI3K, which in turn activated the guanosine exchange factor, which not only converted the inactive Rac (Ras-related C protein)-GDP to Rac-GTP but also activated the Rac1 protein and cell division control protein 42, which are key molecules in promoting lamellipodia and filopodia, respectively. **SG-ME** (**14**) **probably binds to TrkA and potently activated the IKK/NF-κB complex to release the NFκB** from IKK via PKC-ζ activation. NFκB can then be translocated into the nucleus where it binds with a transcription factor (AP-1) to **initiate further transcriptional expression of neurotrophic factors that promoted neurite outgrowth. NFκB is a key transcription factor involved in processes of synaptic plasticity and memory.|**

A Mechanistic Review on Medicinal Mushrooms–Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders

Mushrooms for Depression, Mood, Anxiety, Sleep Quality

Happiness, Motivation, Awe, Enjoyment, Learning, Connection versus isolation–

All very important for brain health and dementia prevention,

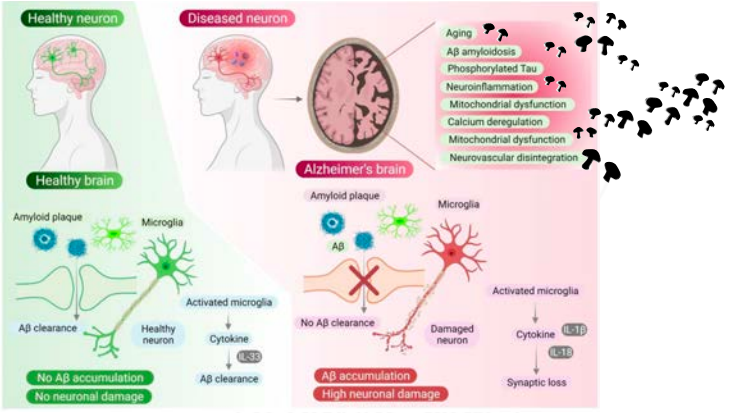
Lucky for us- mushrooms can help with that on many levels too!

Immune balancing actions of mushrooms

Decades of research on it (in addition to centuries of traditional use).
Immune actions have downstream impacts on brain health.
Just about all edible/medicinal mushrooms are going to have these impacts via beta-glucans, phenolic compounds and antioxidants

Mushroom Immune Balance action on brain health

- Helps prevent autoimmune degeneration like MS
- Many different antiviral mechanisms
- Helps to fight infections that can trigger formation of amyloid plaques in the brain, connected to Alzheimers disease. New research shows these plaques often form to encapsulate an infective agent i.e. stealth teeth strep infections etc
- Stealth pathogens will also steal resources, energy and focus from younger, "healthy" individuals i.e. college students with recurrent mono or Lyme, covid long haulers, candid, dysbiosis
- Surveying for cancers



Microfluidic Platforms to Unravel Mysteries of Alzheimer's Disease: How Far Have We Come?

by Pragya Prasanna [1,*], Shweta Rathee [2], Vedanabhatla Rahul [3], Debabrata Mandal [4], Macherla Sharath Chandra Goud [1], Pardeep Yadav [5], Susan Hawthorne [6], Ankur Sharma [7], Piyush Kumar Gupta [7], Shreesh Ojha [8], Niraj Kumar Jha [5], Chiara Villa [9] and Saurabh Kumar Jha [5,*]

dr lindsay chimileski THE BOTANICAL DOCTA

IMPORTANCE OF PREVENTION
NATUROPATHIC DOCS
+ MUSHROOMS EXCELL AT THIS

=antioxidants
=build the blood
=enhance lymph/ emunctories
=immunomodulation
=stabilize blood brain barrier
=provide nutrients needed
=enhance detoxification
=enhance enzyme function
=enhance cellular function

(*mitochondria, controlled cell death, lipid bilayer, signaling*)

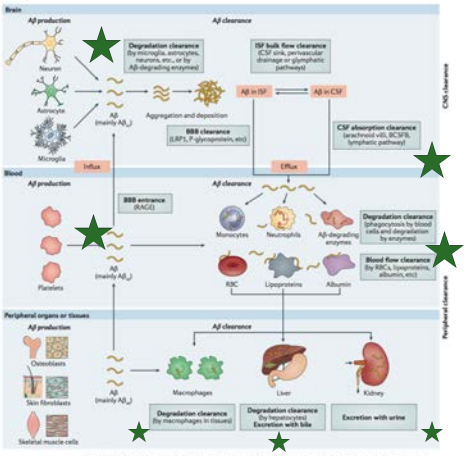
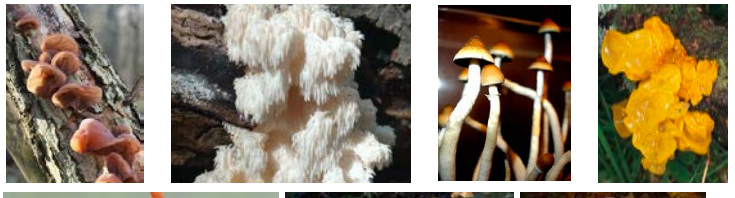


Figure 1 | **Physiological metabolism of Aβ in the brain and periphery.** Amyloid-β (Aβ) is generated by neurons, microglia and astrocytes in the brain, and by platelets, skin fibroblasts, osteoblasts, and skeletal muscle cells in the periphery. The CNS and peripheral pools of Aβ can interact; some Aβ peptides in the CNS are cleared via phagocytosis or proteolytic degradation, whereas others are released into the blood via the blood–brain barrier (BBB), interstitial fluid (ISF) bulk flow or cerebrospinal fluid (CSF) egress pathways. Some Aβ peptides in blood are phagocytosed, including by monocytes or neutrophils, some are degraded by Aβ-degrading enzymes, and some are transported by carriers (such as erythrocytes, albumin and lipoproteins) to peripheral organs or tissues, where they are degraded by macrophages or hepatocytes, or excreted via the liver or kidney. BCSFB, blood–CSF barrier; RAGE, receptor for advanced glycation end products; RBC, red blood cell.

dr lindsay chimileski
THE BOTANICAL SOCIETY



MUSHROOM MATERIA MEDICA
LINDSAY CHIMILESKI

Hot gossip- White button, Cremini, Portobello are all the same species

Agaricus bisporus

***White**: fresh, young; common, inexpensive, champignon*
***Cremini/ Baby Bella:** brown strain of button mushroom & immature Portobello, chestnut brown*
***Portobello**: fully mature, thick, meaty texture; Campellone mushroom, roman mushroom*

J Nutr. 2001 Dec;131(12):3288-93.

White button mushroom phytochemicals inhibit aromatase activity and breast cancer cell proliferation.

Grube BJ[1], Eng ET, Kao YC, Kwon A, Chen S.

Author information

Abstract

Estrogen is a major factor in the development of breast cancer. In situ estrogen production by aromatase/estrogen synthetase in breast cancer plays a dominant role in tumor proliferation. Because natural compounds such as flavones and isoflavones have been shown to be inhibitors of aromatase, it is thought that vegetables that contain these phytochemicals can inhibit aromatase activity and suppress breast cancer cell proliferation. Heat-stable extracts were prepared from vegetables and screened for their ability to inhibit aromatase activity in a human placental microsome assay. The white button mushroom (species Agaricus bisporus) suppressed aromatase activity dose dependently. Enzyme kinetics demonstrated mixed inhibition, suggesting the presence of multiple inhibitors or more than one inhibitory mechanism. "In cell" aromatase activity and cell proliferation were measured using MCF-7aro, an aromatase-transfected breast cancer cell line. Phytochemicals in the mushroom aqueous extract inhibited aromatase activity and proliferation of MCF-7aro cells. These results suggest that diets high in mushrooms may modulate the aromatase activity and function in chemoprevention in postmenopausal women by reducing the in situ production of estrogen.

Vitamin D2–enriched button mushroom (Agaricus bisporus) improves memory in both wild type and APPswe/PS1dE9 transgenic mice

Abstract

Vitamin D deficiency is widespread, affecting over 30% of adult Australians, and increasing up to 80% for at-risk groups including the elderly (age>65). The role for Vitamin D in development of the central nervous system is supported by the association between Vitamin D deficiency and incidence of neurological and psychiatric disorders including Alzheimer's disease (AD). A reported positive relationship between Vitamin D status and cognitive performance suggests that restoring Vitamin D status might provide a cognitive benefit to those with Vitamin D deficiency. Mushrooms are a rich source of ergosterol, which can be converted to Vitamin D3 by treatment with UV light, presenting a new and convenient dietary source of Vitamin D2. We hypothesised that Vitamin D2-enriched mushrooms (VDM) could prevent the cognitive and pathological abnormalities associated with dementia. Two month old wild type (WLD) and AD transgenic (APPSwe/PS1dE9) mice were fed a diet either deficient in Vitamin D2 or a diet which was supplemented with VDM, containing 1±0.2 μg/kg (~1-6 IU/kg) vitamin D2, for 7 months. Effects of the dietary intervention on memory were assessed pre- and post-feeding. Brain sections were evaluated for amyloid β (Aβ) plaque loads and inflammation biomarkers using immuno-histochemical methods. Plasma vitamin D metabolites, Aβ40, Aβ42, calcium, protein and cholesterol were measured using biochemical assays. Compared with mice on the control diet, VDM-fed wild type and AD transgenic mice displayed improved learning and memory, had significantly reduced amyloid plaque load and glial fibrillary acidic protein, and elevated interleukin-10 in the brain. The results suggest that VDM might provide a dietary source of Vitamin D2 and other bioactives for preventing memory impairment in dementia. This study supports the need for a randomised clinical trial to determine whether or not VDM consumption can benefit cognitive performance in the older population.

Auricularia (auricula-judae, polytricha, spp.)

Wood Ear, Jelly Ear, Mu-err
Cloud ear, jelly fungus,
Black Fungus, Tree jelly fish

Caution: blood thinning "szechwan purpura" anticoagulant effect. In 1980, a U.S. case of "Szechwan Purpura" was reported in the New England Journal of Medicine. A 32-year-old U.S. researcher (during an experiment using his own blood platelets for clotting) found after some *50 trials* one morning that his platelets would not agglutinate or release serotonin on exposure to epinephrine. It continued to inhibit platelet response in the researcher and other volunteers for 3-24 days. **Like aspirin (or other platelet inhibitors) this mushroom should not be ingested prior to surgery or in patients with poor blood clotting**.

Traditional Chinese Medicine ☯ Used in TCM cooking as early as 300-200BC.
- ☯ Flavor & Energetics: sweet, neutral; lung, stomach, liver, spleen, kidney, large intestine meridians.
- ☯ Actions: n**ourishes yin and moisturizes**, replenishes qi, revives blood, gently cools to stop bleeding, moistens and clears lung qi, build blood, build stomach qi, nourishing and moistening.
- ☯ Indications: Dry cough, Urine with blood, metrorrhagia, hemorrhoids, blood deficiency.

- ☯ **Heart disease & circulation balancing, Anti-coagulant, Balances cholesterol**
- ☯ **Hypoglycemic, Hepatoprotective, Antiviral, Anti-tumor**
- ☯ **Healthy Aging, Skin Beauty tonic**
- ☯ **Anti-inflammatory for skin, mucus and eyes**
- ☯ **Vitamins: B1, B2, B5** (40% RDA in 100g raw mushroom)**, B6, B9. Minerals: Copper, Iron, Magnesium, Selenium, Zinc, Fiber, protein, calcium, phosphorus.**
- ☯ **Asian culinary staple- adds consistency/texture/crunch more than flavor.**
- ☯ **Contains lecithin for lipid cell membrane health and oxidation. Linoleic acids, soluble fiber, antioxidants.**

Saprophytic, deciduous wood-decaying (Maple, Oak, Ash, European Elder). Found all year round. Clusters gelatinous sporocarp fruiting body, rubbery, flexible, fine surface hairs; edible

Mushroom Medicine for Everyone. Lindsay Chimileski ND LAc RH(AHG)

Auricularia polytricha

Potential use in Alzheimer's and amyloid plaque formation, helps stimulate the enzymes that cleave or breaks down the plaques

Int J Med Mushrooms. 2013;15(3):233-49.

Heat-stable components of wood ear mushroom, Auricularia polytricha (higher Basidiomycetes), inhibit in vitro activity of beta secretase (BACE1).

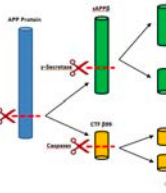
Bennett L[1], Sheean P, Zabaras D, Head R.

Author information

Abstract

The consumption of mushrooms has been linked with protection against dementia, including Alzheimer's disease (AD), by several biological pathways including inhibiting beta-site APP-cleaving enzyme (BACE1), which is responsible for releasing toxic β-amyloid peptide in the brain. We have investigated the capacity of several medicinal mushroom species-Auricularia polytricha (wood ear mushroom), Agaricus bisporus (button mushroom), Flammulina velutipes (winter or enoki mushroom), and Lentinus edodes (shiitake mushroom)-in the regulation of BACE1. Mushrooms were subjected to a generic food-compatible processing method to detect process-stable or process-modified products; the effects of processing were interpreted to infer the chemical classes associated with bioactivity. We have shown previously that in addition to enzyme inhibition, in the presence of the BACE1 proenzyme, heteropolymeric species such as heparin can activate BACE1 by modulating access to the catalytic site. We observed both inhibitory and activating components of the various mushrooms. Only BACE1 inhibitory species were detected in unprocessed and processed forms of A. polytricha, whereas the dominant extracted species from A. bisporus, F. velutipes, and L. edodese were activators of BACE1. It is not known whether activating species were masking the presence of inhibitory species in A. bisporus, F. velutipes, and L. edodes. Inhibitory species were attributed to hispidin-derived polyphenols, whereas activating species were attributed to soluble polysaccharides and possibly low-mass Maillard products produced during processing. Larger molecular BACE1-activating species are unlikely to be bioavailable to brain in contrast with possible brain bioavailability of smaller, lipophilic hispidins.

PMID: 23662612 DOI: 10.1615/IntJMedMushr.v15.i3.20



Mushroom Medicine for Everyone.

Lindsay Chimileski ND LAc RH(AHG)

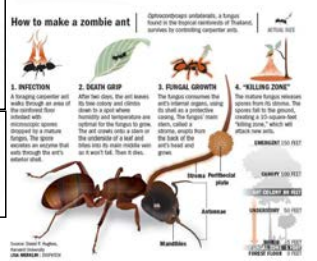
Cordyceps sinensis

Caterpillar fungus
Himalayan Viagra

Adaptogen, Energy Promoting, Anti-tumor, Anti-inflammatory, Antioxidant, Hepatoprotective

Classic Adapotogen: Improves energy, stamina, physical performance and quality of life
Traditional Chinese Uses: Cough, chronic bronchitis, respiratory dysfunctions, kidney disorders, frequent nocturia, male sexual dysfunction, liver disease, dizziness, weakness, waisting and opium addiction Lung, Immune, Adrenal affinity

Immunostimulating polysaccharide galactomannins, cordycepic acid. Amino Acids, Fatty Acids, Polyamines, Ecdysterones, Adenosine, B-Vitamins, polysaccharides, ophiocordin (an antibiotic compound), cordycepin, cordypyridones, nucleosides, bioxanthracenes, sterols, alkenoic acids, and exo-polymers.



Forms of Cordyceps

Cordyceps sinensis

Almost all of the supplements are not true cordyceps sinensis bc of its extremely high price- wild cordyceps costs up to $20,000 per kilogram; rarely even sold in North America.

Cordyceps Cs-4. Cordyceps sinensis is difficult to grow in the lab or on different substrates, still not really affordably cultivated to this day. In the 1980s, scientists made Cordyceps anamorphs, mycelium growth that are unable to produce a mushroom fruiting body.

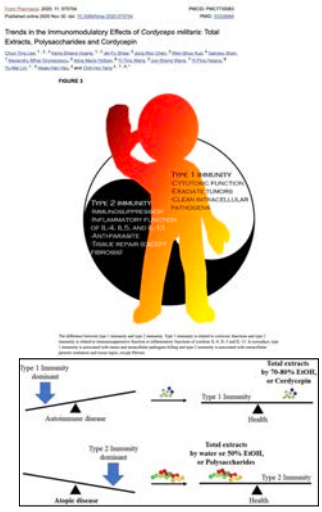
Using liquid fermentation, these anamorphs were grown to create mass amounts of pure mycelium (this method uses a liquid culture mycelium or liquid fermentation nutrients which are then removed, leaving the pure mycelium). These anamorphs were studied extensively and found to produce similar results to the wild Cordyceps sinensis – > now known as Cordyceps Cs-4. Many clinical trials in China, the Chinese government approved its use in TCM hospitals and is recognized as a safe natural product drug. If a Cordyceps supplement is claiming to be *Cordyceps sinensis* and it is made in China, it is almost always Cordyceps Cs-4.

Cordyceps sinensis CS4 liquid grow tanks

Cordyceps myceliated grain

Cordyceps militaris.

Cordyceps species that can be commercially cultivated at scale to produce a mushroom (fruiting body); becoming quite popular. Tests on par with sinensis. Made from the mushroom fruit body= higher levels of the important beta-glucans.

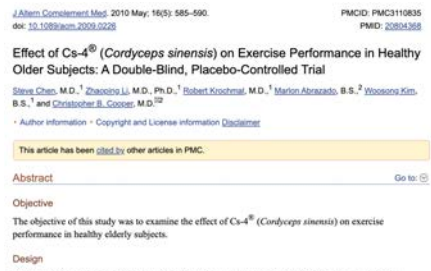


Cordyceps militaris

FIGURE 2

The biological activities of *C. militaris*. 3'-deoxyadenosine (cordycepin), adenosine derivatives, polysaccharides, ergosterol analogs, mannitol, peptides, fibrinolytic enzyme, xanthophylls, aqueous or alcohol extracts, and the powders of *C. militaris* have exhibited specific biological activities. The immunoregulation is one of the important functions of *C. militaris*. Immune response has been divided into type I and type 2, the balance between these two types of immunity is crucial to our health.

Medicinal Mushrooms and Oncology. Lindsay Chimileski ND LAc RH(AHG)


J Altern Complement Med. 2010 May; 16(5): 585–590.
doi: 10.1089/acm.2009.0226
PMCID: PMC3110835
PMID: 20804368

Effect of Cs-4® (*Cordyceps sinensis*) on Exercise Performance in Healthy Older Subjects: A Double-Blind, Placebo-Controlled Trial

Steve Chen, M.D.,[1] Zhaoping Li, M.D., Ph.D.,[1] Robert Krochmal, M.D.,[1] Marlon Abrazado, B.S.,[2] Woosong Kim, B.S.,[1] and Christopher B. Cooper, M.D.[1][2]

Abstract

Objective

The objective of this study was to examine the effect of Cs-4® (*Cordyceps sinensis*) on exercise performance in healthy elderly subjects.

Design

Twenty (20) healthy elderly (age 50–75 years) subjects were enrolled in this double-blind, placebo-controlled, prospective trial. The subjects were taking either Cs-4 333 mg or placebo capsules 3 times a day for 12 weeks.

Measurement

Subjects received baseline screening including physical examination and laboratory tests. Maximal incremental exercise testing was performed on a stationary cycle ergometer using breath-by-breath analysis at baseline and at the completion of the study.

Results

After receiving Cs-4 for 12 weeks, the metabolic threshold (above which lactate accumulates) increased by 10.5% from 0.83 ± 0.06 to 0.93 ± 0.08 L/min ($p < 0.02$) and the ventilatory threshold (above which unbuffered H^+ stimulates ventilation) increased by 8.5% from 1.25 ± 0.11 to 1.36 ± 0.15 L/min. Significant changes in metabolic or ventilatory threshold were not seen for the subjects in the placebo group after 12 weeks, and there were no changes in $\dot{V}O_2$ max in either group.

Conclusion

This pilot study suggests that supplementation with Cs-4 (*Cordyceps sinensis*) improves exercise performance and might contribute to wellness in healthy older subjects.

20 adults, double blind placebo controlled 333mg TID or placebo for 12 weeks. Improved exercise performance & wellness

Cordyceps & Ischemic Brain Injury

Post-ischemic treatment of WIB801C, standardized Cordyceps extract, reduces cerebral ischemic injury via inhibition of inflammatory cell migration

WIB801C, the standardized extract of Cordyceps militaris used to treat rats that had had induced ischemic injuries (no blood flow to certain areas of the brain

WIB801C significantly decreased migration of cultured microglia/macrophages.

This anti-chemotactic activity of WIB-801C was not mediated via adenosine A3 receptors, although cordycepin, the major ingredient of WIB801C, is known as an adenosine receptor agonist.

Post-ischemic treatment with WIB801C significantly reduced the infiltration of ED-1-and MPO-positive inflammatory cells into ischemic lesions in tMCAO rats.

WIB801C-treated rats exhibited significantly decreased infarct volume and cerebral edema, less white matter and blood-brain barrier damages, and improved neurological deficits.

WIB801C also **improved survival rates** over 34 days after ischemia onset.

A significant reduction in infarct volume and neurobehavioral deficits by WIB801C was also observed in rats subjected to pMCAO.

Conclusions: In summary, post-ischemic treatment of WIB801C reduced infiltration of inflammatory cells into ischemic lesions via inhibition of chemotaxis, which confers long-lasting histological and neurological protection in ischemic brain. WIB801C may be a promising anti-ischemic drug candidate with clinically relevant therapeutic time window and safety.

Int J Chron Obstruct Pulmon Dis. 2016; 11: 1721–1731.
Published online 2016 Jul 28. doi: 10.2147/COPD.S107396
PMCID: PMC4968668
PMID: 27555782

The inhibitory mechanism of *Cordyceps sinensis* on cigarette smoke extract-induced senescence in human bronchial epithelial cells

Ailing Liu,[1,2] Jinxiang Wu,[1,*] Aijun Li,[2] Wenxiang Bi,[3] Tian Liu,[1] Liuzhao Cao,[1] Yahui Liu,[1] and Liang Dong[1]

Abstract

Objectives

Cellular senescence is a state of irreversible growth arrest induced either by telomere shortening (replicative senescence) or stress. The bronchial epithelial cell is often injured by inhaled toxic substances, such as cigarette smoke. In the present study, we investigated whether exposure to cigarette smoke extract (CSE) induces senescence of bronchial epithelial cells; and *Cordyceps sinensis* mechanism of inhibition of CSE-induced cellular senescence.

Methods

Human bronchial epithelial cells (16HBE cells) cultured in vitro were treated with CSE and/or *C. sinensis*. p16, p21, and senescence-associated-galactosidase activity were used to detect cellular senescence with immunofluorescence, quantitative polymerase chain reaction, and Western blotting. Reactive oxygen species (ROS), PI3K/AKT/mTOR and their phosphorylated proteins were examined to testify the activation of signaling pathway by ROS fluorescent staining and Western blotting. Then, inhibitors of ROS and PI3K were used to further confirm the function of this pathway.

Results

Cellular senescence was upregulated by CSE treatment, and *C. sinensis* can decrease CSE-induced cellular senescence. Activation of ROS/PI3K/AKT/mTOR signaling pathway was enhanced by CSE treatment, and decreased when *C. sinensis* was added. Blocking ROS/PI3K/AKT/mTOR signaling pathway can attenuate CSE-induced cellular senescence.

Conclusion

CSE can induce cellular senescence in human bronchial epithelial cells, and ROS/PI3K/AKT/mTOR signaling pathway may play an important role in this process. *C. sinensis* can inhibit the CSE-induced senescence.

Keywords: senescence, *Cordyceps sinensis*, ROS/PI3K/AKT/mTOR signaling pathway, COPD

RESULTS:

Cellular senescence was unregulated by CSE (cigarette smoke treatment

C. sinensis can decrease CSE-induced cellular senescence.

Activation of ROS/PI3K/AKT/mTOR signaling pathway was enhanced by CSE treatment, and decreased when *C. sinensis* was added.

Blocking ROS/PI3K/AKT/mTOR signaling pathway can attenuate CSE-induced cellular senescence.

Conclusion

CSE can induce cellular senescence in human bronchial epithelial cells, and ROS/PI3K/AKT/mTOR signaling pathway may play an important role in this process. *C. sinensis* can inhibit the CSE-induced senescence.

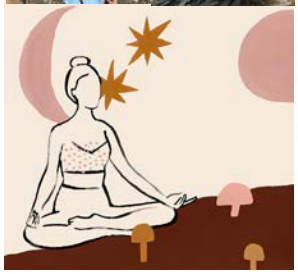
Nootropic Medicinal Mushrooms. Lindsay Chimileski ND LAc RH(AHG)

Ganoderma lucidum

REISHI, Ling Zhi

Mushroom of spiritual potency

adaptogen, immune stimulant, antioxidant



TCM: Tonifies Jing, Qi and Shen. calmness, centeredness, balance, inner awareness and inner strength.

Asia as a tonic herb consumed for the attainment of radiant health, longevity and spiritual attainment.

In the middle ages- used by *mountain hermits, monks, Taoist adepts and spiritual seekers* throughout Asia to help calm the mind, ease tension, strengthen the nerves, strengthen memory, sharpen concentration, improve focus, build will power and, as a result, help build wisdom.

Called the "Mushroom of Spiritual Potency" by these seekers.

Used to improve meditative practices and to protect the body, mind and spirit so that the adept could attain both a long and healthy life.

The Auspicious Fungus

Finding it was a blessing
Great luck/ very special / a gift
The spirits of the mountain favoring you

Rituals & astrology to help find it
Sage naturalist would go into the mountains carrying specific talismans,
a white chicken or a white dog to gain favor of the mountain spirits

Reishi was such a sacred finding, that the mountain spirits would guard it.
If you did not pay honor to them, they would not show you the reishi-
You could walk right by it and not see it.

Only ones who could afford it were the emperors and wealthy
Because it was so special, it is one of the few TCM herbs that was used on its own in formulas, versus the big blends that are common in their formulary.

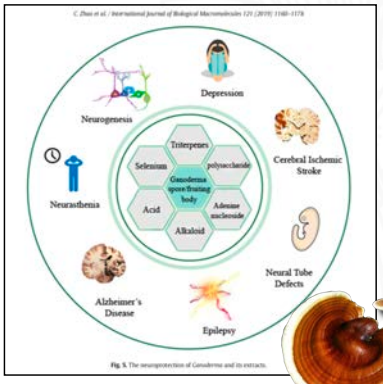
In the "Superior Medicinals" in the TCM texts= safe to take daily with no ill effects and helps you live a better life

Reishi "lightens the spirit"
Daoist immortals said it "makes you fly"
Encourages lucid dreaming and spirit travel

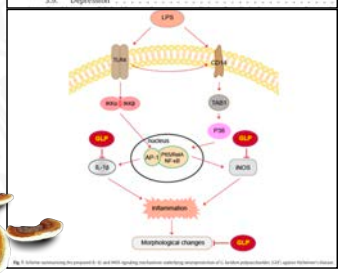
REISHI Research: Brain

Pharmacological effects of natural *Ganoderma* and its extracts on neurological diseases: A comprehensive review

Chen Zhao [a,c], Chunchen Zhang [a], Zheng Xing [c], Zeeshan Ahmad [d], Jing-Song Li [a], Ming-Wei Chang [a,b,*]



3. Pharmacological effects of *Ganoderma* and its extracts on neurological diseases
- 3.1. Abnormal neurogenesis
- 3.2. Alzheimer's disease (AD)
- 3.3. Parkinson's disease (PD)
- 3.4. Cerebrovascular disease (CVD)
- 3.5. Epilepsy
- 3.6. Spinal cord injury (SCI)
- 3.7. Neural tube defects (NTDs)
- 3.8. Neurasthenia
- 3.9. Depression



REISHI Research: Brain

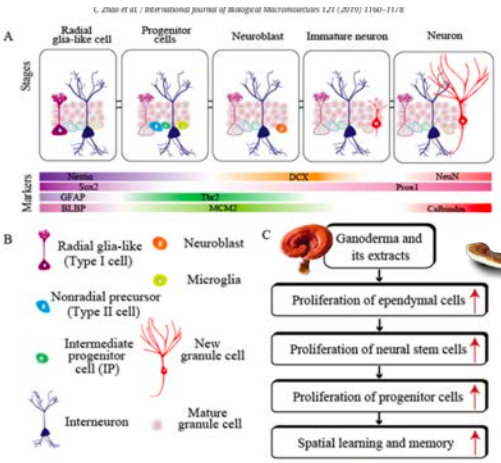


Fig. 6. (A) 5 stages of neurogenesis in sub-granular zone area. (B) Cell types involved in neurogenesis in sub-granular zone [130]. (C) Summarizing the *Ganoderma* effects on neurogenesis.

REISHI Research: Liver and Brain

> Alcohol Clin Exp Res. 2015 Jul;39(7):1128-36. doi: 10.1111/acer.12758. Epub 2015 Jun 8.

Neurometabolic Effect of Altaian Fungus Ganoderma lucidum (Reishi Mushroom) in Rats Under Moderate Alcohol Consumption

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Affiliations + expand

PMID: 26058418 DOI: 10.1111/acer.12758

The Reishi (R) suspension was produced as water extract from Altaian mushrooms. Sprague-Dawley male rats were separated into the following 3 experimental groups: **Group A + R received R (6 days per week) starting 1 week before alcohol exposure, and during the next 3 weeks, they received both R and alcohol; group A received alcohol; and group C received water.**
At the end of experiment, we determined the metabolic profile using proton magnetic resonance spectroscopy ((1) H MRS) of the brain cortex and phosphorus magnetic resonance spectroscopy of the liver. Additionally, the blood cells were collected, and the serum biochemistry and liver histology were performed after euthanasia.

...Moderate alcohol consumption did not cause significant pathological changes in the livers of the experimental animals. However, 20 days of alcohol consumption significantly increased the number of binuclear hepatocytes compared to the control. This effect was mitigated in the rats that received the Reishi extract.

Conclusions: Regular administration of the Reishi suspension improved the energy supply to the brain cortex and decreased the prevalence of inhibitory neurotransmitters that are characteristic of alcohol consumption. The alcohol-induced increase in liver proliferation was significantly suppressed by regular administration of the G. lucidum water suspension.

> Biomed Pharmacother. 2017 Aug;92:1055-1061. doi: 10.1016/j.biopha.2017.06.029. Epub 2017 Jun 10.

Anti-amnesic effects of Ganoderma species: A possible cholinergic and antioxidant mechanism

Ravneet Kaur [1], Varinder Singh [1], Richa Shri [2]

Affiliations + expand

PMID: 28618650 DOI: 10.1016/j.biopha.2017.06.029

AChE inhibitor= Prevention potential Alzheimer's Parkinson's dementia

Cholinesterase inhibitors (also called acetylcholinesterase inhibitors) are **a group of medicines that block the normal breakdown of acetylcholine- keeping it circulating for longer**. Acetylcholine is the main neurotransmitter found in the body and has functions in both the peripheral nervous system and the central nervous system.

REISHI Research: Brain

The present study was designed to systematically evaluate the anti-amnesic effect of selected Ganoderma species i.e. G. mediosinense and G. ramosissimum.

Extracts of selected mushroom species were **evaluated for their antioxidant activity and acetylcholinesterase (AChE) inhibition using in-vitro assays** (DPPH and Ellman tests respectively).

The anti-amnesic potential of the most active extract (i.e. 70% methanol extract of G. mediosinense) was confirmed using mouse model of scopolamine-induced amnesia.

Mice were treated with bioactive extract and donepezil once orally before the induction of amnesia.

Cognitive functions were evaluated using passive shock avoidance (PSA) and novel object recognition (NOR) tests.

The effect on brain AChE activity, brain oxidative stress (TBARS level) and neuronal damage (H & E staining) were also assessed.

In-vitro results showed strong antioxidant and AChE inhibitory activities by G. mediosinense extract (GME). Therefore, it was selected for in-vivo studies.

GME pre-treatment (800mg/kg, p.o.) reversed the effect of scopolamine in mice, evident by significant decrease ($p < 0.05$) in the transfer latency time and increase in object recognition index in PSA and NOR, respectively.
GME significantly reduced the brain AChE activity and oxidative stress.
Histopathological examination of brain tissues showed decrease in vacuolated cytoplasm and increase in pyramidal cells in brain hippocampal and cortical regions.
GME exerts anti-amnesic effect through AChE inhibition and antioxidant mechanisms.

REISHI Research: Brain

> J Ethnopharmacol. 2021 Apr 6;269:113725. doi: 10.1016/j.jep.2020.113725. Epub 2020 Dec 25.

Prophylactic effects of sporoderm-removed Ganoderma lucidum spores in a rat model of streptozotocin-induced sporadic Alzheimer's disease

Hui-Ling Zhao [1], Su-Ying Cui [1], Yu Qin [1], Yu-Tong Liu [1], Xiang-Yu Cui [1], Xiao Hu [1], Nurhumar Kurban [1], Ming-Yan Li [2], Zhen-Hao Li [2], Jing Xu [2], Yong-He Zhang [4]

Affiliations + expand

PMID: 33352241 DOI: 10.1016/j.jep.2020.113725

Free article

Abstract

Ethnopharmacological relevance: Ganoderma lucidum (G. lucidum, Lingzhi), also known as "immortality mushroom" has been broadly used to improve health and longevity for thousands of years in Asia. G. lucidum and its spores have been used to promote health, based on its broad pharmacological and therapeutic activity. This species is recorded in Chinese traditional formula as a nootropic and has been suggested to improve cognitive dysfunction in Alzheimer's disease. However, little is known about the nootropic effects and molecular mechanism of action of G. lucidum spores.

Aim of the study: The present study investigated the protective effects of sporoderm-deficient Ganoderma lucidum spores (RGLS) against learning and memory impairments and its mechanism of action.

Materials and methods: In the Morris water maze, the effects of RGLS on learning and memory impairments were evaluated in a rat model of sporadic Alzheimer's disease that was induced by an intracerebroventricular injection of streptozotocin (STZ). Changes in amyloid β (Aβ) expression, Tau expression and phosphorylation, brain-derived neurotrophic factor (BDNF), and the BDNF receptor tropomyosin-related kinase B (TrkB) in the hippocampus were evaluated by Western blot.

Results: Treatment with RGLS (360 and 720 mg/kg) significantly enhanced memory in the rat model of STZ-induced sporadic Alzheimer's disease and reversed the STZ-induced increases in Aβ expression and Tau protein expression and phosphorylation at Ser199, Ser202, and Ser396. The STZ-induced decreases in neurotrophic factors, including BDNF, TrkB and TrkB phosphorylation at Tyr816, were reversed by treatment with RGLS.

Conclusion: These findings indicate that RGLS prevented learning and memory impairments in the present rat model of STZ-induced sporadic Alzheimer's disease, and these effects depended on a decrease in Aβ-expression and Tau hyperphosphorylation and the modulation of BDNF-TrkB signaling in the hippocampus.

> Exp Toxicol Pathol. 2012 Nov;64(7-8):673-80. doi: 10.1016/j.etp.2010.12.011. Epub 2011 Jan 19.

Neuroprotective effect of preadministration with Ganoderma lucidum spore on rat hippocampus

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Affiliations + expand

PMID: 21242065 DOI: 10.1016/j.etp.2010.12.011

Abstract

The aim of this study was to investigate if preadministration with Ganoderma lucidum spore (GLS) could (1) alleviate oxidative stress and mitochondrial dysfunction in rat hippocampus of intracerebroventricular (ICV) injection of streptozotocin (STZ), (2) protect neurons from apoptosis, and (3) improve cognitive dysfunction. Three groups of Sprague–Dawley rats were preadministrated with GLS at doses of 2.0, 4.0 and 8.0 g/kg, respectively, for 3 weeks before the ICV STZ injury. Thereafter the rats were operated with ICV STZ (1.5 mg/kg) bilaterally on days 1 and 3. The behavioral alterations, oxidative stress indexes, ATP, cytochrome oxidase (CytOx), and histopathology of hippocampal neurons were studied. The results showed that ICV STZ model rats exhibited a significant increase of malondialdehyde (MDA), a significant decrease of glutathione reductase (GR), reduced glutathione (GSH), ATP and CytOx, accompanied with marked impairments in spatial learning and memory, and severe damage of hippocampal neuron. In conclusion, preadministration with GLS at dose of 8.0 g/kg in ICV STZ rats significantly reversed these abnormalities. In conclusion, preadministration with GLS might protect hippocampus from oxidative impairment and energy metabolism disturbance of ICV STZ. This may also provide useful information for future research on the pathogenesis and prevention of Alzheimer's disease.

REISHI Research: Brain

> Oxid Med Cell Longev. 2020 Jan 28;2020:9894037. doi: 10.1155/2020/9894037. eCollection 2020.

Ganoderma lucidum Triterpenoids (GLTs) Reduce Neuronal Apoptosis via Inhibition of ROCK Signal Pathway in APP/PS1 Transgenic Alzheimer's Disease Mice

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Affiliations + expand

PMID: 32089787 PMCID: PMC7008260 DOI: 10.1155/2020/9894037

Free PMC article

Abstract

Alzheimer's disease (AD) is the most common cause of dementia among senior citizen. Ganoderma lucidum triterpenoids (GLTs) have nutritional health benefits and has been shown to promote health and longevity, but a protective effect of GLTs on AD damage has not yet been reported. The objective of this research was to elucidate the phylactic effect of GLTs on AD model mice and cells and to explore its underlying mechanisms. Morris water maze (MWM) test was conducted to detect changes in the cognitive function of mice. Hematoxylin–eosin (HE) staining was applied to observe pathological changes in the hippocampus. Silver nitrate staining was applied to observe the hippocampal neuronal tangles (NFTs). Apoptosis of the hippocampal neurons in mouse brain tissue was determined by TUNEL staining. The expression levels of apoptosis-related protein Bcl2, Bax, and caspase 3/cleaved caspase 3; antioxidative protein Nrf2, NQO1, and HO1; and ROCK signaling pathway–associated proteins ROCK2 and ROCK1 were measured by western blot. *In vivo* experiments show that 5-month-old APP/PS1 mice appeared to have impaired acquisition of spatial learning and GLTs could reduce cognitive impairment in AD mice. Compared to normal mice, the hippocampus of APP/PS1 mouse's brains was severely damaged, while GLTs could alleviate this symptom by inhibiting apoptosis, relieving oxidative damage, and inactivating the ROCK signaling pathway. In *in vitro* cell experiments, Aβ $_{25-35}$ was applied to induce hippocampal neurons into AD model cells. GLTs promoted cell proliferation, facilitated superoxide dismutase (SOD) expression, and inhibited malondialdehyde (MDA) and lactic dehydrogenase (LDH) expression of neurons. Our study highlights that GLTs improve cognitive impairment, alleviate neuronal damage, and inhibit apoptosis in the hippocampus tissues and cells in AD through inhibiting the ROCK signaling

REISHI Research: Brain

> Int J Med Mushrooms. 2013;15(6):555-68. doi: 10.1615/intjmedmushr.v15.i6.40.

Anticonvulsant and neuroprotective effects of oligosaccharides from Lingzhi or Reishi medicinal mushroom, Ganoderma lucidum (Higher Basidiomycetes)

Isaac Tello [1], Victoria Campos-Pena, Elizur Montiel, Veronica Rodriguez, Alma Aguirre-Moreno, Ismael Leon-Rivera, Federico Del Rio-Portilla, Maribel Herrera-Ruiz, Juana Villeda-Hernandez

Affiliations + expand

PMID: 24266379 DOI: 10.1615/intjmedmushr.v15.i6.40

Abstract

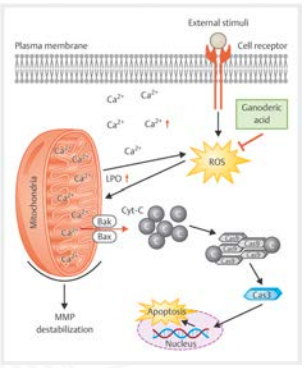
An oligosaccharide fraction isolated from the mycelium of the Lingzhi or Reishi medicinal mushroom Ganoderma lucidum (GLOS) was separated by size-exclusion chromatography. The chemical structure of GLOS consists of a disaccharide repeating unit [→4-β-1-Galf(1→6)-O-(β-Glcp)-1→]n (n=3,4). In addition, this study was undertaken to determine the possible anticonvulsant and neuroprotective effects of GLOS (10–80 mg/kg) on kainic acid (KA)–induced seizures. The behavioral alterations and histopathology of hippocampal neurons were studied. Our results show that GLOS inhibited convulsions in rats from KA–induced seizures, reduced the degeneration pattern in the CA3 region of rats, decreased astrocytic reactivity, and reduced the expression of IL-1β and TNF-α induced by KA. These results indicate a potential anticonvulsant and neuroprotective effects of GLOS.

mycelium of the Lingzhi or Reishi medicinal mushroom Ganoderma lucidum **inhibited convulsions in rats from KA-induced seizures, reduced the degeneration pattern in the CA3 region of rats, decreased astrocytic reactivity, and reduced the expression of IL-1β and TNF-α induced by KA. These results indicate a potential anticonvulsant and neuroprotective effects of GLOS.**

Constituents we care about

Mushroom Neurologically Bio-Active Compounds

Reishi & Epilepsy



β-glucans, lectins, amino acids, lignin, mycin, and vitamins, which have potential antioxidant, anti-inflammatory, and neuroprotective effects [62],[63]. Ganodermasides A–D (**43**–**46**), the biologically active compounds obtained from different parts of *G. lucidum*, increase life span and show anti-aging properties [64],[65],[66]. Other bioactive triterpenoid compounds such as lucidenic acids, 7-oxo-ganoderic acid-Z (**47**), 4,4,1,4α-trimethyl-5α-chol-7,9 (11)-diene-3-oxo-24-oic acid (**48**), ganoderic acid-S1 (**49**), ganolucidic acid-A (**50**), methyl ganoderic acid-A (**51**), and methyl ganoderic acid-B (**52**) from *G. lucidum* are capable of inducing neurite outgrowth

Fig. 9 Schematic representation of **mitochondrial membrane stabilization via action of the antioxidative activity of ganoderic acid (51)**. The excessive accumulation of an excitotoxic insult such as glutamate and its binding on the cell receptor induces ROS generation, which in turn impairs the stabilization of the mitochondrial membrane and its functions in hippocampal neurons. Mitochondrial damage may also be caused by the results of lipid peroxidation of the membrane. **Ganoderic acid A (51) increased the levels of SOD to inhibit the production of ROS, thereby preserving the integrity of the mitochondrial membranes by improving the MMP of the hippocampal neurons. Due to its mitochondrial membrane stabilizing activity, the release of cytochrome C from mitochondria may also be greatly reduced by ganoderic acid (51), and thus control the release of apoptotic proteases such as caspases 3 and 9 to protect the hippocampal neurons against epileptic insults.|**

A Mechanistic Review on Medicinal Mushrooms-Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders

https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1177-4834

Constituents we care about

Mushroom Neurologically Bio-Active Compounds

Reishi and Epilepsy

Epilepsy is a major neurological disorder with frequent seizures due to abnormal neuronal firing and synaptotoxicity and apoptosis of neurons in the cortico-hippocampal region [67]. Several factors such as apoptotic proteins (Bax/Bad) and cytoplasmic organoids are associated with apoptosis in the hippocampal neurons [67]. In the mitochondria of epileptiform hippocampal neurons, the damage is caused by the peroxidation of lipids after the induction of free radicals [67]. It has been experimentally demonstrated that **Ganodermic acids A and B**

play an important role in the regulation of lipid peroxidation and stabilization of the MMP (ψ), thus maintaining the mitochondrial structure [64]. Similarly, apoptosis is associated with **SOD** activity and MMP; thus, apoptosis in epileptic hippocampus neurons is caused via mitochondrial apoptosis pathways.

Ganoderic acids A and B significantly improve SOD activity and maintain the MMP in hippocampus neurons, they protect the hippocampus neurons by inhibiting apoptosis [68],[69]. The ganodermic acid-mediated stabilization of mitochondrial membranes via its antioxidative activity is represented in [Fig. 9].

New identified Lanostane triterpene named Methyl Ganoderate and two known aromatic meroterpenoids, namely, lingzhine E and lingzhine F have been documented to possess neuroprotective activities against H2O2 and aged Aβ-induced cell death in neuroblastoma SHSY5Y cells, an Alzheimer's cell model [70].

A Mechanistic Review on Medicinal Mushrooms-Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders

https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1177-4834

Constituents we care about

Mushroom Neurologically Bio-Active Compounds

Reishi and Epilepsy

Two new Benzendiols, designated as lucidumins B and C, along with two new alkaloids, namely, lucidimine E and ganocochlearine A, have shown remarkable neuroprotective activity against corticosteroid-induced cytotoxicity in PC12 cells [71].

In patients with depressive disorders, glucocorticoids such as corticosterone and cortisol are secreted at a high level due to the dysfunction and hyperactivity of the hypothalamic-pituitary-adrenal axis, which further leads to damage to hippocampal neurons, followed by depressive symptoms [72],[73],[74]. Hence, the **neuroprotective effect of lucidumins and lucidimines against glucocorticoids-induced hippocampus dysfunction may play a protective role in fighting depression.** The above studies indicate that *G. lucidum* may have potential for the treatment of neurodegenerative diseases and other neurological disorders.

=Adaptogenic action for mood and brain health, longevity.

A Mechanistic Review on Medicinal Mushrooms-Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders

https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1177-4834

> Int J Mol Sci. 2021 May 24;22(11):5559. doi: 10.3390/ijms22115559.

Ganoderic Acid A Promotes Amyloid-β Clearance (In Vitro) and Ameliorates Cognitive Deficiency in Alzheimer's Disease (Mouse Model) through Autophagy Induced by Activating Axl

Li-Feng-Rong Qi [1], Shuai Liu [1,2], Yu-Ci Liu [3], Ping Li [3], Xiaojun Xu [1,2]

Affiliations + expand

PMID: 34074054 PMCID: PMC8197357 DOI: 10.3390/ijms22115559

Free PMC article

Abstract

Alzheimer's disease (AD) is thought to be caused by amyloid-β (Aβ) accumulation in the central nervous system due to deficient clearance. The aim of the present study was to investigate the effect of ganoderic acid A (GAA) on Aβ clearance in microglia and its anti-AD activity. Aβ degradation in BV2 microglial cells was determined using an intracellular Aβ clearance assay. GAA

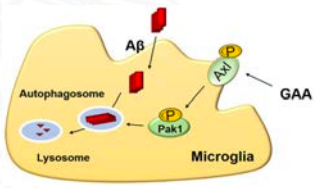


Figure 5 Proposed mechanism of GAA-mediated Aβ clearance in vitro.

> Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2017 Aug 20;39(4):552-561. doi: 10.3881/j.issn.1000-503X.2017.04.015.

Pathological Changes in APP/PS-1 Transgenic Mouse Models of Alzheimer's Disease Treated with Ganoderma Lucidum Preparation

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Affiliations + expand

PMID: 28877835 DOI: 10.3881/j.issn.1000-503X.2017.04.015

Abstract in English, Chinese

Objective To explore the efficacy of ganoderma lucidum preparation(Ling Zhi) in treating APP/PS-1 transgenic mouse models of Alzheimer's disease(AD).Methods APP/PS-1 transgenic mice of 4 months were randomly divided into model group,ganoderma lucidum treatment groups,including high [2250 mg/(kg·d)] and middle [750 mg/(kg·d)] dose groups,i.e.LZ-H and LZ-M groups,and the positive control group(treated with donepezil hydrochloride [2 mg/(kg·d)]) in addition,C57BL/6J wild mice were selected as normal group.The animals were administered for 4 months.Histopathological examinations including hematoxylin-eosin(HE) staining,immunohistochemistry,special staining,and electron microscopy were applied,and then the pathological morphology and structures in different groups were compared. Results The senile plaques and neurofibrillar tangles in the cerebrum and cerebellum were dissolved or disappeared in LZ-H and LZ-M groups.Decrease of amyloid angiopathy was found in LZ-H and LZ-M groups.The immature neurons appeared more in hippocampus and dentate nucleus of LZ-H and LZ-M groups than those in AD model and donepezil hydrochloride groups(hippcampus:F=1.738,P=0.016;dentate nucleus:F=1.924,P=0.026),and these immature neurons differentiated to be neurons.More Purkinje cells loss occurred in AD model mice than that in LZ-H and LZ-M groups(F=9.46,P=0.007;F=9.46,P=0.010).The LZ-H and LZ-M groups had more new neuron stem cells grown up in cerebellum.Electromicroscopic examination showed the hippocampal neurons in LZ-H and LZ-M group were integrated,the nuclear membrane was intact,and the mitochondria in the cytoplasm,endoplasmic reticulum,Golgi bodies,microtubules,and synapses were also complete.The microglial cell showed no abnormality.No toxicity appeared in the pathological specimens of mice treated with ganoderma lucidum preparation.Conclusion The ganoderma lucidum preparation can dissolve and decline or dismiss the senile plaques and neurofibrillar tangles in the brain of AD mice and also reduce the amyloid angiopathy.

REISHI Research: Brain

> Curr Issues Mol Biol. 2021 Jun 15;43(1):385-393. doi: 10.3390/cimb43010030.

Water Extract of Mixed Mushroom Mycelia Grown on a Solid Barley Medium Is Protective against Experimental Focal Cerebral Ischemia

Ji Heun Jeong [1], Shin Hye Kim [1], Mi Na Park [2], Jong Hoa Park [2], Hyun Young Park [3], Chan Eui Song [4], Ji Hyun Moon [1], Ah La Choi [1], Yo Duck Kim [1], Nam Seob Lee [1], Young Gil Jeong [1], Do Kyung Kim [1], Bong Ho Lee [5], Yung Choon Yoo [6], Seung Yun Han [1]

Affiliations + expand

PMID: 34203617 DOI: 10.3390/cimb43010030

Free article

Helps prevent damage from and repairs areas of focal blood loss

Phellinus linteus **(PL),** ***Ganoderma lucidum*** **(GL), and** ***Inonotus obliquus*** **(IO), mixed mushroom mycelia (MMM)**

Rats were subjected to a 90 min middle cerebral artery occlusion and reperfusion, after which a wMMM treatment resulted in significant dose-dependent improvements across a number of parameters.

Furthermore, measurements of intracellular ROS and levels of antioxidant enzymes revealed a **MMM-mediated ROS attenuation and antioxidant enzyme up regulation.**

We suggest that wMMM is neuroprotective against fCI through its **anti-apoptotic and anti-oxidative effects.**

Grifola frondosa

Maitake, hen of the woods, king of the mushrooms

Anti cancer & Immunomodulation: colon, skin, gastric, osteo, breast

- **induce hematopoietic cell differentiation**
- **protect those cells from the toxic effects exerted by chemotherapy**

Antibacterial

Hypoglycemic, blood sugar regulation, decreases insulin resistance

enhancing insulin sensitivity and ameliorating insulin resistance of peripheral target tissues

Polysaccharides can enhance glucose uptake by HepG2 cells, activate the insulin receptor protein in the cell membrane, and increase phosphorylated AktSer473 production, thereby relieving insulin resistance.

Anti-oxidant, lipid balancing, Skin benefits

Human dermal fibroblast experiments suggest that a G. frondosa extracellular polysaccharide (GF-EPS) can protect cells from hydroxyl **radical-induced DNA strand breaks, inhibit matrix metalloproteinase expression, stimulate fibroblasts proliferation, and prevent melanin formation.** In addition, GF-MPS can **stimulate the biosynthesis of collagen,** and was shown to increase the mRNA level of type I collagen in human dermal fibroblasts

Healthy aging & Fertility tonic

Hepatoprotective

down-regulation of expression of cytochrome P450 and TNF-, cell cycle arrest, decrease of the activities of aspartate aminotransferase and alanine aminotransferase, and inhibition of superoxide anion oxygen species and RO

Polysaccharides in *Grifola frondosa* mushroom and their health promoting properties: A review

Xinyu He [1,2], Xiaoxiao Wang [1], Jiacheng Fang [1], Yu Chang [1], Ning Ning [1], Hao Guo [1], Linhong Huang [1,*], Xiaoqiang Huang [1], Zefeng Zhao [1,*]

Submerged Production and Characterization of *Grifola frondosa* Polysaccharides – A New Application to Cosmeceuticals

*Sang Woo Kim[1], Hye Jin Hwang[1], Bum Chun Lee[2] and Jong Won Yun[1]**

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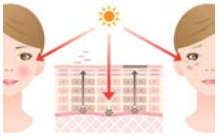
Received: May 30, 2006

Revised version: December 6, 2006

Accepted: December 9, 2006

Summary

Grifola frondosa (maitake) is traditionally called 'the king of mushrooms' and 'the hen of the woods'. Both the fruiting bodies and the mycelium of maitake have been reported to have antitumor and antiviral activities. Recently, submerged culture processes have been developed, with the intention of providing opportunities for increased economic exploitation of maitake. Commonly the aim of these processes is to produce extracellular polysaccharides (EPS), mostly glucans, and to explore their applications, particularly in the cosmetic industry. A wide variety of EPS with different molecular chain length and chemical compositions are produced under different culture conditions. In this article, various biological and physicochemical properties of the EPS of *G. frondosa* (GF-EPS) are described, with a view to applications in the area of functional cosmeceuticals. The GF-EPS, together with GF mycelial extract (GF-MPS), showed antioxidative activity, stimulation of collagen biosynthetic activity, cell proliferation activity, and inhibitory activity of melanogenesis, without significant cytotoxicity. These diverse functionalities suggest that both GF-EPS and GF-MPS can be promising cosmetic ingredients.



Key words: cosmetic ingredients, exopolysaccharide, glucan, *Grifola frondosa* (maitake), human dermal fibroblasts, matrix metalloproteinase, skin aging

Grifola & Memory

> Comparative Study > Mol Nutr Food Res. 2017 Nov;61(11). doi: 10.1002/mnfr.201700313. Epub 2017 Aug 29.

Oral administration of Grifola frondosa polysaccharides improves memory impairment in aged rats via antioxidant action

Zhaoxia Chen [1,2], Yanan Tang [1,2], Along Liu [1,2], Xiaobao Jin [1,2], Jiayong Zhu [1,2], Xuemei Lu [1,2]

Affiliations + expand

PMID: 28752930 DOI: 10.1002/mnfr.201700313

Methods and results: 20-month-old rats were gavaged with **Grifola frondosa polysaccharides (GFP) for 8 weeks.**

Morris **Water Maze test revealed that GFP administration significantly improved memory impairment in aged rats.**

GFP supply was also found to attenuate age-associated changes of brain histology and ultrastructure observed by light microscopy and transmission electron microscopy.

Moreover, the increase of **total antioxidant capacity (T-AOC), glutathione peroxidase (GPx) activity, superoxide dismutase (SOD) activity, catalase (CAT) activity, as well as the decreased nitric oxide (NO) and malondialdehyde (MDA) levels, were consistent with the behavioral results.**

Maitake for Memory & Learning

Int J Med Mushrooms. 2019;21(11):1065-1074. doi: 10.1615/IntJMedMushrooms.2019032914.

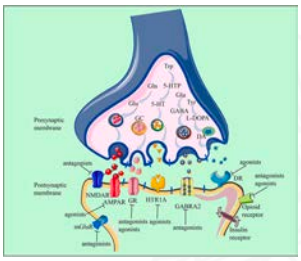
A Polysaccharide Extract from Maitake Culinary-Medicinal Mushroom, Grifola frondosa (Agaricomycetes) Ameliorates Learning and Memory Function in Aluminum Chloride-Induced Amnesia in Mice

In the current study, we aimed to explore the beneficial effect of PGM on learning and memory function in aluminum chloride (AlCl3)-induced amnesia in mice and to explore the underlying mechanisms. Mice were intraperitoneally administered with AlCl3 (60 mg/kg/d) and PGM (5, 10, or 20 mg/kg/d) for 6 weeks consecutively, and then the Morris water maze (MWM) test was conducted to assess the learning and memory function. Hematoxylin-eosin staining was performed to observe the morphology of neurons in the hippocampal dentate gyrus (DG). The expression of p-Tau (Ser396), Tau, p-GluA1 (S845), GluA1, and brain-derived neurotrophic factor (BDNF) proteins was evaluated with western blot.

We found that PGM (5 and 10 mg/kg/d) **significantly improved learning and memory function** and **attenuated histopathological abnormalities in the hippocampal DG region in the AlCl3-treated mice**.

Furthermore, **PGM treatment significantly enhanced the level of AMPAR and BDNF in the hippocampus, while suppressing the tau protein hyperphosphorylation at the Ser396 site. These findings indicated that PGM could significantly attenuate the AlCl3-induced amnesia through the synergistic action of its active component on tau pathology, AMPAR and BDNF signaling pathway.**

Maitake's Antidepressant action



Antidepressant action

Continual effect all five days (no tolerance developed)

No hyperactive side effects

Able to ID the Dectin-1 receptor as a main mechanism because medications that blocked that action, blunted the anti-depressant effect

Results lasted at least 3 days after treatment stopped

Proteo-β-glucan from Maitake (PGM) is a strong immune regulator, and its receptor is called Dectin-1. Cumulative evidence suggests that AMPA receptors are important for the treatment of depression. Here, we report that **PGM treatment leads to a significant antidepressant effect** in the tail suspension test and forced swim test after sixty minutes of treatment in mice. **After five consecutive days of PGM treatment, this antidepressant effect remained. PGM treatment did not show a hyperactive effect in the open field test**. PGM significantly enhanced the expression of its receptor Dectin-1, as well as p-GluA1(S845) and GluA1, but not GluA2 or GluA3 in the prefrontal cortex (PFC) after five days of treatment. **The Dectin-1 inhibitor Laminarin was able to block the antidepressant effect of PGM.** At the synapses of PFC, PGM treatment significantly up-regulated the p-GluA1(S845), GluA1, GluA2, and GluA3 levels. Moreover, PGM's **antidepressant effects and the increase of p-GluA1(S845)/GluA1 lasted for 3 days after stopping treatment.** The AMPA-specific antagonist GYKI 52466 was able to block the antidepressant effect of PGM. **This study identified PGM as a novel antidepressant with clinical potential and a new antidepressant mechanism for regulating prefrontal Dectin-1/AMPA receptor signalling.**

Lindsay Chimileski ND LAc RH(AHG)

The Prefrontal Dectin-1/AMPA Receptor Signaling Pathway Mediates The Robust and Prolonged Antidepressant Effect of Proteo-β-Glucan from Maitake

Hericium erinaceus

LIONS MANE

Hedgehog, monkey head

Trophorestorative

DEMENTIA, parkinson's, MS, NEUROPROTECTIVE

- **Used to treat nerve damage, neuropathy, wound healing**
- **Ability to stimulate the production of nerve growth factor (NGF) ****
- **Anxiety, menopause, MRSA**
- **Wound healing, skin, corneal and gastric ulcers, esophagus cancer**
- **Kills h.pylori, gram positive, gram negative bacteria**
- **Vast cancer research**
- **Super antioxidant= tx for diabetic neuropathies**
- **Lipid balancing, hepatoprotective, counteracts ischemia, antiHTN**

Hericinones and erinacines- strongly stimulate the synthesis of Nerve Growth Factor (NGF). NGF promotes neuron repair and renewal, including myelination. –Plays an essential role in the differentiation and survival of several cell populations in the central and peripheral nervous system.
–Lower than normal levels of NGF linked to early stages of Alzheimer's and dementia NFG also plays a much wider role in maintaining homoeostasis in the body

Cerebrosides: immune reg, anticancer, (some found in many mushrooms, some unique to lions mane)

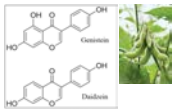
Cerebrosides are glycosphingolipids consisting of a ceramide and a single sugar residue at C-1, thus are usually named monohexosylceramides or ceramide monohexosides.[1] Structurally, ceramide has a long-chain sphin- gosine or sphingol and an amide-linked long-chain fatty acid, with the sugar moiety being either glucose or galactose.

Clinical trials dried fruiting body at a dose of 3-5g/day.
Chinese Phamacopoeia
Gastric ulcers: *daily 500mg/kg*, *which equals up to 25-50g/day*

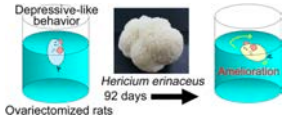
aromatic Hericenones : fruiting body
diterpenoid Erinacines : mycelium

****Critically these molecules are are low molecular weight compounds believed to be able to pass through the blood-brain barrier.****

phytoestrogens: including daidzein and genistein.



Ameliorating Effect of the Edible Mushroom Hericium erinaceus on Depressive-Like Behavior in Ovariectomized Rats



Abstract:

Estrogen deficiency during menopause causes a variety of neurological symptoms, including depression

The edible Lion's Mane mushroom, Hericium erinaceus (Bull.: Fr.) Pers. (HE), is a medicinal mushroom that has the potential for a neuroprotective effect and ameliorating neurological diseases, such as depression, anxiety, and neurodegenerative diseases.

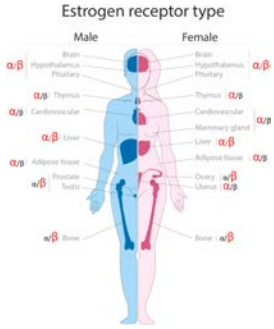
HE contains phytoestrogens, including daidzein and genistein. However, the ameliorating effect of HE on menopausal symptoms is not well understood. Here we investigated the impact of methanol extract of the HE fruiting body on depressive-like behavior in postmenopausal model rats.

Estrogen receptor alpha (ERα) activation causes body weight loss and uterine weight gain. [this was not seen with the Hericium]. Body weight gain and uterine weight loss by estrogen deficiency in ovariectomized (OVX) rats were reversed with 17β-estradiol (E2) but not with HE. Thus, the phytoestrogens in HE may hardly activate ERα .

Estrogen receptor beta (ERβ) is expressed in the brain, and activation of ERβ ameliorates menopausal depressive symptoms. Notably, depressive-like behavior in OVX rats evaluated in forced swim test was reduced by administration of not only E2 but also HE for 92 d. [this was seen with the Hericium].

Long-term activation of ERα increases the risk of breast and uterine cancers.

HE, therefore, may be effective in treating menopausal depression without the risk of carcinogenesis caused by ERα activation.



Estrogen receptor alpha (ERα) activation causes body weight loss and uterine weight gain.

Longterm activation increases risk of breast and uterine cancers.

Hericium does not seem to act on these very much

Estrogen receptor beta (ERβ) expressed in the brain, and activation of ERβ ameliorates menopausal depressive symptoms.

Hericium seemed to activate these

So it may be safer for tx menopausal symptoms without the same cancer risk

Hericium coralloides has corallocins a-c that induce nerve growth and brain derived neurotrophic factor just like lions mane!

Corallocins A–C, Nerve Growth and Brain-Derived Neurotrophic Factor Inducing Metabolites from the Mushroom Hericium coralloides

Kathrin Wittstein et al. J Nat Prod. 2016.

Show details | Full text links | Cite | ...

Abstract

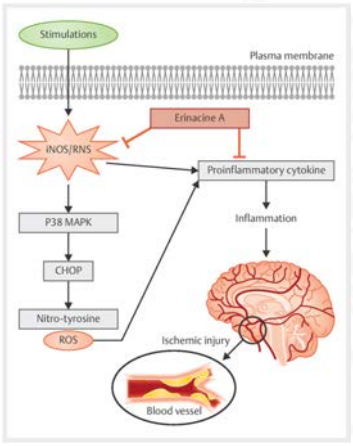
Three new natural products, corallocins A-C (1-3), along with two known compounds were isolated from the mushroom Hericium coralloides. Their benzofuranone and isoindolinone structures were elucidated by spectral methods. All corallocins induced nerve growth factor and/or brain-derived neurotrophic factor expression in human 1321N1 astrocytes. Furthermore, corallocin B showed antiproliferative activity against HUVEC and human cancer cell lines MCF-7 and KB-3-1.

Mushroom Medicine for Everyone.

Lindsay Chimileski ND LAc RH(AHG)

Constituents we care about

Mushroom Neurologically Bio-Active Compounds



Hericium erinaceus

Fig. 10 Schematic description of

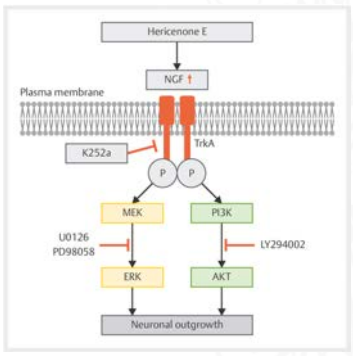
Erinacine A mediated antioxidative and anti-inflammatory activity in the intermittent ischemic brain injury.

An ischemic injury or stroke produces oxidative stress (ROS) that leads to the generation of nitric oxide, a mediator of protein nitrosylation, that leads to the phosphorylation of p38 MAPK and CHOP and the phosphorylated p38 MAPK/CHOP involved in the ER stress signaling pathway-mediated neuronal death. The oxidative damage of the brain also upregulates proinflammatory cytokines. **Erinacine A treatment reduced the levels of iNOS/RNS, phosphorylated p38 MAPK, CHOP, nitrotyrosine protein, and proinflammatory cytokines such as IL-1β, IL-6, and TNF-α in a stroke animal model.**

A Mechanistic Review on Medicinal Mushrooms–Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders
https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1177-4834

Constituents we care about

Mushroom Neurologically Bio-Active Compounds



Hericium erinaceus

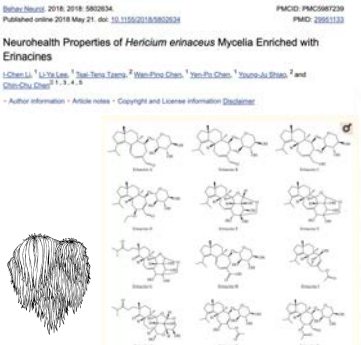
Fig. 11 The involvement of the PI3K/Akt and Erk1/2 signaling pathways in **Hericeone E** induced neuronal outgrowth. **The neuroprotective activity of hericenone E may mimic the action of the endogenous synthesized nerve growth factor that induced neuronal outgrowth by binding with the TrkA receptor, thereby either activating the ERK or PI3K/AKT signaling pathway.**

The involvement of PI3K/AKT or ERK in hericeone E (64)-induced neurite outgrowth was elucidated by use of a specific ERK (U0126 or PD98059) or PI3K class I inhibitor (LY294002), respectively, which abrogated the hericeone E (64)-induced neurite growth or neuritogenesis.|

A Mechanistic Review on Medicinal Mushrooms–Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders

https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1177-4834

Mushroom Medicine with Lindsay Chimileski ND LAc RH



Neurohealth Properties of *Hericium erinaceus* Mycelia Enriched with Erinacines

6. Conclusion

The evidence so far has shown that *H. erinaceus* mycelium enriched with its active compounds is capable of delaying neuronal cell death in rats with neurodegenerative diseases, such as ischemic stroke, Parkinson's disease, Alzheimer's disease, and depression. Moreover, results have indicated that administration of *H. erinaceus* mycelia enriched with its active compounds can promote functional recovery and enhance nerve regeneration in rats with neuropathic pain or prothyroxia. Despite that more clinical research is needed to fully understand the potential applications of erinacine-enriched *Hericium erinaceus* mycelium, the majority of preclinical data strongly suggests that it is safe and offers much-needed neuroprotective applications.

Table 1

Erinacines with biological activities demonstrated *in vitro* and *in vivo*.

Erinacines	Tests	Concentration	Biological activities	Reference
Erinacine A	*In vitro*	1 mM	Induced 250.1 ± 36.2 pg/ml NGF synthesis	[12]
	In vivo	30 mg/kg body weight/day	(1) Reduced amyloid burden by 38.1 ± 19.7% (2) Increased IDE levels by 141.1 ± 63.7%	[20]
	In vivo	1 mg/kg body weight/day	Inhibited DLD-1 tumor growth by 66%	[21]
	In vivo	30 mg/kg body weight/day	(1) Reduced both the size and number of amyloid plaques (2) Increased IDE levels by 303.5% (3) Recovered from impairments in burrowing, nesting, and Morris water maze tasks	[22]
Erinacine B	*In vitro*	1 mM	Induced 129.7 ± 6.5 pg/ml NGF synthesis	[12]
Erinacine C	*In vitro*	1 mM	Induced 299.1 ± 59.6 pg/ml NGF synthesis	[12]
Erinacine D	*In vitro*	1.67 mM	Induced 141.5 ± 18.2 pg/ml NGF synthesis	[14]
Erinacine E	*In vitro*	5 mM	Induced 105.0 ± 5.2 pg/ml NGF synthesis	[13]
	In vitro	IC_{50}	Binding inhibitor for κ-opioid receptor at 0.8 μM	[23]
Erinacine F	*In vitro*	5 mM	Induced 175.0 ± 5.2 pg/ml NGF synthesis	[13]
Erinacine H	*In vitro*	70.8 mM	Induced 31.5 ± 1.7 pg/ml NGF synthesis	[15]
Erinacine S	*In vivo*	30 mg/kg body weight/day	(1) Reduced amyloid burden by 40.2 ± 15.2% (2) Increased IDE levels by 130.5 ± 68.9%	[20]
	In vivo	30 mg/kg body weight/day	(1) Reduced the size of amyloid plaques (2) Increased IDE levels by 269.8% (3) Recovered from impairments in burrowing, nesting, and Morris water maze tasks	[22]

Mushroom medicine

Lions Mane- Antidepressant & Anti-Anxiety

Biomed Res. 2010 Aug;31(4):231-7.

Reduction of depression and anxiety by 4 weeks Hericium erinaceus intake.

Nagano M[1], Shimizu K, Kondo R, Hayashi C, Sato D, Kitagawa K, Ohnuki K.

Author information

1 Department of Clinical Psychology, Kyoto Bunkyo University, Kyoto, Japan.

Abstract

Hericium erinaceus, a well known edible mushroom, has numerous biological activities. Especially hericenones and erinacines isolated from its fruiting body stimulate nerve growth factor (NGF) synthesis, which expects H. erinaceus to have some effects on brain functions and autonomic nervous system. Herein, we investigated the clinical effects of H. erinaceus on menopause, depression, sleep quality and indefinite complaints, using the Kupperman Menopausal Index (KMI), the Center for Epidemiologic Studies Depression Scale (CES-D), the Pittsburgh Sleep Quality Index (PSQI), and the Indefinite Complaints Index (ICI). Thirty females were randomly assigned to either the H. erinaceus (HE) group or the placebo group and took HE cookies or placebo cookies for 4 weeks. Each of the CES-D and the ICI score after the HE intake was significantly lower than that before. In two terms of the ICI, "insentive" and "palpitatio", each of the mean score of the HE group was significantly lower than the placebo group. "Concentration", "irritating" and "anxious" tended to be lower than the placebo group. Our results show that HE intake has the possibility to reduce depression and anxiety and these results suggest a different mechanism from NGF-enhancing action of H. erinaceus.

PMID: 20834180

30 women going through menopause
Hericium 0.5g fruiting body powder or placebo cookies for 4 weeks
Improved Symptoms- less depression, insensitivity, anxiety, frustration, and palpitations than those taking placebo

Mushroom Medicine for Everyone.

Lindsay Chimileski ND LAc RH(AHG)

Lions Mane-Neuron Inflammation moderator

Antioxidants (Basel). 2019 Aug 1;8(8). pii: E261. doi: 10.3390/antiox8080261.

Lion's Mane Mushroom, *Hericium erinaceus* (Bull.: Fr.) Pers. Suppresses H_2O_2-Induced Oxidative Damage and LPS-Induced Inflammation in HT22 Hippocampal Neurons and BV2 Microglia.

Kushairi N[1,2], Phan CW[1,3], Sabaratnam V[1], Davis P[4,5], Naidu M[1,2].

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2 Department of Anatomy, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia.
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5 Department of Anatomy, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia. rosiepamela@um.edu.my.

Abstract

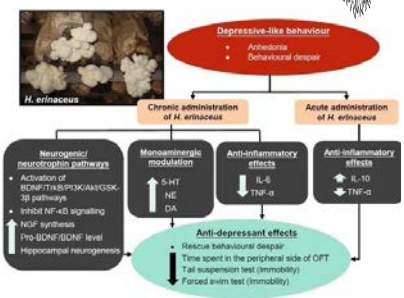
Oxidative stress and inflammation in neuron-glia system are key factors in the pathogenesis of neurodegenerative diseases. As synthetic drugs may cause side effects, natural products have gained recognition for the prevention or management of diseases. In this study, hot water (HE-HWA) and ethanolic (HE-ETH) extracts of the basidiocarps of *Hericium erinaceus* mushroom were investigated for their neuroprotective and anti-inflammatory activities against hydrogen peroxide (H_2O_2)-induced neurotoxicity in HT22 mouse hippocampal neurons and lipopolysaccharide (LPS)-induced BV2 microglial activation respectively. HE-ETH showed potent neuroprotective activity by significantly ($p < 0.0001$) increasing the viability of H_2O_2-treated neurons. This was accompanied by significant reduction in reactive oxygen species (ROS) ($p < 0.05$) and improvement of the antioxidant enzyme catalase (CAT) ($p < 0.05$) and glutathione (GSH) content ($p < 0.01$). Besides, HE-ETH significantly improved mitochondrial membrane potential (MMP) ($p < 0.05$) and ATP production ($p < 0.0001$) while reducing mitochondrial toxicity ($p < 0.001$), Bcl-2-associated X (Bax) gene expression ($p < 0.05$) and nuclear apoptosis ($p < 0.0001$). However, gene expression of Nuclear factor erythroid 2-related factor 2 (Nrf2), heme oxygenase 1 (HO-1) and NAD(P)H quinone dehydrogenase 1 (NQO1) were unaffected ($p > 0.05$). HE-ETH also significantly ($p < 0.0001$) reduced nitric oxide (NO) level in LPS-treated BV2 indicating an anti-inflammatory activity in the microglia. These findings demonstrated HE-ETH maybe a potential neuroprotective and anti-inflammatory agent in neuron-glia environment.

KEYWORDS: Hericium erinaceus; anti-inflammation; anticoxidants; mushroom; neuroprotection

Mushroom medicine

Lindsay Chimileski ND Lac RH

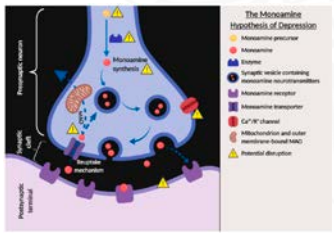
Lions Mane- Antidepressant Action

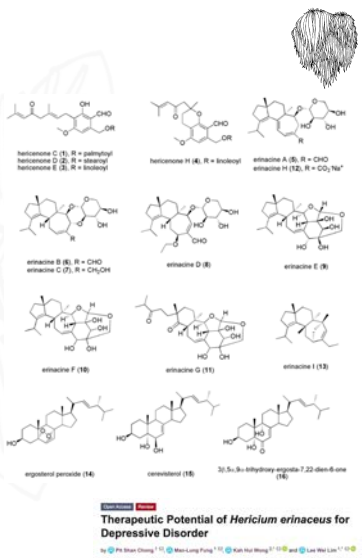


Therapeutic Potential of *Hericium erinaceus* for Depressive Disorder

Lions Mane- Antidepressant Action

Lions mane also targets:
Neurotrophic/Neurogenic Hypothesis and Inflammatory Hypothesis

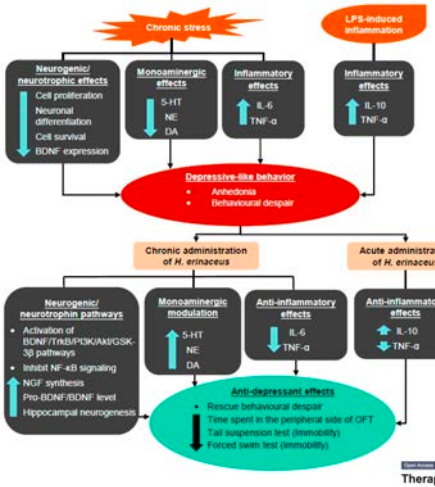




Therapeutic Potential of *Hericium erinaceus* for Depressive Disorder

Mushroom Medicine with Lindsay Chimileski ND LAc RH

Lions Mane- Antidepressant Action



Therapeutic Potential of *Hericium erinaceus* for Depressive Disorder

Lions Mane- Mood, Sleep & Obesity

Evid Based Complement Alternat Med. 2019 Apr 18;2019:7861297. doi: 10.1155/2019/7861297. eCollection 2019.

***Hericium erinaceus* Improves Mood and Sleep Disorders in Patients Affected by Overweight or Obesity: Could Circulating Pro-BDNF and BDNF Be Potential Biomarkers?**

Luisella Vigna [1], Federica Morelli [1], Gianna M Agnelli [1], Filomena Napolitano [2], Daniela Ratto [3], Alessandra Occhinegro [3], Carmine Di Iorio [3], Elena Savino [4], Carolina Gironetta [4], Federico Brandalise [4], Paola Rossi [3]

Affiliations + expand

PMID: 31118969 PMCID: PMC6500611 DOI: 10.1155/2019/7861297

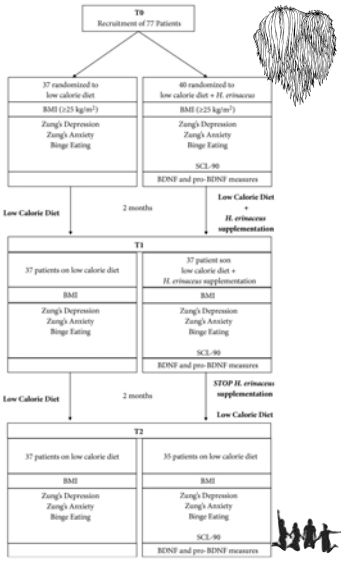
Free PMC article

Abstract

Epidemiological data indicate that subjects affected by obesity have an increased risk of developing mood disorders. The relationship between obesity and mood disorders is bidirectional. We assessed whether a Hericium erinaceus treatment improved depression, anxiety, sleep, and binge eating disorders after 8 weeks of supplementation in subjects affected by overweight or obesity under a low calorie diet regimen. Looking for a possible clinical biomarker, we assessed the serum balance between brain-derived neurotrophic factor (BDNF) and its precursor pro-BDNF before and after H. erinaceus supplementation. Seventy-seven volunteers affected by overweight or obesity were recruited at the offices of the Department of Preventive Medicine, Luigi Devoto Clinic of Work, Obesity Centre, at the RCCS Foundation Policlinico Hospital of Milan (Italy). Patients were recruited only if they had a mood and/or sleep disorder and/or were binge eating as evaluated through self-assessment questionnaires. We used two different enzyme-linked immunosorbent assays kits to discriminate circulating levels of pro-BDNF and BDNF. Eight weeks of oral H. erinaceus supplementation decreased depression, anxiety, and sleep disorders. H. erinaceus supplementation improved mood disorders of a depressive-anxious nature and the quality of the nocturnal rest. H. erinaceus increased circulating pro-BDNF levels without any significant change in BDNF circulating levels.

8 weeks of oral *H. erinaceus* supplementation decreased depression, anxiety, and sleep disorders. *H. erinaceus* supplementation improved mood disorders of a depressive-anxious nature and the quality of the nocturnal rest. *H. erinaceus* increased circulating pro-BDNF levels without any significant change in BDNF circulating levels.

brain-derived neurotrophic factor (BDNF) and its precursor pro-BDNF



Lions Mane- Mood, Sleep & Obesity

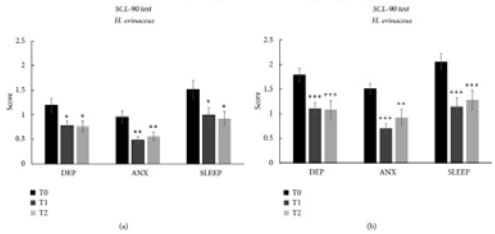
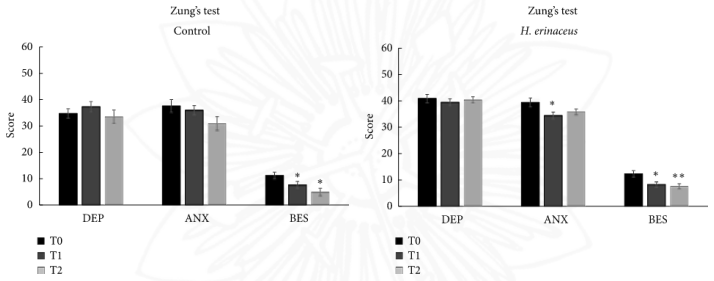


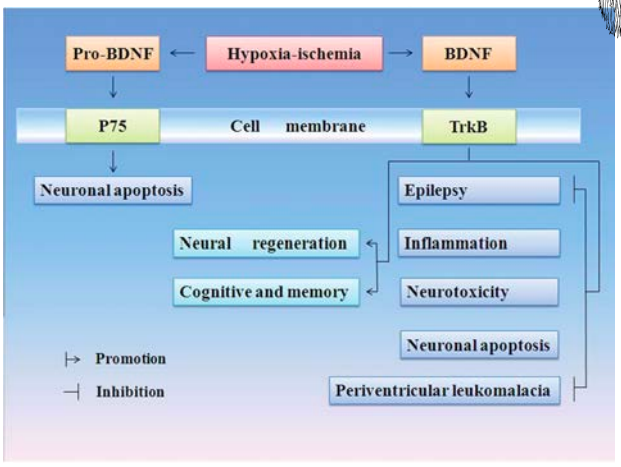
Figure 3 (a) Mean score values ± SEM obtained by means of SCL-90 in *H. erinaceus* group before (T0), after (T1), and in *H. erinaceus* wash-out condition (T2) in (DEP), anxiety (ANX), and sleep disorders (SLEEP). (b) Patients selected for symptomatology before (T0), after (T1), and in *H. erinaceus* wash-out condition (T2). The ∗p<0.05 and ∗∗p<0.01 obtained by the comparison versus T0 (according one-way ANOVA, Tukey post hoc test). The comparison of values between T1 and T2 does not show any statistically significant differences.

Lions Mane- Mood, Sleep & Obesity



Mean values ± SEM of Zung's depression (DEP), Zung's anxiety (ANX), and binge eating scale (BES) tested by self-evaluation: (a) control and (b) *H. erinaceus* groups before (T0), after (T1), and in *H. erinaceus*. (c) Patients in control condition selected for symptomatology in T0, T1, and T2. (d) Patients selected for symptomatology before (T0), after (T1), and in *H. erinaceus* wash-out condition (T2). p<0.05 and p<0.01 were obtained by the comparison versus T0 in any experimental group (according to two-way ANOVA). The comparison of values between T1 and T2 does not show any statistically significant differences.

Lions Mane- Mood, Sleep & Obesity



Lions Mane- Mood, Sleep & Obesity

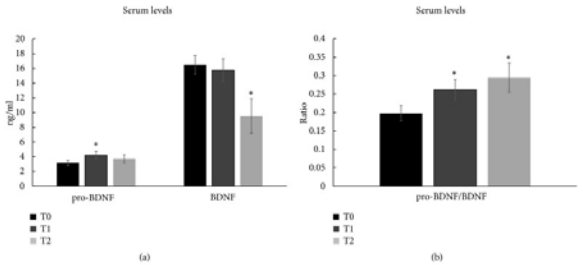


Figure 5 (a) Pro-BDNF, BDNF, and (b) pro-BDNF/BDNF ratio serum levels ± SEM in patients treated with *H. erinaceus* at T0, T1, *and* T2. ∗p<0.05 indicates significant differences between different time versus T0 tested by paired Student's t-test. The comparison of values between T1 and T2 does not show any statistically significant differences.

Randomized Controlled Trial | Phytother Res. 2009 Mar;23(3):367-72. doi: 10.1002/ptr.2634.

Improving effects of the mushroom Yamabushitake (Hericium erinaceus) on mild cognitive impairment: a double-blind placebo-controlled clinical trial

Koichiro Mori [1], Satoshi Inatomi, Kenzi Ouchi, Yoshihito Azumi, Takashi Tuchida

Affiliations + expand

PMID: 18844328 DOI: 10.1002/ptr.2634

Abstract

A double-blind, parallel-group, placebo-controlled trial was performed on 50- to 80-year-old Japanese men and women diagnosed with mild cognitive impairment in order to examine the efficacy of oral administration of Yamabushitake (Hericium erinaceus), an edible mushroom, for improving cognitive impairment, using a cognitive function scale based on the Revised Hasegawa Dementia Scale (HDS-R). After 2 weeks of preliminary examination, 30 subjects were randomized into two 15-person groups, one of which was given Yamabushitake and the other given a placebo. The subjects of the Yamabushitake group took four 250 mg tablets containing 96% of Yamabushitake dry powder three times a day for 16 weeks. After termination of the intake, the subjects were observed for the next 4 weeks. At weeks 8, 12 and 16 of the trial, the Yamabushitake group showed significantly increased scores on the cognitive function scale compared with the placebo group. The Yamabushitake group's scores increased with the duration of intake, but at week 4 after the termination of the 16 weeks intake, the scores decreased significantly. Laboratory tests showed no adverse effect of Yamabushitake. The results obtained in this study suggest that Yamabushitake is effective in improving mild cognitive impairment.

(c) 2008 John Wiley & Sons, Ltd.

Lions Mane & Cognitive Health

A double-blind, parallel-group, placebo-controlled trial

50- to 80-year-old Japanese men and women diagnosed with mild cognitive impairment

using a cognitive function scale

30 subjects were randomized into two 15-person groups, one of which was given Yamabushitake and the other given a placebo.

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Laboratory tests showed no adverse effect of Yamabushitake. The results obtained in this study suggest that Yamabushitake is effective in improving mild cognitive impairment.

Lindsay Chimileski ND LAc RH(AHG)

> Fiziol Zh. 2003;49(1):38-45.

The influence of Hericium erinaceus extract on myelination process in vitro

E V Kolotushkina [1], M G Moldavan, K Yu Voronin, G G Skibo

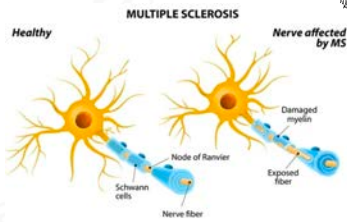
Affiliations + expand

PMID: 12675022

44 Cite

Abstract

Myelin sheaths, wrapping axons, perform the following important functions: support, protection, feeding and isolation. Injury of myelin compact structure leads to an impairment and severe illness of the nerve system. Exact mechanisms underlying the myelination process and myelin sheaths' damage have not established yet. Therefore search for substances, which provide regulatory and protective effects on the normal myelination as well as stimulating action on the remyelination after myelin damage, is of special interest. Recently it was shown that extract from mushroom Hericium erinaceus had activating action on the nerve tissue. So the aim of the present work was to study an influence of an extract from H. erinaceus on the cerebellar cells and the process of myelination in



Obtained data revealed the normal growth of the nerve and glial cells with extract at cultivating.
No pathologic or toxic action of the extract has been found.
The cell ultrastructure was intact and similar to that observed in vivo.
The process of myelination in the presence of the extract began earlier as compared to controls and was characterised by a higher rate.
Thus, extract of H. erinaceus promoted normal development of cultivated cerebellar cells and demonstrated a regulatory effect on the process of myelin genesis process in vitro.

Mushroom Medicine with Lindsay Chimileski ND LAc RH

Abstract: Lion's Mane Mushroom Study

Study Methods

We conducted an acute randomized, placebo-controlled, double-blinded, cross-over intervention study using *H. erinaceus* fruiting body extract (3g of 10:1 extract). **Eighteen healthy participants aged 18-35 completed cognitive and mood assessments at baseline and 90 minutes post-consumption.**

Results

No significant effect was observed for composite measures of global cognitive function and mood. However, **participants exhibited improved performance specifically on the pegboard test at 90 minutes following a single dose of *H. erinaceus*.**

Conclusion & Future Research

Acute consumption showed no significant overall improvement in cognitive performance. Future research should investigate chronic supplementation effects, optimal dosage, time to peak concentration of bioactives, and potential mechanisms of action.

Surendran G, Saye J, Binti Mohd Jalil S, Spreadborough J, Duong K, Shatwan IM, Lilley D, Heinrich M, Dodd GF, Surendran S. Acute effects of a standardised extract of *Hericium erinaceus* (Lion's Mane mushroom) on cognition and mood in healthy younger adults: a double-blind randomised placebo-controlled study. Front Nutr. 2025 Apr 10;12:1405796. doi: 10.3389/fnut.2025.1405796. PMID: 40276537; PMCID: PMC12018234.

Inonotus obliquus

Chaga

Antioxidant,
Antineurodegenerative
Adaptogen, Endurance
Immunomodulation
Cancer research
Blood sugar regulation

Triterpenoids
Inotodiol
Trametonolic acid
Betulinic acid

Melanin

vitamin B2, vitamin D, calcium, iron, magnesium, phosphorus, manganese

sclerotium

MANY cancer modulating actions- antitumor, anti-mutagenic, antiviral, immunomodulating, allergy lowering
In vitro, animal studies mostly, some human trials- colon cancers hepatomas, *selective apoptosis in tumor cells with no effects on healthy cells* reduced toxicity associated with radiation, and inhibited melanoma cell growth in animal models
Anti-diabetic and blood sugar balancing actions
Immune system focused adaptogen– for those who catch viruses when run down, ie. Cold sores etc
Analgesic, Anti-inflammatory and pain-relieving properties
Reduced oxidative stress in lymphocytes from patients with inflammatory bowel disease.
Cognition-enhancing and antioxidant activities
Increased exercise endurance and biological measures related to fatigue
CAUTIONS: May interact with anticoagulant and anti-diabetic drugs. High in oxalates and excessive intake may have toxic effects because of this- kidney stones, bladder sensitivity and spasms.

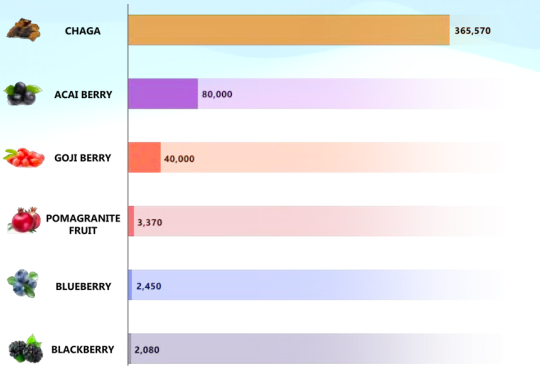
Medicinal Mushrooms Lindsay Chimileski ND LAc RH(AHG)

Grows predominantly on birch trees, but may also be found on ash, elm, beech, alder

CHAGA

Chaga has the highest ORAC score ever recorded in any natural food! 6.5 times more than Acai berry.

O.R.A.C.
Oxygen Radical Absorbance Capacity
Antioxidant Level



dr lindsay chimileski
THE BOTANICAL SOUTH

Chaga, Memory & Learning

Mouse study
Mice given amnesia with scopolamine then treated with chaga extract
Showed improvements in memory and learning
Decreased oxidative stress, increased SOD and glutathione
Inhibits excess Acetylcholine esterase (the enzyme that breaks it down) to increase/balance acetylcholine levels.

> Food Funct. 2011 Jun;2(6):320-7. doi: 10.1039/c1fo10037h. Epub 2011 Jun 6.

Amelioration of scopolamine induced cognitive dysfunction and oxidative stress by Inonotus obliquus – a medicinal mushroom

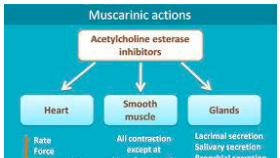
Vijayasree Vayalanekore Giridharan [1], Rajarajan Amirthalingam Thandavarayan, Tetsuya Konishi

Affiliations + expand

PMID: 21779570 DOI: 10.1039/c1fo10037h

Abstract

The present study was aimed to investigate the cognitive enhancing and anti-oxidant activities of Inonotus obliquus (Chaga) against scopolamine-induced experimental amnesia. Methanolic extract of Chaga (MEC) at 50 and 100 mg kg (-1)doses were administered orally for 7 days to amnesic mice. Learning and memory was assessed by passive avoidance task (PAT) and Morris water maze (MWM) test. Tacrine (THA, 10 mg kg (-1), orally (p.o)) used as a reference drug. To elucidate the mechanism of the cognitive enhancing activity of MEC, the activities of acetylcholinesterase (AChE), anti-oxidant enzymes, the levels of acetylcholine (ACh) and nitrite of mice brain homogenates were evaluated. MEC treatment for 7 days significantly improved the learning and memory as measured by PAT and MWM paradigms. Further, MEC significantly reduced the oxidative-nitritive stress, as evidenced by a decrease in malondialdehyde and nitrite levels and restored the glutathione and superoxide dismutase levels in a dose dependent manner. In addition, MEC treatment significantly decreased the AChE activity in both the salt and detergent-soluble fraction of brain homogenates. Further, treatment with MEC restored the levels of ACh as did THA. Thus, the significant cognitive enhancement observed in mice after MEC administration is closely related to higher brain anti-oxidant properties and inhibition of AChE activity. These findings stress the critical impact of Chaga, a medicinal mushroom, on the higher brain functions like learning and memory.



- **Acetylcholine is used all throughout the brain and body, huge impact on functionality and mental health**
- **Paying attention, memory, learning, spatial awareness, arousal.**
- **Acetylcholine binds to receptors on the muscle fiber to cause contraction.**
- **Depletion is associated with Alzheimer's,**
- **specifically loss of AchE enzyme**

Mushroom Medicine for Everyone.

Lindsay Chimileski ND LAc RH(AHG)

Review > Appl Biochem Biotechnol. 2021 Dec;193(12):4197-4213.
doi: 10.1007/s12010-021-03670-1. Epub 2021 Sep 15.

Recent Advances on Bioactive Ingredients of Morchella esculenta

Haishan Wu [1], Jing Chen [2 3], Jingjiet Li [4], Yuting Liu [1], Hyun Jin Park [5], Liu Yang [6]

Affiliations + expand
PMID: 34524632 DOI: 10.1007/s12010-021-03670-1

Yellow Morel
Morchella esculenta

Bioactive ingredients:
Polysaccharides
Polyphenolic compounds
Proteins, and protein hydrolysates
Triterpenoids

Morchella esculenta polysaccharides (MEP) possess multiple bioactivities such as antioxidant, anti-inflammation, immunoregulation, hypoglycemic activity, atherosclerosis prevention and antitumor ability.

The substances extracted from both natural collected and submerged fermented M. esculenta are promising for antioxidants, immunomodulation, anti-cancer and anti-inflammatory applications.

> Molecules. 2021 Mar 8;26(5):1459. doi: 10.3390/molecules26051459.

Isolation, Characterization, and Medicinal Potential of Polysaccharides of *Morchella esculenta*

Syed Lal Badshah [1], Anila Riaz [1], Akhtar Muhammad [1], Gülsen Tel Çayan [2], Fatih Çayan [2], Mehmet Emin Duru [2], Nasir Ahmad [3], Abdul-Hamid Emwas [4], Mariusz Jaremko [4]

Affiliations + expand
PMID: 33800212 PMCID: PMC7962536 DOI: 10.3390/molecules26051459
Free PMC article

Abstract

Mushroom polysaccharides are active medicinal compounds that possess immune-modulatory and anticancer properties. Currently, the mushroom polysaccharides krestin, lentinan, and polysaccharopeptides are used as anticancer drugs. They are an unexplored source of natural products with huge potential in both the medicinal and nutraceutical industries. The northern parts of Pakistan have a rich biodiversity of mushrooms that grow during different seasons of the year. Here we selected an edible Morchella esculenta (true morels) of the Ascomycota group for polysaccharide isolation and characterization. Polysaccharopeptides and polysaccharides from this mushroom were isolated using the green chemistry, hot water treatment method. Fourier transform infrared spectroscopy revealed the sugar nature and possible beta-glucan type structure of these polysaccharides. Antioxidant assays showed that the deproteinized polysaccharides have moderate free radical scavenging activity. These isolated polysaccharides exhibited good acetylcholinesterase (AChE) and butyryl cholinesterase (BChE) inhibition activities. Therefore, these polysaccharides may be valuable for the treatment of Alzheimer's and Parkinson's diseases. Further bioassays are needed to discover the true potential of M. esculenta polysaccharides for medicinal purposes.

Keywords: Morchella esculenta; anticholinesterase activity; antioxidant; polysaccharopeptides; tyrosinase inhibition.

Morels & Alzheimer's & Parkinson's Prevention

Antioxidants
Polysaccharopeptides
Beta glucans
AChE inhibitor
–> Alzheimer's Parkinson's dementia Prevention potential

Multiple Sclerosis & Phellinus igniarius

Biomed Res Int. 2014; 2014: 218274. PMCID: PMC3922003
Published online 2014 Jan 27. doi: 10.1155/2014/218274 PMID: 24592383

A Mushroom Extract Piwep from *Phellinus igniarius* Ameliorates Experimental Autoimmune Encephalomyelitis by Inhibiting Immune Cell Infiltration in the Spinal Cord

Lan Li, [1] Guang Wu, [2] Bo Young Choi, [3] Bong Geom Jang, [2] Jin Hee Kim, [2] Gi Ho Sung, [2] Jae Youl Cho, [4] Sang Won Suh, [2,*] and Hyoung Jin Park [1,2,*]

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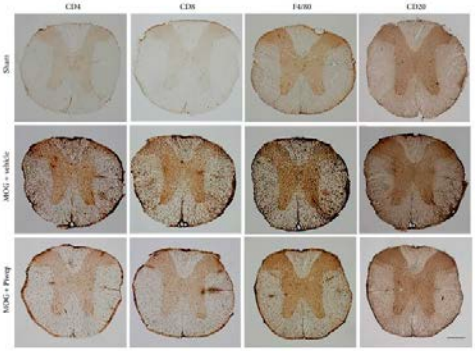
This article has been cited by other articles in PMC.

Abstract Go to: +

The present study aimed to evaluate the therapeutic potential of a mushroom extract from *Phellinus igniarius* in an animal model of multiple sclerosis. The medicinal mushroom, *Phellinus igniarius*, contains biologically active compounds that modulate the human immune system. Experimental autoimmune encephalomyelitis (EAE) was induced by immunization with myelin oligodendrocyte glycoprotein (MOG 35–55) in C57BL/6 female mice. A water-ethanol extract of *Phellinus igniarius* (Piwep) was delivered intraperitoneally every other day for the entire experimental course. Three weeks after the initial immunization, demyelination and immune cell infiltration in the spinal cord were examined. Piwep injection profoundly decreased the daily incidence rate and clinical score of EAE. The Piwep-mediated inhibition of the clinical course of EAE was accompanied by suppression of demyelination and infiltration of encephalitogenic immune cells including CD4+ T cells, CD8+ T cells, macrophages, and B cells in the spinal cord. Piwep reduced expression of vascular cell adhesion molecule-1 (VCAM-1) in the spinal cord and integrin-α_4 in the lymph node of EAE mice. Piwep also inhibited proliferation of lymphocytes and secretion of interferon-γ in the lymph node of EAE mice. The results suggest that a mushroom extract, Piwep, may have a high therapeutic potential for ameliorating multiple sclerosis progression.

"meshima" translates to "women's island"
in Japanese as it supports women's health
black hoof mushroom, Conk Mushroom

Multiple Sclerosis & Phellinus igniarius



Sham

Control
Just MOG myelin oligodendrocyte glycoprotein

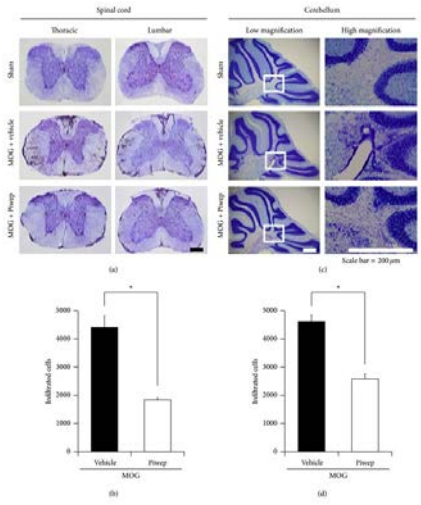
MOG and Piwep
water-ethanol extract of *Phellinus igniarius*

Piwep treatment attenuates EAE-induced immune cell infiltration into white matter of spinal cord in mice. PFA fixed sections of the thoracic spinal cord were immunohistochemically stained with antibodies against cell surface molecules such as CD4, CD8, F4/80, and CD20. Immunostaining revealed that T cell, B cell, and microglia/ macrophage labeled cells extensively infiltrated the white matter of EAE mice (MOG + vehicle). However, Piwep treatment reduced the infiltration of immune cells into the white matter of the spinal cords in EAE mice (MOG + Piwep). Scale bar represents 100 μm.

Biomed Res Int. 2014; 2014: 218274.
Published online 2014 Jan 27. doi: 10.1155/2014/218274

Clear, visible differences in autoimmune cell infiltration/ staining/ inflammation – Much less in those with Phellinus

Multiple Sclerosis & Phellinus igniarius



Poria cocos & Alzheimer's

> Neuroreport. 2021 May 19;32(8):727-737. doi: 10.1097/WNR.0000000000001648.

Poria cocos polysaccharide attenuates damage of nervus in Alzheimer's disease rat model induced by D-galactose and aluminum trichloride

Xibin Zhou [1], Yuxing Zhang, Yiqian Jiang, Chunxiang Zhou, Yun Ling

Affiliations + expand
PMID: 33913927 DOI: 10.1097/WNR.0000000000001648

Abstract

Poria cocos polysaccharide (PCP) is a compound from Poria cocos, and which is used as a classical tonic agent. This article aims to investigate the effects of PCP on neuronal damage of hippocampus and cognitive function in a rat model of Alzheimer's disease induced by D-galactose and aluminum trichloride. Oxiracetam (ORC) was used as a positive drug in this experiment. The rats were treated with PCP at doses of 100, 200 and 300 mg/kg/day for 30 days and ORC at dose of 346 mg/kg/day after modeling. The results of behavioral test showed that PCP could prevent cognitive decline in Alzheimer's disease rats as assessed by Y-maze test and Morris water maze test. Results of hippocampus slices showed that neurons were integrated and regularly arranged in the groups, which were administered along with PCP. Moreover, PCP could reduce neuronal apoptosis in hippocampus of Alzheimer's disease rats. Furthermore, the activities of superoxide dismutase in the hippocampus were elevated by PCP administration, while acetyl cholinesterase, reactive oxygen, malondialdehyde and inflammatory factors levels were reduced. In addition, we found PCP could attenuate MAPK/NF-κB signal pathway in the hippocampus. All results illustrated that PCP could exert neuroprotective effects at least partly through alleviating oxidative stress, apoptosis, inflammation and inhibiting the MAPK/NF-κB pathway in Alzheimer's disease rats induced by D-galactose and aluminum trichloride.

Poria Anti-Amnesia

J Ethnopharmacol. 2020 Aug 10;258:112566. doi: 10.1016/j.jep.2020.112566. Epub 2020 Jan 9.

Poria cocos water extract ameliorates the behavioral deficits induced by unpredictable chronic mild stress in rats by down-regulating inflammation

Yun-Ju Huang [1], Nai-Yuan Hsu [1], Kuan-Hung Lu [1], Yu-En Lin [1], Shih-Hang Lin [1], Yun-Sheng Lu [2], Wei-Ting Liu [2], Mei-Hsing Chen [3], Lee-Yan Sheen [4]

Affiliations + expand

PMID: 31926986 DOI: 10.1016/j.jep.2020.112566

Abstract

Ethnopharmacological relevance: Poria cocos is a medicinal mushroom of the Polyporaceae family with antioxidant and anti-inflammatory activities, which has been used for its sedative, diuretic and tonic effects in traditional medicine for several hundred years.

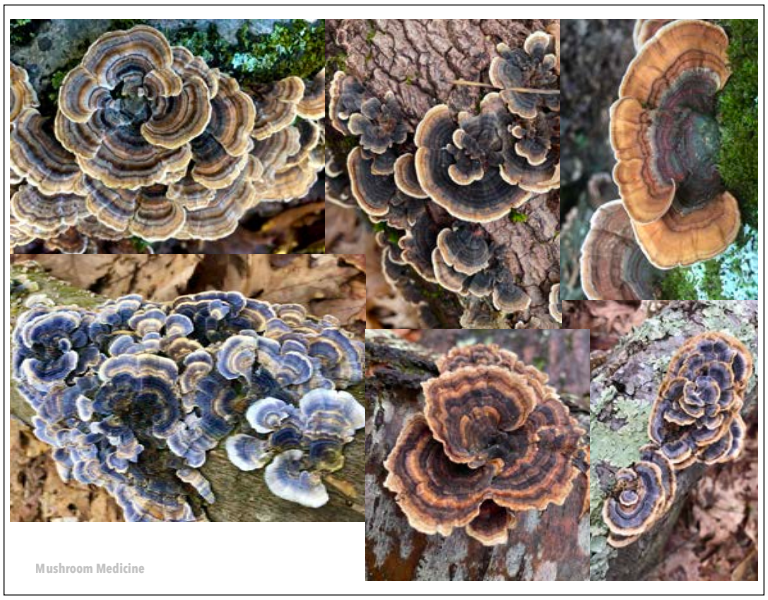
Aim of study: Considering that depression is an inflammatory related mental disease, this study investigated the antidepressant-like effects of water extract of P. cocos in a rodent animal model.

Materials and methods: Rats that were exposed to a forced swimming test (FST) for 28 consecutive days, and unpredictable chronic mild stress (UCMS) for five weeks underwent treatment with P. cocos water extract (PCW) (doses: 100, 300 and 900 mg/kg body weight [bw]; administered by gavage). Dopamine (DA), serotonin (5-HT) and their metabolites in the frontal cortex of rats were measured.

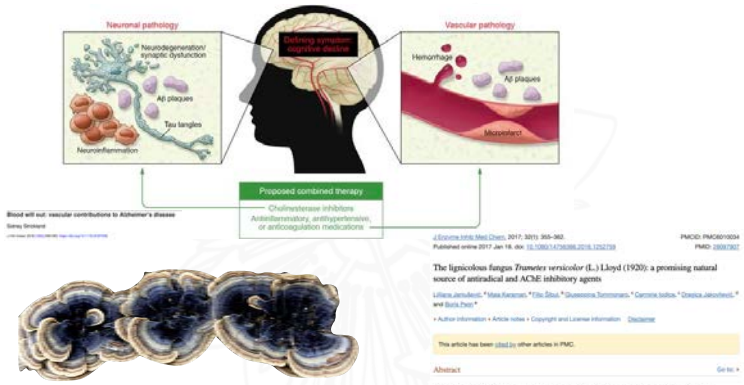
Results: Our results firstly showed that sucrose preference during the UCMS-paradigm was increased and immobility time in the FST was reduced with administration of PCW. In addition, PCW significantly attenuated UCMS-induced turnover rate of DA and 5-HT in the frontal cortex. Moreover, PCW inhibited UCMS-induced activated inflammatory response, reflected by reduced expression in the frontal cortex of p38, NF-κB and TNF-α.

Conclusions: Our results strongly suggest that PCW exhibits a potent antidepressant-like effect via regulation of monoaminergic neurotransmission and inactivation of inflammation, and that P. cocos may be considered as a traditional herbal potential medicine for the treatment of depression.

Keywords: Antidepressant-like effects; Forced swimming test; Monoamine; Poria cocos; Unpredictable chronic mild stress.



Turkey Tails & Alzheimer's



Blood will out: vascular contributions to Alzheimer's disease

Cholinesterase inhibition (like Donepezil)
High in antioxidants, free radical scavenging activity
Flavonoids like baicalin and quercetin

J Enzyme Inhib Med Chem. 2017; 32(1): 355–362. PMCID: PMC6010034
Published online 2017 Jan 18. doi: 10.1080/14756366.2016.1252759 PMID: 28097907

The lignicolous fungus *Trametes versicolor* (L.) Lloyd (1920): a promising natural source of antiradical and AChE inhibitory agents

Liliana Jamuđević, Maja Karaman, Filip Šibul, Giuseppina Tommonaro, Carmine Iodice, Dragica Jakovljević, and Boris Pavlović

Abstract

This study aimed to determine antiradical (DPPH• and •OH) and acetylcholinesterase (AChE) inhibitory activities along with chemical composition of autochtonous fungal species *Trametes versicolor* (Serbia). A total of 38 phenolic compounds with notable presence of phenolic acids were identified using HPLC/MS-MS. Its water extract exhibited the highest antiradical activity against •OH (3.21 μg/mL), among the rest due to the presence of gallic, *p*-coumaric and caffeic acids. At the concentration of 100 μg/mL, the same extract displayed a profound AChE inhibitory activity (80.53%) *in liquid*, compared to donepezil (89.05%), a drug in clinical practice used as positive control. The flavonoids baicalein and quercetin may be responsible compounds for the AChE inhibitory activity observed. These findings have demonstrated considerable potential of *T. versicolor* water extract as a natural source of antioxidant(s) and/or AChE inhibitor(s) to be eventually used as drug-like compounds or food supplements in the treatment of Alzheimer's disease.

Mushroom Medicine for Everyone. Lindsay Chimileski ND LAc RH(AHG)

Turkey Tails & Alzheimer's

J Enzyme Inhib Med Chem. 2017; 32(1): 355–362. PMCID: PMC6010034
Published online 2017 Jan 18. doi: 10.1080/14756366.2016.1252759 PMID: 28097907

The lignicolous fungus *Trametes versicolor* (L.) Lloyd (1920): a promising natural source of antiradical and AChE inhibitory agents

Liliana Jamuđević, Maja Karaman, Filip Šibul, Giuseppina Tommonaro, Carmine Iodice, Dragica Jakovljević, and Boris Pavlović

Cholinesterase inhibition of different phenolic compounds from turkey tails

Baicalein as the most potent inhibitor; combined with the quercertin likely most AchE activity

Apigenin, baicalein, kaempferol and quercetin expressed inhibitory effect above 90% at 100 μM.

Daidzein also inhibited the respective enzyme, at the lower extent.

***p*-hydroxybenzoic acid was found is and is also known to exhibit the Cholinesterase inhibition**

Also terpenoids, flavonoids and other phenolic substances also show inhibition of AChE activity.

Polyphenolic and polysaccharide compounds are linked to each other

The water soluble triterpenoid compounds in the H2O turkey tail extract may also contribute both to the antioxidant activity and synergistic effect of these compounds with polysaccharides, phenols and flavonoids as suggested by others

Table 4.

Correlation (R^2) between content of compounds (TF, TPs, TPR and PSH) and antiradical activities.

		TPhC	TFC	TPSH
H_2O			R^2	
	DPPH•	0.53	0.03	**0.66**
	•OH	0.50	0.42	0.30
EtOH				
	DPPH•	**0.79**	**0.97***	0.75
	•OH	0.58	0.89	0.75
MeOH				
	DPPH•	**0.87**	0.48	**0.88**
	•OH	0.27	0.03	0.07

Open in a separate window

*Significant correlation coefficient (R^2) ($p < .05$).
Bold numbers indicate the highest values.
TPhC: total phenol content; TFC: total flavonoid content; TPSH: total polysaccharides; H_2O: water extract of *T. versicolor*; EtOH: ethanolic extract of *T. versicolor*; MeOH: methanolic extract of *T. versicolor*.

Turkey Tails & Alzheimer's

Quantification of particular phenolics by HPLC-MS/MS.

Class	Compound	Extract (μg/g dw) PSH	H_2O	EtOH	MeOH
Flavones	Apigenin	1.57	1.71	0.93	0.23
	Baicalein	**43.00**	**21.60**	8.04	3.63
	Luteolin	2.01	1.47	1.05	1.19
	Chrysoeriol	1.68	1.79	1.21	0.74
	Vitexin	2.06	1.56	1.98	1.19
	Apigenin-7-O-Glucoside	2.37	1.41	1.34	0.54
	Luteolin-7-O-glucoside	0.78	0.91	0.78	0.26
	Apiin	2.86	1.82	2.07	0.86
	Baicalin	**9.95**	**10.7**	**8.88**	**6.27**
Flavonols	Kaempferol	1.69	2.15	1.96	1.58
	Quercetin	**33.70**	**31.20**	**29.90**	**29.30**
	Isorhamnetin	**21.40**	**14.60**	9.36	8.97
	Quercitrin	0.89	1.62	1.81	1.93
	Kaempferol-3-O-Glucoside	1.68	1.71	1.86	0.80
	Hyperoside	0.85	0.68	0.11	0.43
	Quercetin-3-O-Glucoside	0.96	0.31	1.72	0.59
	Rutin	1.01	1.11	1.34	0.53
Flavanone	Naringenin	1.82	1.70	1.82	1.06
Flavanols	Catechin	nd	**17.20**	5.91	21.90
Bifavonoid	Amentoflavone	**32.40**	**17.20**	7.79	6.60
Isoflavonoids	Daidzein	**0.86**	**0.53**	nd	nd
	Genistein	0.51	0.37	0.30	0.21
Hydroxybenzoic acids	*p*-Hydroxybenzoic acid	10.10	**141.00**	**465.00**	**184.00**
	Protocatechuic acid	2.06	1.82	**18.20**	8.57
	Gentisic acid	nd	nd	32.10	24.90
	Vanillic acid	nd	nd	**45.60**	**44.70**
	Gallic acid	9.30	11.40	16.80	22.00
	Syringic acid	nd	6.02	**59.10**	30.10
Hydroxycinnamic acids	*p*-Coumaric acid	1.56	1.21	1.49	1.28
	o-Coumaric acid	0.81	1.16	0.79	0.74
	Ferulic acid	2.12	nd	2.66	2.12
	Caffeic acid	1.72	1.53	3.26	2.33
Coumarins	Esculetin	nd	0.78	**26.20**	2.87
	Scopoletin	4.22	1.66	0.59	nd
	Umbelliferon	1.40	1.13	1.37	1.13
Cyclohexanecarboxylic acid	Quinic acid	2.72	**80.40**	8.84	**98.70**
Chlorogenic acid	5-O-caffeoylquinic acid	2.29	2.93	4.13	2.41
Total		**206.27**	**384.39**	**776.29**	**514.66**

nd – not detected, peak not observed; the concentration is lower than the LOD.

Bold numbers indicate the highest values of the respective compound.

PSH: polysaccharide extract of *T. versicolor*; H_2O: water extract of *T. versicolor*; EtOH: ethanolic extract of *T. versicolor*; MeOH: methanolic extract of *T. versicolor*.

J Enzyme Inhib Med Chem. 2017; 32(1): 355–362. PMCID: PMC6010034
Published online 2017 Jan 18. doi: 10.1080/14756366.2016.1252759 PMID: 28097907

The lignicolous fungus *Trametes versicolor* (L.) Lloyd (1920): a promising natural source of antiradical and AChE inhibitory agents

Liliana Jamuđević, Maja Karaman, Filip Šibul, Giuseppina Tommonaro, Carmine Iodice, Dragica Jakovljević, and Boris Pavlović

Mushrooms for Neuronal Health & as Antioxidant

Review > J Tradit Complement Med. 2013 Jan;3(1):62-8. doi: 10.4103/2225-4110.106549.

Neuronal health - can culinary and medicinal mushrooms help?

Vikineswary Sabaratnam [1], Wong Kah-Hui [2], Murali Naidu [2], Pamela Rosie David [2]

Affiliations + expand

PMID: 24716157 PMCID: PMC3924982 DOI: 10.4103/2225-4110.106549

Free PMC article

Abstract

Hericium erinaceus a culinary and medicinal mushroom is a well established candidate for brain and nerve health. Ganoderma lucidum, Grifola frondosa and Sarcodon scabrosus have been reported to have neurite outgrowth and neuronal health benefits. The number of mushrooms, however, studied for neurohealth activity are few compared to the more than 2 000 species of edible and / or medicinal mushrooms identified. In the on-going search for other potent culinary and / or medicinal mushrooms, indigenous mushrooms used in traditional medicines such as Lignosus rhinocerotis and Ganoderma neo-japonicum are also being investigated. Further, the edible mushroom, Pleurotus giganteus can be a potential candidate, too. Can these edible and medicinal mushrooms be tapped to tackle the health concerns of the aging population which is projected to be more than 80-90 million of people age 65 and above in 2050 who may be affected by age-related neurodegenerative disorders. Scientific validation is needed if these mushrooms are to be considered and this can be achieved by understanding the molecular and biochemical mechanisms involved in the stimulation of neurite outgrowth. Though it is difficult to extrapolate the in vitro studies to what may happen in the human brain, studies have shown that there can be improvemen in cognitive abilities of the aged if the mushroom is incorporated in their daily diets.

Keywords: Ganoderma neo-japonicum; Hericium erinaceus; Lignosus rhinocerotis; Mushrooms; Nerve regeneration; Neurite outgrowth; Neuronal health; Pleurotus giganteus.

Mushrooms for Neuronal Health & as Antioxidant

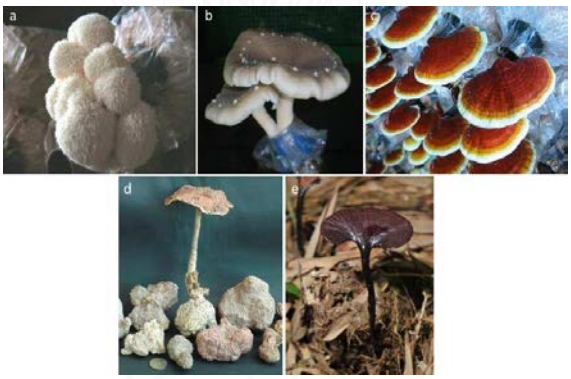


Plate 1 Selected culinary and medicinal medicinal mushrooms with neurite outgrowth stimulatory activity. a: *H. erinaceus*; b: *P. giganteus*; c: *G. lucidium*; d: *L. rhinocerotis*; d: *G.neo-japonicum*

Mushrooms for Neuronal Health & as Antioxidant

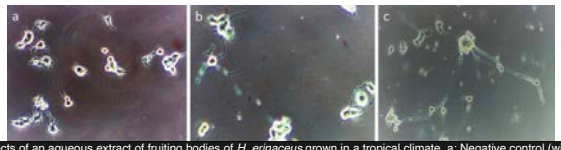


Figure 1 The effects of an aqueous extract of fruiting bodies of *H. erinaceus* grown in a tropical climate. a: Negative control (without treatmen b: NGF (20 ng/ml); c: Aqueous extract of *H. erinaceus* (extensive neurite outgrowth)

Figure 2 The morphology of PC-12Adh cells. Arrows indicate neurite extensions. a: Negative control - F-12K medium only; b: Positive control 50 ng/mL (w/v) of NGF; c: 50 ug/mL of *G. neo-japonicum*

Figure 3 Neurofilament staining to confirm neurite outgrowth

Mushrooms for Neuronal Health & as Antioxidant

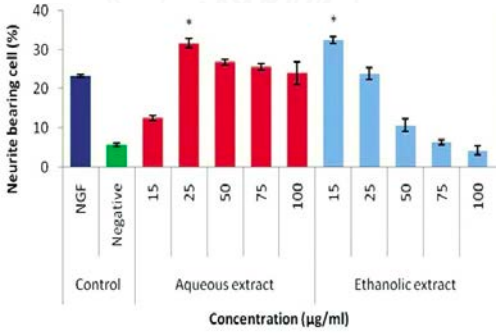


Figure 4 Effects of NGF and *P. giganteus* extracts on neurite outgrowth using PC12 as an *in vitro* model. * $P < 0.05$ compared to NGF (the positive control)[29]

Psychedelics & Entheogens

Connected, Community, Tapping into the Collective Consciousness
Individualized Trauma healing/ Mushroom Guides

Neuroplasticity and new neural networks and connections
Training brain adaptability and learning/ unlearning
Balancing default mode network
Potential to retrain awe response and childlike wonder when paired with nature

Amanita muscaria toadstools demonstrating the range of colours and fruiting body shapes observed for this species. The scales seen on the caps of this species are remnants of the universal veil that surrounds the immature fruiting body (Copyright © Alan Rockefeller).

B. Toxic compounds produced by Amanita fungi.

Huge potential for pain control, anxiety, depression etc depending on the constitution of the individual / circumstances.

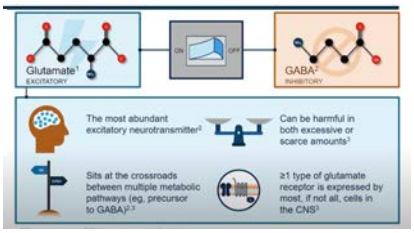
Ibotenic acid acts as an agonist of the glutamate at the *N*-methyl-d-aspartate (NMDA) glutamate receptors while muscimol is a gamma-aminobutyric acid (GABA) agonist, targeting GABAA receptor.
Amanita species is responsible for amatoxin and the very deadly death cap mushro great caution needed distinguishing between the edible and very deadly species

Fly Agaric

Amanita muscaria

Ibotenic acid= glutamate agonist at the *N*-methyl-d-aspartate (NMDA) glutamate receptors

while Muscimol=GABA agonist, targeting GABAA receptor (gamma-aminobutyric acid)



The excitatory effects characterized by elation, giddiness, hyperactivity, muscle tremors, and distortion of space and time begin approximately 30 minutes to 2 hours after ingestion and are likely to be mediated by ibotenic acid.

Following is a phase of tiredness and deep sleep, in which it may be difficult to arouse the patient. During this phase, vivid hallucinations and manic excitement may oscillate with periods of deep sleep. The duration of effect is up to 12 hours. Prolonged sleep with *A. muscaria* ingestion requires only observation and supportive care. Tonic-clonic seizures are reported, but occurrences are rare.

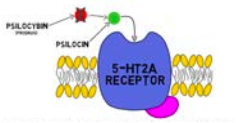
Mushroom Medicine for Everyone. Lindsay Chimileski ND LAc RH(AHG)

***Psilocybe cubensis*- over 200 known strains**
***Psilocybe semilanceata*- liberty caps**
***Psilocybe azurescens*- flying saucer**
***Psilocybe tampanensis*- Magic truffles, philosopher's stone**
***Psilocybe cyanescens*- Wavy Caps**
***Copelandia cyanescens/ Panaeolus cyanescens*- Blue meanies (different from p.cubensis blue meanies strain)**
***Psilocybe caerulescens*- Landslide mushrooms**

Psilocybe

Psilocybin

"magic mushrooms"



Psilocybin and psilocin, indolealkylamines, are structurally similar to the neurotransmitter serotonin (5-hydroxytryptamine or 5-HT). Two other tryptamines – baeocystin and norbaeocystin – could be present but are thought to be less active.

Psilocin mainly interacts with 5-HT1A, 5-HT2A and 5-HT2C receptor subtypes: a mixed receptor agonist.

Unlike MDMA, Psilocybe do not just flood the brain with serotonin. They target a specific subtype of serotonin receptor–the 5-HT2A receptor–to which they bind directly, thereby activating it.

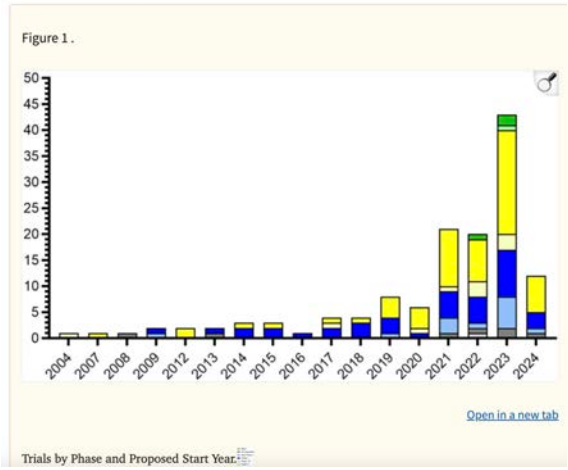
The 5-HT2A receptor is known to play a key role in regulating mood, anxiety, schizophrenia and consciousness

Many trials- micro and macro dosing PTSD, OCD, Migraines, PD, Anxiety, Suicide etc.

Hallucinogenic mushroom use found in the Sahara Desert and date back to 7000 to 9000 years ago.
Traditionally used by Mayans, aztec and many other native tribes throughout Mexico and California

MushWomb Medicine *Lindsay Chimileski* ND LAc RH(AHG)

The Promise of Therapeutic Psilocybin: An Evaluation of the 134 Clinical Trials, 54 Potential Indications, and 0 Marketing Approvals on ClinicalTrials.gov



The Therapeutic Potential of Psilocybin

by Henry Lowe [1,2,3,4], Ngeh Toyang [2,3], Blair Steele [1,*], Henkel Valentine [1], Justin Grant [1,5], Amza Ali [1,5], Wilfred Ngwa [6] and Lorenzo Gordon [7]

Table 3. Psychic vs. somatic effects of psilocybin.

Psychic Effects in Humans and Animals (in Medium Dose (12–20 mg p.o.)	Somatic Effects in Humans (Barely Noticeable/Secondary Pharmacological Effects) [5]
	At 8–12 mg p.o., i.m.:
1. Stimulation of affect/affective activation [5],	1. Mydriasis [189],
2. Hypnagogic experience [5],	2. Accelerated heart frequency [189],
3. Dreams [5],	3. Slowed heart frequency [189],
4. Enhanced ability for introspection [5],	4. Hypotension [189],
5. Mystical-type experience, which predicted the success of the therapy and likelihood of persisting positive benefits [9,15],	5. Hypertension [189],
6. Illusions [5],	6. Nausea [189],
7. Synaesthesia [5], and	7. Increased reflex tendineae [189],
8. Alterations of thought and time sense [5],	8. Decreased reflex tendineae [189],
	9. Dysmetria [189], and
	10. Tremors [189]
	At 0.11 mg/kg p.o, similar effects were observed in another study [190]. At 1.5 mg increased to 25 mg p.o. in three doses per day, for 21 consecutive days, another study reported no significant aberrations in the parameters above [191].

Mushroom Medicine with Lindsay Chimileski ND LAc RH

The Therapeutic Potential of Psilocybin

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Table 1. The potential therapeutic window of psilocybin-assisted therapy, that is, diseased states in which psilocybin-assisted therapy is being explored.

		Diseased State/Condition	Reference
1.		Alcohol dependence	[23–25]
2.		Stimulant dependence	[25]
3.		Cocaine addiction	[26,27]
4.		Tobacco addiction	[25,28–30]
5.		Nicotine addiction	[26,29]
6.		Opioid addiction	[25]
7.		Cannabis dependence	[25]
		Anxiety disorders such as:	
	i.	Post-traumatic stress disorder (PTSD),	[26]
	ii.	Generalized anxiety disorder (GAD),	[26]
8.	iii.	Obsessive–compulsive disorder (OCD)	[31,32]
	iv.	Advanced-stage cancer-related anxiety	[33–37]
	v.	Psychological distress associated with existential crisis of terminal disease	[26]
	vi.	Adjustment disorder with anxiety	[26,38]
9.		Cancer-related depression	[33–37,39]
10.		Treatment-resistant depression	[40–44]
11.		Major Depressive Disorder	[45]
12.		Severe existential depression	[26,33,36]
13.		Suicidality (ideation and actual attempts)	[13,46]
14.		Cluster ("suicide") headaches	[6,47]
15.		Chronic pain	[48–50]
16.		Intractable phantom pain	[51]
17.		Demoralization	[52]
18.		Demoralization in older, long-term AIDS survivor men (OLTAS)	[53]
19.		Dysfunctional social cognition	[54]
20.		Maladaptive narcissism	[55]
21.		Borderline Personality Disorder (BPD)	[56,57]
22.		Narcissistic Personality Disorder (NPD)	[58–60]
23.		Epilepsy	[61]
24.		Psychopathy	[54]
25.		Emotional dysregulation and violence against one's partner	[62–64]
26.		Inflammation	[49]

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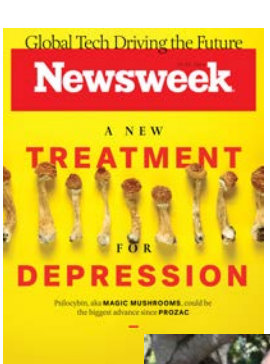
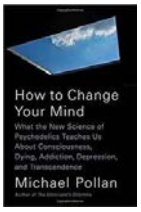
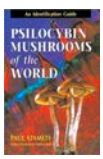






Mushroom medicine

Lindsay Chimileski ND Lac RH

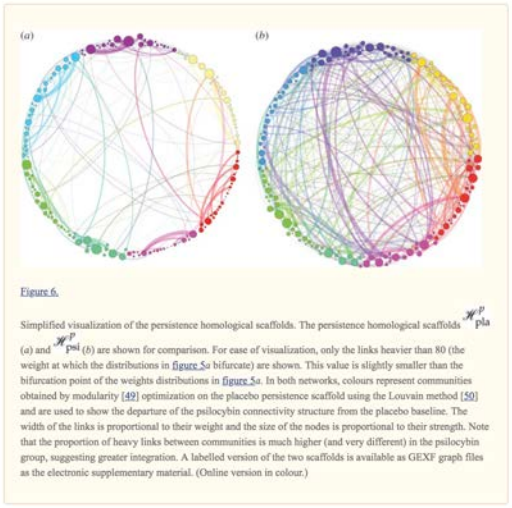


Figure 6.

Simplified visualization of the persistence homological scaffolds. The persistence homological scaffolds $\mathcal{H}^P_{pla}$ (*a*) and $\mathcal{H}^P_{psi}$ (*b*) are shown for comparison. For ease of visualization, only the links heavier than 80 (the weight at which the distributions in figure 5*a* bifurcate) are shown. This value is slightly smaller than the bifurcation point of the weights distributions in figure 5*a*. In both networks, colours represent communities obtained by modularity [49] optimization on the placebo persistence scaffold using the Louvain method [50] and are used to show the departure of the psilocybin connectivity structure from the placebo baseline. The width of the links is proportional to their weight and the size of the nodes is proportional to their strength. Note that the proportion of heavy links between communities is much higher (and very different) in the psilocybin group, suggesting greater integration. A labelled version of the two scaffolds is available as GEXF graph files as the electronic supplementary material. (Online version in colour.)

Stoned Ape theory- role in development of language

Terrence McKenna

New Research on Ancient Mushrooms

Lindsay Chimileski ND Lac RH

SSRIs target the 5-ht1a receptor

Behavior and emotional responses, regulating your hunger, thirst, response to pain, levels of pleasure, sexual satisfaction, anger and aggressive behavior

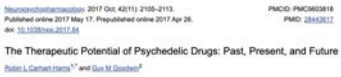
SSRIs target the 5-ht1a receptor
Changes our tolerance to stress by
Encouraging patiences and emotional resistance
but it can BLUNTING
They help us TOLERATE stress.
Cope with things that are hard; grin and bear it
Anti stress/ pro coping

Psychedelics target the 5-ht2a receptor
Adapt and change
Outside of just the limbic system
Related to neuroplasticity
Environmental sensitivity
Learning and UNLEARNING
Adaption and change
Enhance sensitivity
Facilitate emotional release
Pro-therapeutic

Psychedelics target the 5-ht2a receptor

a measure of the brain's overall flexibility or readiness to encounter unpredictable stimuli and they found that it correlated with intelligence

–Not just grinning and bearing it; actually making space to adapt ourselves or environments to impact change
–May be 1-3 or less frequent doses can have such lasting impact
5-HT2A receptors are in the high level association regions of the brain influencing cognition, perception.
–Lowest activity in the PMC or brain areas more connected to motor function

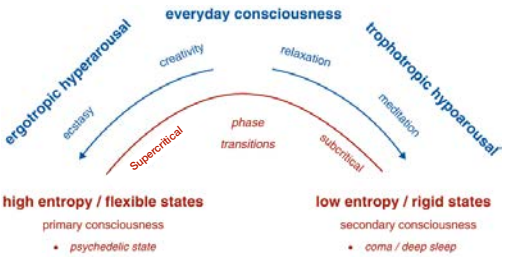


Neuropsychopharmacology 2017 Oct; 42(11): 2105–2113. Published online 2017 May 17. Prepublished online 2017 Apr 26. doi: 10.1038/npp.2017.84 PMCID: PMC5603818 PMID: 28443617

The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future

Robin L Carhart-Harris[1,*] and Guy M Goodwin[2]

MushWomb Medicine



high entropy / flexible states

primary consciousness

- *psychedelic state*
- *dreaming*
- *psychosis*
- *creative thinking*

low entropy / rigid states

secondary consciousness

- *coma / deep sleep*
- *depression*
- *addiction*
- *rigid thinking*

Home › Ayahuasca Healing and Science › Chapter

Psychedelic Medicines: A Paradigm Shift from Pharmacological Substitution Towards Transformation-Based Psychiatry

Milan Scheidegger

Chapter | First Online: 16 April 2021

MushWomb Medicine

Lindsay Chimileski ND LAc RH(AHG)

https://ericazelfand.com/

Great trainings & resources

The Default Mode Network (DMN)

Those with depression / addiction / OCD may benefit from "the ability of psychedelics to disrupt stereotyped patterns of thought and behavior by disintegrating the patterns of [neural] activity upon which they rest."

~ Robin Carhart-Harris, as quoted in How to Change Your Mind by Michael Pollan

Mushroom Medicine for Everyone. Lindsay Chimileski ND LAc RH(AHG)

SINGLE DOSE psilocybin vs. single dose niacin

Follow ups showed improvements 4.5 years after!

Anxiety, Depression, Hopelessness, Demoralization, Death Anxiety

J Psychopharmacol. 2020 Feb;34(2):155-166. doi: 10.1177/0269881119897615. Epub 2020 Jan 9.

Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer

Gabrielle I Agin-Liebes [1 2], Tara Malone [2 3], Matthew M Yalch [1], Sarah E Mennenga [2], K Linnae Ponté [4], Jeffrey Guss [2 3 5], Anthony P Bossis [2 3 5], Jim Grigsby [6 7], Stacy Fischer [6 7], Stephen Ross [2 3 5]

Affiliations + expand

PMID: 31916890 DOI: 10.1177/0269881119897615

Abstract

Background: A recently published randomized controlled trial compared single-dose psilocybin with single-dose niacin in conjunction with psychotherapy in participants with cancer-related psychiatric distress. Results suggested that psilocybin-assisted psychotherapy facilitated improvements in psychiatric and existential distress, quality of life, and spiritual well-being up to seven weeks prior to the crossover. At the 6.5-month follow-up, after the crossover, 60–80% of participants continued to meet criteria for clinically significant antidepressant or anxiolytic responses.

Methods: The present study is a long-term within-subjects follow-up analysis of self-reported symptomatology involving a subset of participants that completed the parent trial. All 16 participants who were still alive were contacted, and 15 participants agreed to participate at an average of 3.2 and 4.5 years following psilocybin administration.

Results: Reductions in anxiety, depression, hopelessness, demoralization, and death anxiety were sustained at the first and second follow-ups. Within-group effect sizes were large. At the second (4.5 year) follow-up approximately 60–80% of participants met criteria for clinically significant antidepressant or anxiolytic responses. Participants overwhelmingly (71-100%) attributed positive life changes to the psilocybin-assisted therapy experience and rated it among the most personally meaningful and spiritually significant experiences of their lives.

Conclusion: These findings suggest that psilocybin-assisted psychotherapy holds promise in promoting long-term relief from cancer-related psychiatric distress. Limited conclusions, however, can be drawn regarding the efficacy of this therapy due to the crossover design of the parent study. Nonetheless, the present study adds to the emerging literature base suggesting that psilocybin-facilitated therapy may enhance the psychological, emotional, and spiritual well-being of patients with life-threatening cancer.

Trial registration: ClinicalTrials.gov NCT00957359.

Keywords: Psilocybin; anxiety; cancer; depression; psychedelic.

Psilocybin with psychological support for treatment-resistant depression: six-month follow-up

Abstract

Rationale

Recent clinical trials are reporting marked improvements in mental health outcomes with psychedelic drug-assisted psychotherapy.

Objectives

Here, we report on safety and efficacy outcomes for up to 6 months in an open-label trial of psilocybin for treatment-resistant depression.

Methods

Twenty patients (six females) with (mostly) severe, unipolar, treatment-resistant major depression received two oral doses of psilocybin (10 and 25 mg, 7 days apart) in a supportive setting. Depressive symptoms were assessed from 1 week to 6 months post-treatment, with the self-rated QIDS-SR16 as the primary outcome measure.

Results

Treatment was generally well tolerated. Relative to baseline, marked reductions in depressive symptoms were observed for the first 5 weeks post-treatment (Cohen's $d = 2.2$ at week 1 and 2.3 at week 5, both $p < 0.001$), nine and four patients met the criteria for response and remission at week 5. Results remained positive at 3 and 6 months (Cohen's $d = 1.5$ and 1.4, respectively, both $p < 0.001$). No patients sought conventional antidepressant treatment within 5 weeks of psilocybin. Reductions in depressive symptoms at 5 weeks were predicted by the quality of the acute psychedelic experience.

Conclusions

Although limited conclusions can be drawn about treatment efficacy from open-label trials, tolerability was good, effect sizes large and symptom improvements appeared rapidly after just two psilocybin treatment sessions and remained significant 6 months post-treatment in a treatment-resistant cohort. Psilocybin represents a promising paradigm for unresponsive depression that warrants further research in double-blind randomised control trials.

20 patients, severe unipolar treatment-resistant depression.
Two doses 1 week apart.

No negative side effects
Reduction in depressive symptoms for 5 weeks post tx and 3, 6 month checks.

No one sought other treatment for depression first 5 weeks

Quality reports of the psychedelic experience predicted level and length of decrease in depressive symptoms

Review > Psychiatry Res. 2020 Feb;284:112749. doi: 10.1016/j.psychres.2020.112749. Epub 2020 Jan 2.

The experimental effects of psilocybin on symptoms of anxiety and depression: A meta-analysis

Simon B Goldberg [1], Brian T Pace [2], Christopher R Nicholas [3], Charles L Raison [4], Paul R Hutson [5]

Affiliations + expand

PMID: 31931272 DOI: 10.1016/j.psychres.2020.112749

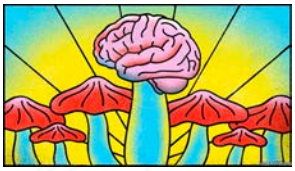
Abstract

The current meta-analysis examined the effects of psilocybin in combination with behavioral interventions on anxiety and depression in samples with elevated symptoms. Across four studies (one uncontrolled; three randomized, placebo-controlled; N = 117), within-group pre-post and pre-follow-up effects on anxiety and depression were large (Hedges' gs=1.16 to 1.47) and statistically significant. Across three placebo-controlled studies, pre-post placebo-controlled effects were also large (gs = 0.82 to 0.83) and statistically significant. No serious adverse events were reported. Limitations include the small number of studies and risk for bias within studies. Results tentatively support future research on psilocybin for the treatment of anxiety and depression.

Keywords: Anxiety; Depression; Psilocybin.

Conflict of interest statement

Declaration of competing interest The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Christopher R. Nicholas received salary offsets from Usona Institute. In the prior 12 months, Charles L. Raison has served as a consultant for Usona Institute, Alkermes and Shire. All other authors declare that there is no conflict of interest.



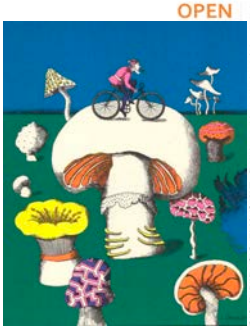
n=117

"Effects on anxiety and depression were large and statistically significant. No serious adverse effects."

12 healthy volunteers - 25mg/70kg(or 154.3 lbs) dose
Assessment 1 day before, 1 week after, 1 month after
More brain changes initially, still positive affect with reduced anxiety 1 month out
Resting-state functional connections across the brain increased
=influences emotional and brain plasticity, lightens negative affect

SCIENTIFIC REPORTS
nature research

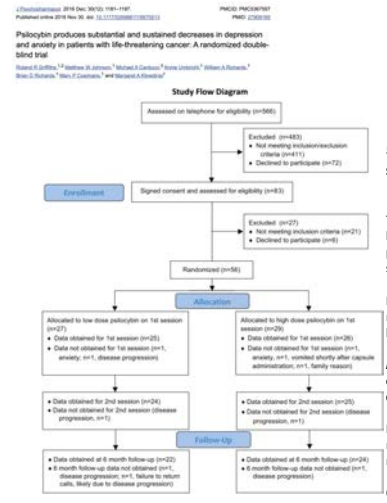
OPEN



Emotions and brain function are altered up to one month after a single high dose of psilocybin

Frederick S. Barrett[1*], Manoj K. Doss[1], Nathan D. Sepeda[1], James J. Pekar[2,3] & Roland R. Griffiths[1,4]

Psilocybin is a classic psychedelic compound that may have efficacy for the treatment of mood and substance use disorders. Acute psilocybin effects include reduced negative mood, increased positive mood, and reduced amygdala response to negative affective stimuli. However, no study has investigated the long-term, enduring impact of psilocybin on negative affect and associated brain function. Twelve healthy volunteers (7F/5M) completed an open-label pilot study including assessments 1-day before, 1-week after, and 1-month after receiving a 25 mg/70 kg dose of psilocybin to test the hypothesis that psilocybin administration leads to enduring changes in affect and neural correlates of affect. One-week post-psilocybin, negative affect and amygdala response to facial affect stimuli were reduced, whereas positive affect and dorsal lateral prefrontal and medial orbitofrontal cortex responses to emotionally-conflicting stimuli were increased. One-month post-psilocybin, negative affective and amygdala response to facial affect stimuli returned to baseline levels while positive affect remained elevated, and trait anxiety was reduced. Finally, the number of significant resting-state functional connections across the brain increased from baseline to 1-week and 1-month post-psilocybin. These preliminary findings suggest that psilocybin may increase emotional and brain plasticity, and the reported findings support the hypothesis that negative affect may be a therapeutic target for psilocybin.



2 doses & long term/6 month follow up

51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety.

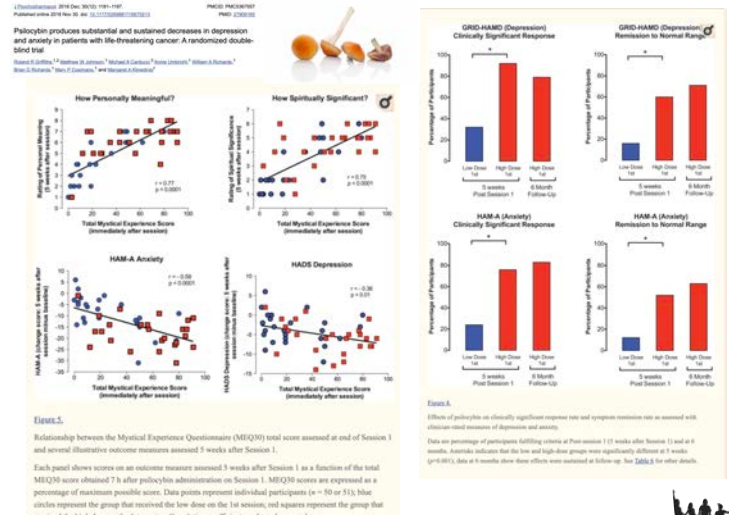
This randomized, double-blind, cross-over trial investigated the effects of a very low (placebo-like) dose (1 or 3 mg/70 kg) vs. a high dose (22 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 5 weeks between sessions and a 6-month follow-up.

High-dose psilocybin produced large decreases in clinician- and self-rated measures of depressed mood and anxiety, along with increases in quality of life, life meaning, and optimism, and decreases in death anxiety.

At 6-month follow-up, these changes were sustained, with about 80% of participants continuing to show clinically significant decreases in depressed mood and anxiety.

Participants attributed improvements in attitudes about life/self, mood, relationships, and spirituality to the high-dose experience, with >80% endorsing moderately or greater increased well-being/life satisfaction.

Community observer ratings showed corresponding changes. Mystical-type psilocybin experience on session day mediated the effect of psilocybin dose on therapeutic outcomes.



Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial

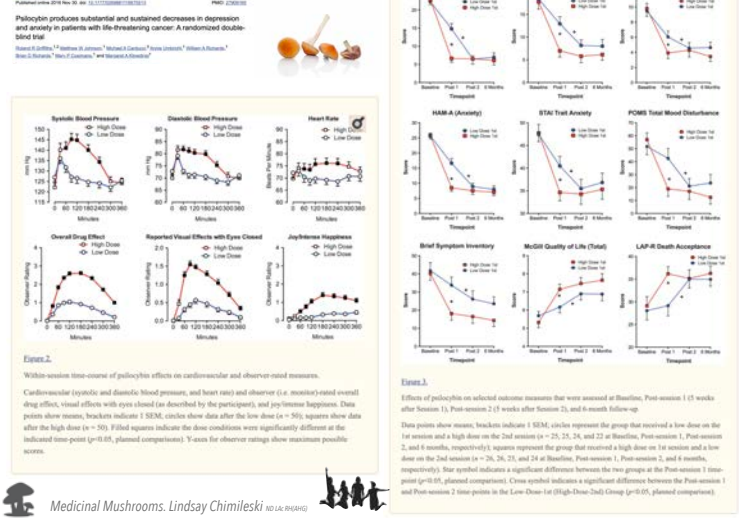


Figure 2.

Within-session time-course of psilocybin effects on cardiovascular and observer-rated measures.

Cardiovascular (systolic and diastolic blood pressure, and heart rate) and observer (i.e. monitor)-rated overall drug effect, visual effects with eyes closed (as described by the participant), and joy/intense happiness. Data points show means; brackets indicate 1 SEM; circles show data after the low dose (n = 50); squares show data after the high dose (n = 50). Filled squares indicate the dose conditions were significantly different at the indicated time-point ($p<0.05$, planned comparisons). Y-axes for observer ratings show maximum possible scores.

Figure 3.

Effects of psilocybin on selected outcome measures that were assessed at Baseline, Post-session 1 (5 weeks after Session 1), Post-session 2 (5 weeks after Session 2), and 6-month follow-up

Data points show means; brackets indicate 1 SEM; circles represent the group that received a low dose on the 1st session and a high dose on the 2nd session (n = 25, 25, 24, and 22 at Baseline, Post-session 1, Post-session 2, and 6 months, respectively); squares represent the group that received a high dose on 1st session and a low dose on the 2nd session (n = 26, 26, 25, and 24 at Baseline, Post-session 1, Post-session 2, and 6 months, respectively). Star symbol indicates a significant difference between the two groups at the Post-session 1 time-point ($p<0.05$, planned comparison). Cross symbol indicates a significant difference between the Post-session 1 and Post-session 2 time-points in the Low-Dose-1st (High-Dose-2nd) Group ($p<0.05$, planned comparison).

Medicinal Mushrooms. Lindsay Chimileski ND LAc RH(AHG)

Acta Psychiatr Scand. 2018 Nov;138(5):368-378. doi: 10.1111/acps.12904. Epub 2018 Jun 19.

Effects of psilocybin therapy on personality structure.

Erritzoe D[1], Roseman L[1], Nour MM[2,3], MacLean K[4], Kaelen M[1], Nutt DJ[1], Carhart-Harris RL[1].

Author information

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Abstract

OBJECTIVE: To explore whether psilocybin with psychological support modulates personality parameters in patients suffering from treatment-resistant depression (TRD).

METHOD: Twenty patients with moderate or severe, unipolar, TRD received oral psilocybin (10 and 25 mg, one week apart) in a supportive setting. Personality was assessed at baseline and at 3-month follow-up using the Revised NEO Personality Inventory (NEO-PI-R), the subjective psilocybin experience with Altered State of Consciousness (ASC) scale, and depressive symptoms with QIDS-SR16.

RESULTS: Neuroticism scores significantly decreased while Extraversion increased following psilocybin therapy. These changes were in the direction of the normative NEO-PI-R data and were both predicted, in an exploratory analysis, by the degree of insightfulness experienced during the psilocybin session. Openness scores also significantly increased following psilocybin, whereas Conscientiousness showed trend-level increases, and Agreeableness did not change.

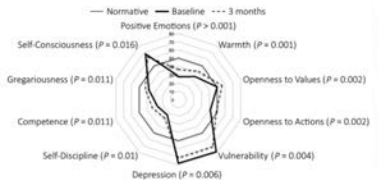
CONCLUSION: Our observation of changes in personality measures after psilocybin therapy was mostly consistent with reports of personality change in relation to conventional antidepressant treatment, although the pronounced increases in Extraversion and Openness might constitute an effect more specific to psychedelic therapy. This needs further exploration in future controlled studies, as do the brain mechanisms of postpsychedelic personality change.

Mushroom medicine

Lindsay Chimileski ND Lac RH

PMC full text: Acta Psychiatr Scand. 2018 Nov; 138(5): 368–378.
Published online 2018 Jun 19. doi: 10.1111/acps.12904

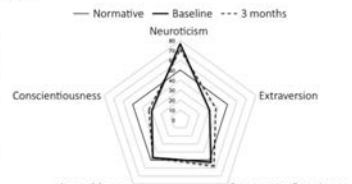
Figure 2



Facet T-scores scores at baseline (solid thick line) and at 3-month follow-up (dotted line), with normative data

PMC full text: Acta Psychiatr Scand. 2018 Nov; 138(5): 368–378.
Published online 2018 Jun 19. doi: 10.1111/acps.12904

Figure 1



Trait T-scores scores at baseline (solid thick line) and at 3-month follow-up (dotted line). T-scores calculated with the use of means and standard deviations from a combined sample of 500 healthy women and 500 healthy men (NEO-PI-R manual). The normative data (solid thin line) are represented by normalized scores of 50.

Mushroom medicine

Lindsay Chimileski ND Lac RH

Research

JAMA Psychiatry | Original Investigation

Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder
A Randomized Clinical Trial

Alan K. Davis, PhD; Frederick S. Barrett, PhD; Darrick G. May, MD; Mary P. Cosimano, MSW; Nathan D. Sepeda, BS; Matthew W. Johnson, PhD; Patrick H. Finan, PhD; Roland R. Griffiths, PhD

IMPORTANCE Major depressive disorder (MDD) is a substantial public health burden, but current treatments have limited effectiveness and adherence. Recent evidence suggests that 1 or 2 administrations of psilocybin with psychological support produces antidepressant effects in patients with cancer and in those with treatment-resistant depression.

OBJECTIVE To investigate the effect of psilocybin therapy in patients with MDD.

DESIGN, SETTING, AND PARTICIPANTS This randomized, waiting list-controlled clinical trial was conducted at the Center for Psychedelic and Consciousness Research at Johns Hopkins Bayview Medical Center in Baltimore, Maryland. Adults aged 21 to 75 years with an MDD diagnosis, not currently using antidepressant medications, and without histories of psychotic disorder, serious suicide attempt, or hospitalization were eligible to participate. Enrollment occurred between August 2017 and April 2019, and the 4-week primary outcome assessments were completed in July 2019. A total of 27 participants were randomized to an immediate treatment condition group (n = 15) or delayed treatment condition group (waiting list control condition; n = 12). Data analysis was conducted from July 1, 2019, to July 31, 2020, and included participants who completed the intervention (evaluable population).

INTERVENTIONS Two psilocybin sessions (session 1: 20 mg/70 kg; session 2: 30 mg/70 kg) were given (administered in opaque gelatin capsules with approximately 100 mL of water) in the context of supportive psychotherapy (approximately 11 hours). Participants were randomized to begin treatment immediately or after an 8-week delay.

Editorial
Author Audio Interview
Supplemental content

JAMA Psychiatry | Original Investigation

Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder
A Randomized Clinical Trial

Alan K. Davis, PhD; Frederick S. Barrett, PhD; Darrick G. May, MD; Mary P. Cosimano, MSW; Nathan D. Sepeda, BS; Matthew W. Johnson, PhD;

MAIN OUTCOMES AND MEASURES The primary outcome, depression severity was assessed with the GRID-Hamilton Depression Rating Scale (GRID-HAMD) scores at baseline (score of ≥17 required for enrollment) and weeks 5 and 8 after enrollment for the delayed treatment group, which corresponded to weeks 1 and 4 after the intervention for the immediate treatment group. Secondary outcomes included the Quick Inventory of Depressive Symptomatology-Self Rated (QIDS-SR).

RESULTS Of the randomized participants, 24 of 27 (89%) completed the intervention and the week 1 and week 4 postsession assessments. This population had a mean (SD) age of 39.8 (12.2) years, was composed of 16 women (67%), and had a mean (SD) baseline GRID-HAMD score of 22.8 (3.9). The mean (SD) GRID-HAMD scores at weeks 1 and 4 (8.0 [7.1] and 8.5 [5.7]) in the immediate treatment group were statistically significantly lower than the scores at the comparable time points of weeks 5 and 8 (23.8 [5.4] and 23.5 [6.0]) in the delayed treatment group. The effect sizes were large at week 5 (Cohen d = 2.2; 95% CI, 1.4-3.0; P < .001) and week 8 (Cohen d = 2.6; 95% CI, 1.7-3.6; P < .001). The QIDS-SR documented a rapid decrease in mean (SD) depression score from baseline to day 1 after session 1 (16.7 [3.5] vs 6.3 [4.4]; Cohen d = 3.0; 95% CI, 1.9-4.0; P < .001), which remained statistically significantly reduced through the week 4 follow-up (6.0 [5.7]; Cohen d = 3.1; 95% CI, 1.9-4.2; P < .001). In the overall sample, 16 participants (67%) at week 1 and 17 (71%) at week 4 had a clinically significant response to the intervention (≥50% reduction in GRID-HAMD score), and 14 participants (58%) at week 1 and 13 participants (54%) at week 4 were in remission (≤7 GRID-HAMD score).

CONCLUSIONS AND RELEVANCE Findings suggest that psilocybin with therapy is efficacious in treating MDD, thus extending the results of previous studies of this intervention in patients with cancer and depression and of a nonrandomized study in patients with treatment-resistant depression.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03181529

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2020.3285
Published online November 4, 2020.

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Randomized Controlled Trial > J Psychopharmacol. 2022 Feb;36(2):151-158.
doi: 10.1177/0269881121073759.

Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: Prospective 12-month follow-up

Natalie Gukasyan [1], Alan K Davis [1, 2], Frederick S Barrett [1], Mary P Cosimano [1], Nathan D Sepeda [1], Matthew W Johnson [1], Roland R Griffiths [1, 3]

Affiliations + expand

PMID: 35166158 PMCID: PMC8864328 DOI: 10.1177/0269881121073759

Methods: This randomized, waiting-list controlled study enrolled 27 patients aged 21-75 with moderate to severe unipolar depression (GRID-Hamilton Depression Rating Scale (GRID-HAMD) ≥ 17). Participants were randomized to an immediate or delayed (8 weeks) treatment condition in which they received two doses of psilocybin with supportive psychotherapy. Twenty-four participants completed both psilocybin sessions and were followed through 12 months following their second dose.

Results: All 24 participants attended all follow-up visits through the 12-month timepoint. Large decreases from baseline in GRID-HAMD scores were observed at 1-, 3-, 6-, and 12-month follow-up (Cohen d = 2.3, 2.0, 2.6, and 2.4, respectively).

Treatment response at 12 months:

(≥50% reduction in GRID-HAMD score from baseline) 75%

Remission 58%, at 12 months.

There were no serious adverse events judged to be related to psilocybin in the long-term follow-up period, and no participants reported psilocybin use outside of the context of the study.

Participant ratings of personal meaning, spiritual experience, and mystical experience after sessions predicted increased well-being at 12 months, but did not predict improvement in depression.

Conclusions: These findings demonstrate that the substantial antidepressant effects of psilocybin-assisted therapy may be durable at least through 12 months following acute intervention in some patients.

Lindsay Chimileski ND LAc RH(AHG)

Clinical Trial > Nat Med. 2022 Apr;28(4):844-851. doi: 10.1038/s41591-022-01744-z. Epub 2022 Apr 11.

Increased global integration in the brain after psilocybin therapy for depression

Richard E Daws [1 2], Christopher Timmermann [3 4], Bruna Giribaldi [4], James D Sexton [4], Matthew B Wall [5 6 7], David Erritzoe [4], Leor Roseman [4], David Nutt [4], Robin Carhart-Harris [4 8]

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PMID: 35411074 DOI: 10.1038/s41591-022-01744-z

Abstract Psilocybin therapy shows antidepressant potential, but its therapeutic actions are not well understood. We assessed the subacute impact of psilocybin on brain function in two clinical trials of depression.

1. **Just Psilocybin:** The first was an open-label trial of orally administered psilocybin (10 mg and 25 mg, 7 d apart) in patients with treatment-resistant depression. Functional magnetic resonance imaging (fMRI) was recorded at baseline and 1 d after the 25-mg dose. Beck's depression inventory was the primary outcome measure (MR/J00460X/1).
2. **Double-blind phase II randomized controlled trial comparing psilocybin therapy with escitalopram.**

   Patients with major depressive disorder received either 2 × 25 mg oral psilocybin, 3 weeks apart, plus 6 weeks of daily placebo ('psilocybin arm') or 2 × 1 mg oral psilocybin, 3 weeks apart, plus 6 weeks of daily escitalopram (10-20 mg) ('escitalopram arm'). fMRI was recorded at baseline and 3 weeks after the second psilocybin dose.

In both trials, the antidepressant response to psilocybin was rapid, sustained and correlated with decreases in fMRI brain network modularity, implying that psilocybin's antidepressant action may depend on a global increase in brain network integration.

Network cartography analyses indicated that 5-HT2A receptor-rich higher-order functional networks became more functionally interconnected and flexible after psilocybin treatment.

The antidepressant response to escitalopram was milder and *no changes in brain network organization were observed.* Consistent efficacy-related brain changes, correlating with robust antidepressant effects across two studies, suggest an antidepressant mechanism for psilocybin therapy: global increases in brain network integration.

Parkinson's Disease

UCSF University of California San Francisco

Psilocybin Therapy for Depression and Anxiety in Parkinson's Disease: A Pilot Study

Recruiting Now

Parkinson's Disease (PD) is a devastating neurodegenerative disorder with growing impact worldwide. Depression and anxiety are common in PD and linked to poor quality of life and high health care costs. Unfortunately, treatment options for patients are limited. Though previous studies have found that psilocybin may be helpful for people with depression and anxiety, all of these studies have excluded patients with PD or any other neurodegenerative disorder. As a result, we lack critical information about the safety, tolerability, and feasibility of this treatment for people living with PD. In this study, our goal is to fill that gap. If successful, this project will lay the groundwork for a larger randomized placebo-controlled study of psilocybin therapy for treating PD-associated depression and anxiety.

I'M INTERESTED

Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers

Joseph M. Rootman, Pamela Kryskow, Kalin Harvey, Paul Stamets, Eesmyal Santos-Brault, Kim P. C. Kuypers, Vince Polito, Francoise Bourzat & Zach Walsh

Scientific Reports 11, Article number: 22479 (2021) | Cite this article

574k Accesses | 8 Citations | 587 Altmetric | Metrics

Abstract

The use of psychedelic substances at sub-sensorium '*microdoses*', has gained popular academic interest for reported positive effects on wellness and cognition. The present study describes microdosing practices, motivations and mental health among a sample of self-selected *microdosers* ($n = 4050$) and non-microdosers ($n = 4653$) via a mobile application. Psilocybin was the most commonly used microdose substances in our sample (85%) and we identified diverse microdose practices with regard to dosage, frequency, and the practice of *stacking* which involves combining psilocybin with non-psychedelic substances such as Lion's Mane mushrooms, chocolate, and niacin. Microdosers were generally similar to non-microdosing controls with regard to demographics, but were more likely to report a history of mental health concerns. Among individuals reporting mental health concerns, microdosers exhibited lower levels of depression, anxiety, and stress across gender. Health and wellness-related motives were the most prominent motives across microdosers in general, and were more prominent among females and among individuals who reported mental health concerns. Our results indicate health and wellness motives and perceived mental health benefits among microdosers, and highlight the need for further research into the mental health consequences of microdosing including studies with rigorous longitudinal designs.

MicroDosing

Clinical Trial > Nat Med. 2023 Aug;29(8):1947-1953. doi: 10.1038/s41591-023-02455-9. Epub 2023 Jul 24.

Psilocybin therapy for females with anorexia nervosa: a phase 1, open-label feasibility study

Stephanie Knatz Peck [1], Samantha Shao [2], Tessa Gruen [2 3], Kevin Yang [2], Alexandra Babakanian [2], Julie Trim [2], Daphna M Finn [2], Walter H Kaye [4]

Affiliations + expand

PMID: 37488291 PMCID: PMC10427429 DOI: 10.1038/s41591-023-02455-9

Free PMC article

Abstract

Anorexia nervosa (AN) is a deadly illness with no proven treatments to reverse core symptoms and no medications approved by the US Food and Drug Administration. Novel treatments are urgently needed to improve clinical outcomes. In this open-label feasibility study, 10 adult female participants (mean body mass index 19.7 kg m^{-2}; s.d. 3.7) who met Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for AN or pAN (partial remission) were recruited to a study conducted at an academic clinical research institute. Participants received a single 25-mg dose of synthetic psilocybin in conjunction with psychological support. The primary aim was to assess safety, tolerability and feasibility at post-treatment by incidences and occurrences of adverse events (AEs) and clinically significant changes in electrocardiogram (ECG), laboratory tests, vital signs and suicidality. No clinically significant changes were observed in ECG, vital signs or suicidality. Two participants developed asymptomatic hypoglycemia at post-treatment, which resolved within 24 h. No other clinically significant changes were observed in laboratory values. All AEs were mild and transient in nature. Participants' qualitative perceptions suggest that the treatment was acceptable for most participants. Results suggest that psilocybin therapy is safe, tolerable and acceptable for female AN, which is a promising finding given physiological dangers and problems with treatment engagement. ClinicalTrials.gov identifier NCT04661514 .

Sub-acute effects of psilocybin on EEG correlates of neural plasticity in major depression: Relationship to symptoms

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PMID: 37392016 DOI: 10.1177/02698811231179800

Abstract

Background: Evidence suggests that serotonergic psychedelics (e.g. psilocybin), have rapid-acting and long-lasting antidepressant effects after a single dose. However, the mechanism underlying these effects remain unclear. One proposed mechanism is that these drugs promote neuroplasticity. However, this has not been conclusively demonstrated in humans.

Aims: We hypothesized that relative to placebo, psilocybin would: (1) increase electroencephalographic (EEG) correlates of neuroplasticity, (2) reduce depression symptoms, and (3) changes in EEG would correlate with improvements in depression.

Methods: In this double-blind, placebo-controlled, within-subject study, individuals with major depressive disorder (MDD; $n = 19$) were administered placebo followed by psilocybin (0.3 mg/kg) in a fixed order (placebo, followed by psilocybin 4 weeks later). EEG indices of neuroplasticity (tetanus-induced long-term potentiation) as assessed via auditory evoked theta (4–8 Hz) power and measures of depression (GRID Hamilton Rating Scale for Depression-17 (GRID-HAM-D-17)) were measured at several time-points after placebo and psilocybin (24 h and 2 weeks after each session).

Results: EEG theta power doubled in amplitude 2 weeks after a single psychedelic dose of psilocybin but not after placebo. Further, improvements in depression symptoms 2 weeks after psilocybin were correlated with increases in theta power.

Conclusions: The increased theta power observed represents evidence of sustained changes in the brain following psilocybin. Given the correlation with enhancement in depressive symptoms, changes in theta may represent an EEG biomarker of the sustained effects of psilocybin, and may shed light on potential mechanisms of psilocybin's antidepressant effect. Taken together, these results complement the emerging notion that psilocybin, and perhaps other psychedelics, can produce long-term alterations in neuroplasticity.

Clinical Trial > J Clin Psychiatry. 2006 Nov;67(11):1735-40. doi: 10.4088/jcp.v67n1110.

Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder

OCD

Francisco A Moreno [1], Christopher B Wiegand, E Keolani Taitano, Pedro L Delgado

Affiliations + expand

PMID: 17196053 DOI: 10.4088/jcp.v67n1110

Abstract Background: Anecdotal reports suggest that psychedelic agents may relieve symptoms of obsessive-compulsive disorder (OCD).

This modified double-blind study investigated the safety, tolerability, and clinical effects of psilocybin, a potent 5-HT(1A) and 5-HT(2A/2C) agonist, in patients with OCD.

Method: Nine subjects with DSM-IV-defined OCD and no other current major psychiatric disorder participated in up to 4 single-dose exposures to psilocybin in doses ranging from sub-hallucinogenic to frankly hallucinogenic. Low (100 microg/kg), medium (200 microg/kg), and high (300 microg/kg) doses were assigned in that order, and a very low dose (25 microg/kg) was inserted randomly and in double-blind fashion at any time after the first dose. Testing days were separated by at least 1 week. Each session was conducted over an 8-hour period in a controlled environment in an outpatient clinic; subjects were then transferred to a psychiatric inpatient unit for overnight observation. The Yale-Brown Obsessive Compulsive Scale (YBOCS) and a visual analog scale measuring overall obsessive-compulsive symptom severity were administered at 0, 4, 8, and 24 hours post-ingestion. The Hallucinogen Rating Scale was administered at 8 hours, and vital signs were recorded at 0, 1, 4, 8, and 24 hours after ingestion. The study was conducted from November 2001 to November 2004.

Results: Nine subjects were administered a total of 29 psilocybin doses. One subject experienced transient hypertension without relation to anxiety or somatic symptoms, but no other significant adverse effects were observed. **Marked decreases in OCD symptoms of variable degrees were observed in all subjects during 1 or more of the testing sessions (23%-100% decrease in YBOCS score)**.

Repeated-measures analysis of variance for all YBOCS values revealed a significant main effect of time on Wilks lambda ($F = 9.86$, $df = 3,3$; $p = .046$), but no significant effect of dose ($F = 2.25$, $df = 3,3$; $p = .261$) or interaction of time and dose ($F = 0.923$, $df = 9,45$; $p = .515$). **Improvement generally lasted past the 24-hour timepoint.**

Conclusions: In a controlled clinical environment, psilocybin was safely used in subjects with OCD and was associated with acute reductions in core OCD symptoms in several subjects.

History of psychedelic use linked to decreased suicidal tendency
Those who did not use psychedelics in the past
And used opioids now, higher risk of suicide

The moderating effect of psychedelics on the prospective relationship between prescription opioid use and suicide risk among marginalized women

Methods: Data (2010-2017) were drawn from a community-based, prospective open cohort of marginalized women in Vancouver, Canada. Extended Cox regression analyses examined the moderating effect of psychedelic use on the association between other illicit drug use and incidence of suicidal ideation or attempt over follow-up.

Results: Of 340 women without suicidal ideation or attempt at baseline, 16% (n=53) reported a first suicidal episode during follow-up, with an incidence density of 4.63 per 100 person-years (95% confidence interval 3.53-6.07). In unadjusted analysis, **psychedelic use moderated the relationship between prescription opioid use and suicide risk**:

among women who did not use psychedelics, prescription opioid use increased the hazard of suicide (hazard ratio 2.91; 95% confidence interval 1.40-6.03)

whereas prescription opioid use was not associated with increased suicidal ideation or attempt among those who used psychedelics (hazard ratio 0.69; 95% confidence interval 0.27-1.73) (interaction term p-value: 0.016). **The moderating effect of psychedelics remained significant when adjusted for confounders** (interaction term p-value: 0.036).

Conclusions: Psychedelic use had a protective moderating effect on the relationship between prescription opioid use and suicide risk. In the context of a severe public health crisis around prescription opioids and lack of addiction services tailored to marginalized women, this study supports calls for innovative, evidence-based and trauma-informed interventions, including further research on the potential benefits of psychedelics

Does psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalised women in a Canadian setting

Objective: This study aimed to longitudinally investigate whether ever having used a psychedelic drug can have a protective effect on incidence of suicidality among marginalised women. **Design:** Longitudinal community-based cohort study. **Setting:** Data were drawn from a prospective, community-based cohort of marginalised women in Metro Vancouver, Canada.

Participants: 766 women completed the baseline questionnaire between January 2010 and August 2014. Participants who did not report suicidality at baseline and who completed at least one follow-up visit were included.

Main outcome measure: Extended Cox regression was used to **model predictors of new suicidality (suicide ideation or attempts) over 54-month follow-up.**

Results: Nearly half (46%; n=355) of participants reported prior suicidality and were thus excluded from the present analyses. **Of 290 women eligible at baseline, 11% (n=31) reported recent suicidality during follow-up,** with an incidence density of 4.42 per 100 person-years (95% CI 3.10 to 6.30).

In multivariable analysis, reported lifetime psychedelic drug use was associated with a 60% reduced hazard for suicidality (adjusted HR (AHR) 0.40; 95% CI 0.17 to 0.94).

Crystal methamphetamine use (AHR 3.25; 95% CI 1.47 to 7.21) and childhood abuse (AHR 3.54; 95% CI 1.49 to 8.40) remained independent predictors of suicidality.

Conclusion: The high rate of suicidality identified in this study is of major concern. Alongside emerging evidence on the potential of psychedelic-assisted therapy to treat some mental illness and addiction issues, our findings demonstrate that naturalistic psychedelic drug use is independently associated with reduced suicidality, while other illicit drug use and childhood trauma predispose women to suicidality. While observational, this study supports calls for further investigation of the therapeutic utility o psychedelic drugs in treating poor mental health and promoting mental wellness.

MushWomb Medicine

Psychedelics as a novel approach to treating autoimmune conditions

Caitlin Thompson [1], Attila Szabo [2]

Affiliations + expand
PMID: 33035575 DOI: 10.1016/j.imlet.2020.10.001
Free article

Abstract

With a rise in the incidence of autoimmune diseases (AiD), health care providers continue to seek out more efficacious treatment approaches for the AiD patient population. Classic serotonergic psychedelics have recently been gaining public and professional interest as novel interventions to a number of mental health afflictions. Psychedelics have also been shown to be able to modulate immune functions, however, while there has been great interest to researching into their psychotherapeutic applications, there has so far been very little exploration into the potential to treat inflammatory and immune-related diseases with these compounds. A handful of studies from a variety of fields suggest that psychedelics may offer a potential novel application in the treatment of pathologies related to autoimmunity. We propose that psychedelics hold the potential to attenuate or even resolve autoimmunity by targeting psychosomatic origins, maladaptive chronic stress responses, inflammatory pathways, immune modulation and enteric microbiome populations.

Keywords: Autoimmunity; Gut microbiota; Inflammation; Psychedelics; Psychoneuroendocrinology; Psychoneuroimmunology.

Table 1. Receptor modulatory and physiological effects of psychedelics.

Classic psychedelics	Receptors of interest in Autoimmune Disease	Resulting effect	References
LSD	5-HT2A (partial agonism)	TNFα, IL-6, IL-2	[59,110]
	TrK-B (agonism)	"BDNF, " mTOR	
Psilocybin	Trk-B (agonism)	"BDNF, " mTOR	[110]
DMT & 5-MeO-DMT	Sig1R (agonism)	"IL-10, IL-1β, IL-6, TNFα CXCL8/IL-8	[38,69,82,103 ,126]
	5-HT2A (agonism)	"BDNF, " mTOR	
	Trk-B (agonism)	Glu excitotoxicity	
		ROS damage	
		Cell apoptosis	
mescaline (peyote)	Trk-B (agonism)	"BDNF, " mTOR	[110,125]
		penicillin resistant staphylococcus bacteria	
ayahuasca (DMT & Harmala alkaloids)	5-HT2A	Cortisol	[99,110]
	Sig1R	"BDNF, " mTOR	
	Trk-B		

MushWomb Medicine

Lindsay Chimileski ND LAc RH(AHG)

Review > Immunol Lett. 2020 Dec;228:45-54. doi: 10.1016/j.imlet.2020.10.001. Epub 2020 Oct 7.

Psychedelics as a novel approach to treating autoimmune conditions

Caitlin Thompson [1], Attila Szabo [2]

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PMID: 33035575 DOI: 10.1016/j.imlet.2020.10.001

Abstract

With a rise in the incidence of autoimmune diseases (AiD), health care providers continue to seek out more efficacious treatment approaches for the AiD patient population. Classic serotonergic psychedelics have recently been gaining public and professional interest as novel interventions to a number of mental health afflictions. **Psychedelics have also been shown to be able to modulate immune functions, however, while there has been great interest to researching into their psychotherapeutic applications, there has so far been very little exploration into the potential to treat inflammatory and immune-related diseases with these compounds**
A handful of studies from a variety of fields suggest that psychedelics do indeed have effects in the body that may attenuate the outcome of AiD.

This literature review explores existing evidence that psychedelic compounds may offer a potential novel application in the treatment of pathologies related to autoimmunity.
We propose that psychedelics hold the potential to attenuate or even resolve autoimmunity by targeting psychosomatic origins, maladaptive chronic stress responses, inflammatory pathways, immune modulation and enteric microbiome populations.

2.1. The link between autoimmunity and mental disorders

The comorbidity between autoimmune conditions and mental and mood disorders, such as MDD, anxiety, schizophrenia, and bipolar disorder has become apparent in the last two decades [8,[23], [24], [25]]. There is a higher risk of developing clinical depression or mood disorders if one has been diagnosed with an autoimmune condition [24]. While there is certainly argument that the burden of having an autoimmune condition could contribute to MDD, **researchers suggest that depression and anxiety symptoms could perhaps be a result of autoimmune mechanisms and resulting inflammation occurring in the nervous system, or *via* dysregulated inflammatory cytokine loops between peripheral and brain-resident immune cells** [11,26]. Potentially by their immunomodulatory activity and in part through the mobilization of **cell-intrinsic neuroprotective mechanisms, psychedelics may represent a promising intervention for autoimmune-related depression and other mental illness.**

MushWomb Medicine

Lindsay Chimileski ND LAc RH(AHG)

Table 1
Receptor modulatory and physiological effects of psychedelics.

Classic psychedelics	Receptors of interest in Autoimmune Disease	Resulting effect	References
LSD	5-HT2A (partial agonism)	TNFα, IL-6, IL-2	[59,110]
	TrK-B (agonism)	"BDNF, " mTOR	
Psilocybin	Trk-B (agonism)	"BDNF, " mTOR	[110]
DMT & 5-MeO-DMT	Sig1R (agonism)	"IL-10, IL-1β, IL-6, TNFα CXCL8/IL-8	[38,69,82, 110,126]
	5-HT2A (agonism)	"BDNF, " mTOR	
	Trk-B (agonism)	Glu excitotoxicity	
		ROS damage	
		Cell apoptosis	
mescaline (peyote)	Trk-B (agonism)	"BDNF, " mTOR	[110,125]
		penicillin resistant staphylococcus bacteria	
ayahuasca (DMT & Harmala alkaloids)	5-HT2A	Cortisol	[99,110]
	Sig1R	"BDNF, " mTOR	
	Trk-B		
Non-classicpsychedelics	Receptors of interest in Autoimmune Disease	Resulting effect	References
Ketamine	NMDA Glu (antagonism)	"BDNF, " mTOR, Glu excitotoxicity IL-6, TNFα	[48,49,64, 65]
MDMA (in assisted psychotherapy)	VMAT, SERT	Amygdala response	[36,97]
		HPA-axis dysregulation	
Harmine/Harmaline	MAO (inhibitor)	"5-HT, NF-kB, HSV-2 "NK cell numbers/ activity, Glu excitotoxicity	[78,79, 106,123]
Ibogaine/ Noribogaine (metabolite)	5-HT2A (partial agonism)	"BDNF, " mTOR	[110]
	Sig1R (agonism)		
	TrK-B (agonism)		

mTOR action directly related to psychedelic-induced neuritogenesis, suggesting that BDNF and psychedelics possess a shared mechanism for promoting neuritogenesis through an mTOR-related process of protein synthesis in synaptogenesis

Likely directly related to 5-HT2A
receptor agonist activity of classic psychedelics, given that when ketanserin, a 5-HT2A antagonist, is administered the neuroplastic effects of DMT, LSD, and DOI are gone

Shown potential in interacting with neurogenic pathways, such as Tropomyosin receptor kinase B (Trk-B) and (mTOR) (the mammalian target of rapamycin), in an equivalent manner to the neurotrophin protein brain-derived neurotrophic factor (BDNF)

Review > Immunol Lett. 2020 Dec;228:45-54. doi: 10.1016/j.imlet.2020.10.001. Epub 2020 Oct 7.

Psychedelics as a novel approach to treating autoimmune conditions

Caitlin Thompson [1], Attila Szabo [2]

Affiliations + expand
PMID: 33035575 DOI: 10.1016/j.imlet.2020.10.001

Mu

Li

Meta-Analysis > J Psychopharmacol. 2019 Sep;33(9):1088-1101. doi: 10.1177/0269881119845793. Epub 2019 May 14.

Cessation and reduction in alcohol consumption and misuse after psychedelic use

Albert Garcia-Romeu [1], Alan K Davis [2], Fire Erowid [3], Earth Erowid [3], Roland R Griffiths [1 2], Matthew W Johnson [1]

Affiliations + expand
PMID: 31064460 DOI: 10.1177/0269881119845793

Abstract

Background: Meta-analysis of randomized studies using lysergic acid diethylamide (LSD) for alcohol use disorder (AUD) showed large, significant effects for LSD efficacy compared to control conditions. Clinical studies suggest potential anti-addiction effects of LSD and mechanistically-related classic psychedelics for alcohol and other substance use disorders.

Aims: To supplement clinical studies, reports of psychedelic use in naturalistic settings can provide further data regarding potential effects of psychedelics on alcohol use.

Methods: An anonymous online survey of individuals with prior AUD reporting cessation or reduction in alcohol use following psychedelic use in non-clinical settings.

Results: 343 respondents, mostly White (89%), males (78%), in the USA (60%) completed the survey. Participants reported seven years of problematic alcohol use on average before the psychedelic experience to which they attributed reduced alcohol consumption, with 72% meeting retrospective criteria for severe AUD. Most reported taking a moderate or high dose of LSD (38%) or psilocybin (36%), followed by significant reduction in alcohol consumption. **After the psychedelic experience 83% no longer met AUD criteria. Participants rated their psychedelic experience as highly meaningful and insightful, with 28% endorsing psychedelic-associated changes in life priorities or values as facilitating reduced alcohol misuse.** Greater psychedelic dose, insight, mystical-type effects, and personal meaning of experiences were associated with a greater reduction in alcohol consumption, controlling for prior alcohol consumption and related distress

Conclusions: Although results cannot demonstrate causality, they suggest that naturalistic psychedelic use may lead to cessation or reduction in problematic alcohol use, supporting further investigation of psychedelic-assisted treatment for AUD.

Keywords: Psychedelics; alcohol; hallucinogens; lysergic acid diethylamide (LSD); psilocybin.

Addiction and alcohol misuse disorders

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Participants reported seven years of problematic alcohol use on average before the psychedelic experience to which they attributed reduced alcohol consumption, with 72% meeting retrospective criteria for severe AUD.
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Greater psychedelic dose, insight, mystical-type effects, and personal meaning of experiences were associated with a greater reduction in alcohol consumption, controlling for prior alcohol consumption and related distress

Teachers to heal a broken society

MushWomb Medicine

Lindsay Chimileski ND LAc RH(AHG)

Clinical Trial > Am J Drug Alcohol Abuse. 2017 Jan;43(1):55-60. doi: 10.3109/00952990.2016.1170135. Epub 2016 Jul 21.

Long-term follow-up of psilocybin-facilitated smoking cessation

Matthew W Johnson [1], Albert Garcia-Romeu [1], Roland R Griffiths [1 2]

Affiliations + expand
PMID: 27441452 PMCID: PMC5641975 DOI: 10.3109/00952990.2016.1170135
Free PMC article

Abstract

Background: A recent open-label pilot study (N = 15) found that two to three moderate to high doses (20 and 30 mg/70 kg) of the serotonin 2A receptor agonist, **psilocybin, in combination with cognitive behavioral therapy (CBT) for smoking cessation, resulted in substantially higher 6-month smoking abstinence rates than are typically observed with other medications or CBT alone.**

Objectives: To assess long-term effects of a psilocybin-facilitated smoking cessation program at ≥12 months after psilocybin administration.

Methods: The present report describes biologically verified smoking abstinence outcomes of the previous pilot study at ≥12 months, and related data on subjective effects of psilocybin.

Results: All **15 participants completed a 12-month follow-up**, and 12 (80%) returned for a long-term (≥16 months) follow-up, with a mean interval of 30 months (range = 16-57 months) between target-quit date (i.e., first psilocybin session) and long-term follow-up. At 12-month follow-up, 10 participants (67%) were confirmed as smoking abstinent. **At long-term follow-up, nine participants (60%) were confirmed as smoking abstinent. At 12-month follow-up 13 participants (86.7%) rated their psilocybin experiences among the five most personally meaningful and spiritually significant experiences of their lives.**

Conclusion: These results suggest that in the context of a structured treatment program, psilocybin holds considerable promise in promoting long-term smoking abstinence. The present study adds to recent and historical evidence suggesting high success rates when using classic psychedelics in the treatment of addiction. Further research investigating psilocybin-facilitated treatment of substance use disorders is warranted.

They sell Nicotine gum and patch as "statistically significant" at 6-15%! and you have to keep using them as replacement vs.

2-3 high doses with CBT

Psilocybin and CBT therapy = 60% smoking abstinent at long term follow up

Fungi Wisdom Apprenticeship. Lindsay Chimileski ND LAc RH(AHG)

Mushrooms reset apathy to help us be more connected & empathetic humans

Clinical Trial > Neuropharmacology. 2018 Nov;142:263-269.
doi: 10.1016/j.neuropharm.2017.12.041. Epub 2017 Dec 27.

Increased amygdala responses to emotional faces after psilocybin for treatment-resistant depression

Leor Roseman [1], Lysia Demetriou [2], Matthew B Wall [3], David J Nutt [4], Robin L Carhart-Harris [4]

Affiliations + expand

PMID: 29288686 DOI: 10.1016/j.neuropharm.2017.12.041

Abstract

Recent evidence indicates that psilocybin with psychological support may be effective for treating depression. Some studies have found that patients with depression show heightened amygdala responses to fearful faces and there is reliable evidence that treatment with SSRIs attenuates amygdala responses (Ma, 2015). We hypothesized that amygdala responses to emotional faces would be altered post-treatment with psilocybin. In this open-label study, **20 individuals diagnosed with moderate to severe, treatment-resistant depression, underwent two separate dosing sessions with psilocybin.**

Psychological support was provided before, during and after these sessions and 19 completed fMRI scans one week prior to the first session and one day after the second and last.

Neutral, fearful and happy faces were presented in the scanner and analyses focused on the amygdala.

Group results revealed rapid and enduring improvements in depressive symptoms post psilocybin. Increased responses to fearful and happy faces were observed in the right amygdala post-treatment, and right amygdala increases to fearful versus neutral faces were predictive of clinical improvements at 1-week.

Psilocybin with psychological support was associated with increased amygdala responses to emotional stimuli, an opposite effect to previous findings with SSRIs.

This suggests fundamental differences in these treatments' therapeutic actions, **with SSRIs mitigating negative emotions and psilocybin allowing patients to confront and work through them**. Based on the present results, we propose that psilocybin with psychological support is a treatment approach that potentially revives emotional responsiveness in depression, enabling patients to reconnect with their emotions.

> J Psychopharmacol. 2018 Jul;32(7):749-755. doi: 10.1177/0269881118771782. Epub 2018 May 29.

Psychedelic use and intimate partner violence: The role of emotion regulation

Michelle S Thiessen [1], Zach Walsh [1], Brian M Bird [2], Adele Lafrance [3]

Affiliations + expand

PMID: 29807492 DOI: 10.1177/0269881118771782

Abstract

Background: Recent evidence suggests that psychedelic use predicts reduced perpetration of intimate partner violence among men involved in the criminal justice system. However, the extent to which this association generalizes to community samples has not been examined, and potential mechanisms underlying this association have not been directly explored.

Aims: The present study examined the association between lifetime psychedelic use and intimate partner violence among a community sample of men and women. The study also tested the extent to which the associations were mediated by improved emotion regulation.

Methods: We surveyed 1266 community members aged 16-70 (mean age=22.78, standard deviation =7.71) using an online questionnaire that queried substance use, emotional regulation, and intimate partner violence. Respondents were coded as psychedelic users if they reported one or more instance of using lysergic acid diethylamide and/or psilocybin mushrooms in their lifetime. Results/ outcomes: **Males reporting any experience using lysergic acid diethylamide and/or psilocybin mushrooms had decreased odds of perpetrating physical violence against their current partner (odds ratio=0.42, p<0.05).**

Furthermore, our analyses revealed that male psychedelic users reported better emotion regulation when compared to males with no history of psychedelic use. Better emotion regulation mediated the relationship between psychedelic use and lower perpetration of intimate partner violence. This relationship did not extend to females within our sample.

Conclusions/interpretation: These findings extend prior research showing a negative relationship between psychedelic use and intimate partner violence, and highlight the potential role of emotion regulation in this association.

TOOLS FOR BETTER EMOTIONAL REGULATION

To help our men

To help our women

Better regulated society?!

Less violence and crime for all

Teachers to heal a broken society

Silo Pharma's drug - SPU-21, arthritogenic joint homing peptides utilizing psilocybin - has demonstrated it significantly inhibited arthritic progression in the animal model, and the company is carrying out further studies at UMB.

Cybin, a Canadian life sciences startup focused on developing psychedelic pharmaceutical products to treat mental disorders, raised 45 million Canadian Dollars ($34 million) in a private placement,

Stamets is patenting using Psilocybin with lions mane and niacin

US 20180021326A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2018/0021326 A1**

Stamets (43) **Pub. Date: Jan. 25, 2018**

(54) **COMPOSITIONS AND METHODS FOR ENHANCING NEUROREGENERATION AND COGNITION BY COMBINING MUSHROOM EXTRACTS CONTAINING ACTIVE INGREDIENTS PSILOCIN OR PSILOCYBIN WITH ERINACINES OR HERICENONES ENHANCED WITH NIACIN**

(71) Applicant: **Paul Edward Stamets**, Shelton, WA (US)

(72) Inventor: **Paul Edward Stamets**, Shelton, WA (US)

(21) Appl. No.: **15/494,503**

(22) Filed: **Apr. 23, 2017**

Related U.S. Application Data

(60) Provisional application No. 62/365,982, filed on Jul. 23, 2016.

Publication Classification

(51) **Int. Cl.**

A61K 31/455	(2006.01)
A61K 31/675	(2006.01)
A61K 36/07	(2006.01)
A61K 31/4045	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/455*** (2013.01); ***A61K 31/4045*** (2013.01); ***A61K 31/675*** (2013.01); ***A61K 36/07*** (2013.01)

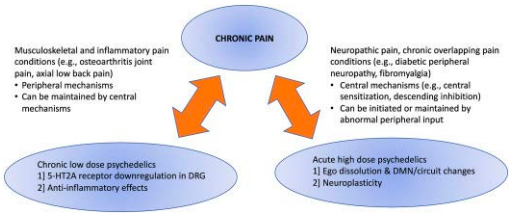
(57) **ABSTRACT**

Methods and compositions are disclosed for enhancing neurogenesis, resolving neuropathy and improving neurological health and functioning using fungal extracts and their active ingredients, including species of mushrooms and mycelia containing psilocybin and psilocin, combined with erinacines and hericenones or fungal extracts containing those active ingredients, with the addition of nicotinic acid. The compositions may optionally be combined with nervine plants.

https://psychedelichealth.co.uk/2022/06/24/silo-pharma-to-utilise-psilocybin-for-autoimmune-diseases/

Neuropharmacology

Are psychedelic medicines the reset for chronic pain? Preliminary findings and research needs



Review > Reg Anesth Pain Med. 2020 Jul;45(7):486-494. doi: 10.1136/rapm-2020-101273. Epub 2020 May 4.

Chronic pain and psychedelics: a review and proposed mechanism of action

Joel P Castellanos [1], Chris Woolley [2], Kelly Amanda Bruno [2], Fadel Zeidan [2], Adam Halberstadt [3], Timothy Furnish [2]

Affiliations + expand

PMID: 32371500 DOI: 10.1136/rapm-2020-101273

Abstract

The development of chronic pain is a complex mechanism that is still not fully understood. Multiple somatic and visceral afferent pain signals, when experienced over time, cause a strengthening of certain neural circuitry through peripheral and central sensitization, resulting in the physical and emotional perceptual chronic pain experience.

The mind-altering qualities of psychedelics have been attributed, through serotonin 2A (5-HT2A) receptor agonism, to 'reset' areas of functional connectivity (FC) in the brain that play prominent roles in many central neuropathic states.

Psychedelic substances have a generally favorable safety profile, especially when compared with opioid analgesics.

Clinical evidence to date for their use for chronic pain is limited; however, several studies and reports over the past 50 years have shown potential analgesic benefit in cancer pain, phantom limb pain and cluster headache.

While the mechanisms by which the classic psychedelics may provide analgesia are not clear, several possibilities exist given the similarity between 5-HT2A activation pathways of psychedelics and the nociceptive modulation pathways in humans.

Additionally, the alterations in FC seen with psychedelic use suggest a way that these agents could help reverse the changes in neural connections seen in chronic pain states.

Given the current state of the opioid epidemic and limited efficacy of non-opioid analgesics, it is time to consider further research on psychedelics as analgesics in order to improve the lives of patients with chronic pain conditions.

Clinical Trial

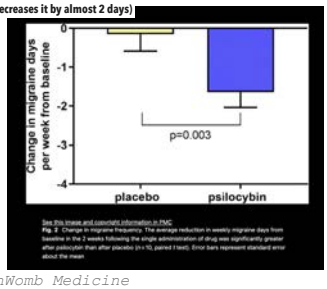
Exploratory Controlled Study of the Migraine-Suppressing Effects of Psilocybin

Subjects maintained headache diaries starting 2 weeks before the first session until 2 weeks after the second session. Physiological and psychological drug effects were monitored during sessions and several follow-up contacts with subjects were carried out to assure safety of study procedures.

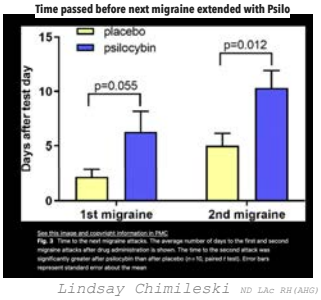
Ten subjects were included in the final analysis. **Over the 2-week period measured after single administration, the reduction in weekly migraine days from baseline was significantly greater after psilocybin** (mean, - 1.65 (95% CI: - 2.53 to - 0.77) days/week) than after placebo (- 0.15 (- 1.13 to 0.83) days/week; p = 0.003, t(9) = 4.11). *Changes in migraine frequency in the 2 weeks after psilocybin were not correlated with the intensity of acute psychotropic effects during drug administration.*

Psilocybin was well-tolerated; there were no unexpected or serious adverse events or withdrawals due to adverse events. This exploratory study suggests there is an enduring therapeutic effect in migraine headache after a single administration of psilocybin.

Migraine Frequency (note negative bars- placebo barely decreased frequency, while psilocybin decreases it by almost 2 days)



Time passed before next migraine extended with Psilo



Randomized Controlled Trial | Headache. 2022 Nov;62(10):1383-1394. doi: 10.1111/head.14420. Epub 2022 Nov 23.

Exploratory investigation of a patient-informed low-dose psilocybin pulse regimen in the suppression of cluster headache: Results from a randomized, double-blind, placebo-controlled trial

Emmanuelle A D Schindler [1 2], N Andrew Sewell [3 4], Christopher H Gottschalk [1], Christina Luddy [4 5], L Taylor Flynn [4 5], Yuliang Zhu [4 5], Hayley Lindsey [1 2], Brian P Pittman [6], Nicholas V Cozzi [4 7], Deepak C D'Souza [4 5]

Affiliations + expand

PMID: 36416492 DOI: 10.1111/head.14420

Abstract

Objective: Using a patient-informed regimen, we conducted an exploratory randomized, double-blind, placebo-controlled study to systematically investigate the effects of psilocybin in cluster headache.

14 final participants

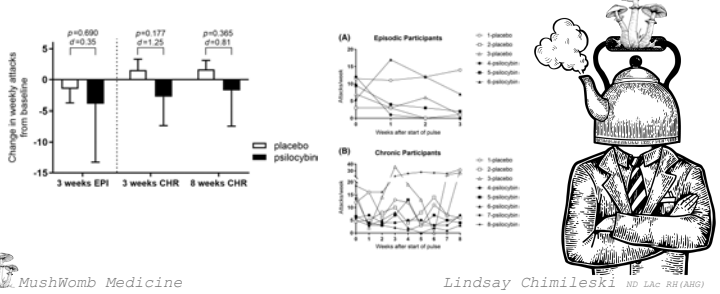
In the 3 weeks after the start of the pulse regimen, the change in cluster attack frequency was

Placebo 0.03 (95% confidence interval [CI] -2.6 to 2.6) attacks/week (baseline 8.9 [95% CI 3.8 to 14.0])

Psilocybin-3.2 (95% CI -8.3 to 1.9) attacks/week with (baseline 9.6 [95% CI 5.6 to 13.6]; p = 0.251).

Group difference in change from baseline had a moderate effect size (d = 0.69). The effect size was small in episodic participants (d = 0.35) but large in chronic participants (d = 1.25), which remained over the entire 8-week period measured (d = 0.81).

Changes in cluster attack frequency were not correlated with the intensity of acute psychotropic effects during psilocybin administration. Psilocybin was well-tolerated without any unexpected or serious adverse events.



MushWomb Medicine Lindsay Chimileski ND LAc RH(AHG)

J Psychoactive Drugs. 2023 Jan-Mar;55(1):73-84. doi: 10.1080/02791072.2021.2022817. Epub 2022 Jan 10.

Knowledge, Perceptions, and Use of Psychedelics among Individuals with Fibromyalgia

Nicolas G Glynos [1 2], Jennifer Pierce [3], Alan K Davis [4 5], Jenna McAfee [3], Kevin F Boehnke [3]

Affiliations + expand

PMID: 35001856 DOI: 10.1080/02791072.2021.2022817

Abstract Fibromyalgia (FM) is a difficult to treat chronic pain condition for which there is strong interest in alternative treatments. There is growing interest in the potential of psychedelic substances (e.g., psilocybin) in conjunction with psychotherapy to treat chronic pain. Via a cross-sectional, anonymous, online survey, we aimed to characterize knowledge, perceptions, and past use of serotonergic ("classic") and non-serotonergic psychedelics among a population of individuals with FM, and to investigate interest in psychedelic-based FM treatments.

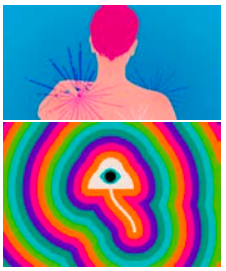
Among a North American population of **354 participants with FM, 29.9% reported past use of a psychedelic, with lysergic acid diethylamide (LSD) and psilocybin mushrooms being most commonly used.**

Perceptions of benefit from psychedelic use were generally neutral (59.4%) or positive (36.8%), with <3% reporting negative impacts on overall health or pain symptoms.

Among 12 participants who used psychedelics with intentions of treating chronic pain, 11 reported improved symptoms.

Regardless of past use, the majority of participants believed that psychedelics have potential for chronic pain treatments and would be willing to participate in a psychedelic-based clinical trial for their pain. These findings support the need for additional studies to understand the potential and effectiveness of psychedelic substances in managing FM symptoms.

Many surveys style studies gauging specific populations experience and interest in **participating psychedelic trials for their condition**



MushWomb Medicine Lindsay Chimileski ND LAc RH(AHG)

The Relationship between Mushroom Intake and Cognitive Performance

An Epidemiological Study in the European Investigation of Cancer-Norfolk Cohort (EPIC-Norfolk)

Study Design

Longitudinal 18-year study with three health check points measuring mushroom intake via food frequency questionnaires and cognitive performance assessment at the final health check.

Key Findings

At follow up, mushroom consumers displayed better cognitive performance than non-consumers across multiple cognitive domains. This relationship was observed to be dose-dependent, with those consuming 1 or more portions per week showing the highest cognitive scores.

Conclusions

Regular mushroom consumers displayed better cognitive performance across multiple domains.

Regular mushroom consumption may benefit cognitive function during aging. Dose-dependent relationship observed, with highest cognitive scores in those consuming 1+ portions weekly.

Cha S, Bell L, Williams CM. The Relationship between Mushroom Intake and Cognitive Performance: An Epidemiological Study in the European Investigation of Cancer-Norfolk Cohort (EPIC-Norfolk). Nutrients. 2024 Jan 25;16(3):353. doi: 10.3390/nu16030353. PMID: 38337638; PMCID: PMC10857520.

Psilocybin's Effects on Brain Networks and Therapeutic Potential

Therapeutic Effects and Neuroplasticity: A single dose of psilocybin (a psychedelic causing distortions of space-time perception and ego dissolution) produces rapid and persistent therapeutic effects in human clinical trials.

Study Design and Methodology

- **Study tracked individual-specific brain changes with longitudinal precision functional mapping** (approximately 18 MRI visits per participant).
- **Healthy adults were monitored before, during, and for 3 weeks after high-dose psilocybin (25 mg) and methylphenidate (40 mg), with follow-up psilocybin dose 6-12 months later.**

Acute Brain Network Effects

- **Psilocybin massively disrupted functional connectivity (FC) in cortex and subcortex, causing more than threefold greater change than methylphenidate.**
- FC changes resulted from brain desynchronization across spatial scales (areal, global), dissolving network distinctions by reducing correlations within and anticorrelations between networks.
- **Strongest psilocybin-driven FC changes occurred in the default mode network**, which connects to anterior hippocampus and is thought to create our sense of space, time and self.
- Individual differences in FC changes strongly linked to subjective psychedelic experience.
- Performing a perceptual task reduced psilocybin-driven FC changes.

Long-term Brain Changes and Implications

- Psilocybin caused persistent decrease in FC between anterior hippocampus and default mode network, lasting for weeks.
- Persistent reduction of hippocampal-default mode network connectivity may represent a neuroanatomical and mechanistic correlate of the proplasticity and therapeutic effects of psychedelics.

Siegel JS, Subramanian S, Perry D, Kay BP, Gordon EM, Laumann TO, Reneau TR, Metcalf NV, Chacko RV, Gratton C, Horan C, Krimmel SR, Shimony JS, Schweiger JA, Wong DF, Bender DA, Scheidter KM, Whiting FI, Padawer-Curry JA, Shinohara RT, Chen Y, Moser J, Yacoub E, Nelson SM, Vizioli L, Fair DA, Lenze EJ, Carhart-Harris R, Raison CL, Raichle ME, Snyder AZ, Nicol GE, Dosenbach NUF. Psilocybin desynchronizes the human brain. Nature. 2024 Aug;632(8023):131-138. doi: 10.1038/s41586-024-07624-5. Epub 2024 Jul 17. PMID: 39020167; PMCID: PMC11291293.

Psilocybin for Bipolar II Depression

A 12-week nonrandomized trial conducted at Sheppard Pratt Hospital showing promising results for treatment-resistant bipolar depression.

Study Population

15 participants

6 male, 9 female

18 to 65 years , Mean age: 37.8 years

with Bipolar II disorder in a current depressive episode lasting >3 months with

Documented insufficient benefit with at least 2 pharmacologic treatments during the current episode

Intervention

Single 25mg dose of synthetic psilocybin administered during an 8-hour session with therapist support.

Psychotropic medications discontinued ≥2 weeks before dosing with 3 preparation and 3 integration sessions.

Outcome Measures

Primary: Montgomery-Åsberg Depression Rating Scale (MADRS) at 3 weeks

Secondary: MADRS at 12 weeks, QIDS-SR (self-rated depression), Q-LES-Q-SF (quality of life)

Safety: CSSRS (suicidality), YMRS (mania symptoms)

Significant Results

Mean MADRS Depression reduction at week 3: -24.00 points (Cohen's d = 4.08, p < .001)

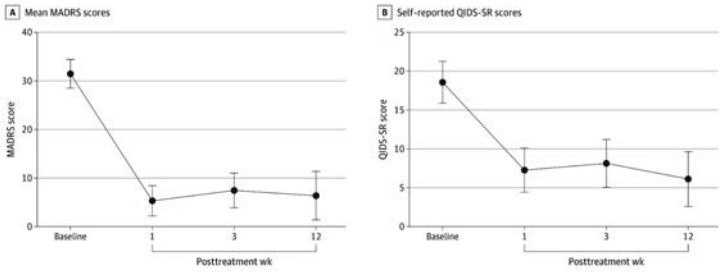
Week 3: 12/15 participants met response criteria, 11/15 met remission criteria

Study endpoint: 12/15 met both response and remission criteria

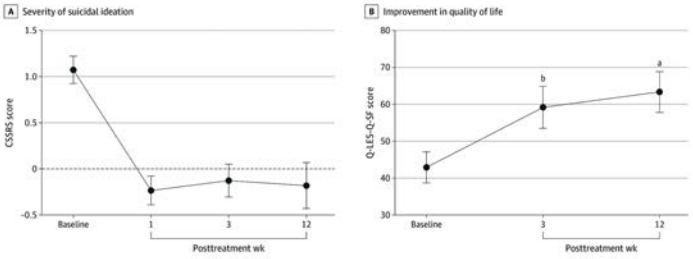
No significant changes in YMRS or CSSRS (safety measures)

Conclusion: Findings suggest efficacy and safety of psilocybin with psychotherapy in BDII depression, supporting further research of psychedelics in this population.

Aaronson ST, van der Vaart A, Miller T, LaPratt J, Swartz K, Shoultz A, Lauterbach M, Sackeim HA, Suppes T. Single-Dose Synthetic Psilocybin With Psychotherapy for Treatment-Resistant Bipolar Type II Major Depressive Episodes: A Nonrandomized Open-Label Trial. JAMA Psychiatry. 2024 Jun 1;81(6):555-562. doi: 10.1001/jamapsychiatry.2023.4685. Erratum in: JAMA Psychiatry. 2024 Jun 1;81(6):634. doi: 10.1001/jamapsychiatry.2024.0481. PMID: 38055270; PMCID: PMC10701666.



dr lindsay chimileski



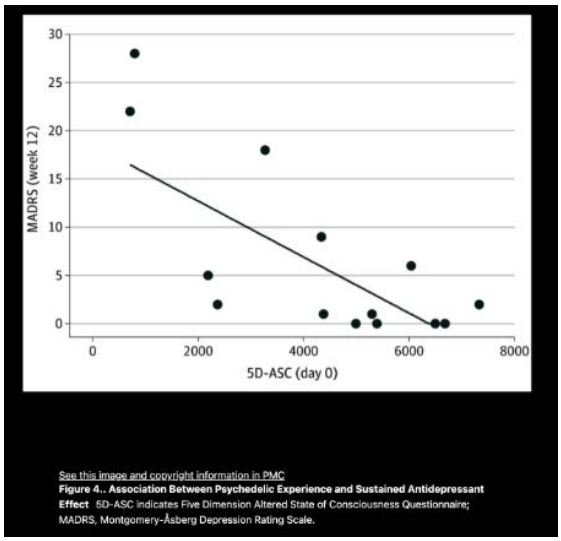


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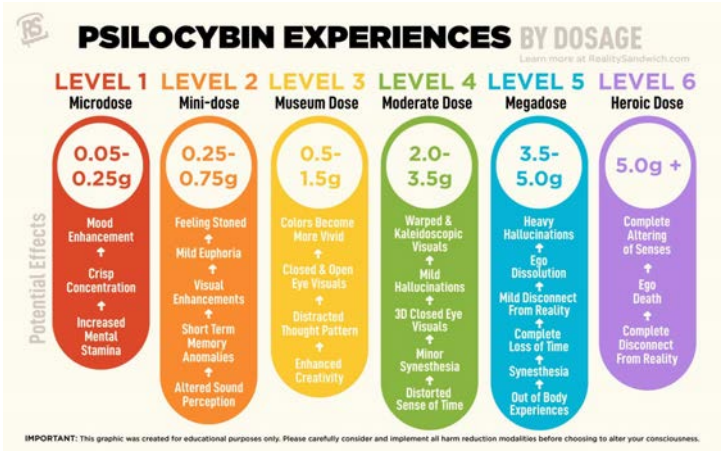
Figure 4.. Association Between Psychedelic Experience and Sustained Antidepressant Effect 5D-ASC indicates Five Dimension Altered State of Consciousness Questionnaire; MADRS, Montgomery-Åsberg Depression Rating Scale.



dr lindsay chimileski

Psychedelic Micro Dose, Harm Reduction and Integration Information & Resources

Micro dose Mushroom Range: 0.1-0.5g

Microdose.me
Microdosingsurvery.com

Month of, followed by break periods.
Fadiman Method 1 day on, 2 days off for
Stamets 4 days on, 3 days off

Stamets Stack

Introspection into your day / journaling/ surveys of your experience

Integration Counseling and Journal Prompts

Working with therapist/support team ongoingly etc.

zendoproject

ZENDO PROJECT

Create a safe space
Sitting, not guiding
Talking through, not down
Difficult is not necessarily bad

Flight Instructions
Encourage exploration within the visions
[and trip sitters to ensure safe physical environment]

Allow yourself to see what the medicine is showing you

1. **If you see a door, open it**
2. **If you see a staircase go up or down it**
3. **If you feel like you see a monster, face it instead of running**
4. **Remember to breathe**

Mushroom Medicine for Everyone. Lindsay Chimileski ND LAc RH(AHG)

Medicinal Mushroom Dosing
is going to vary greatly depending on your goals and the extraction forms you are using.

Price, digestion are the main limiting factors, very safe. Minimal digestive upset usually only adverse reaction.

Whole mushroom powder doses or dried range from 2 to 16 to 50 grams in divided doses. At least 6g in most for therapeutic dose.

Can be prescribed as a tea, soup or food (fresh or dried) too!

Tinctures, Standardized extracts can be dosed lower but more often than not, the goal is still to get to high doses when really using mushrooms as a targeted therapy. Still will be beneficial at lower doses though, just more for vitality, wellness, prevention side.

Chinese Pharmacopoeia Doses

Maitake 2 to 25 grams of whole powder daily.

Oysters: 3-9 grams daily

Chaga: Powder is 1-3grams daily

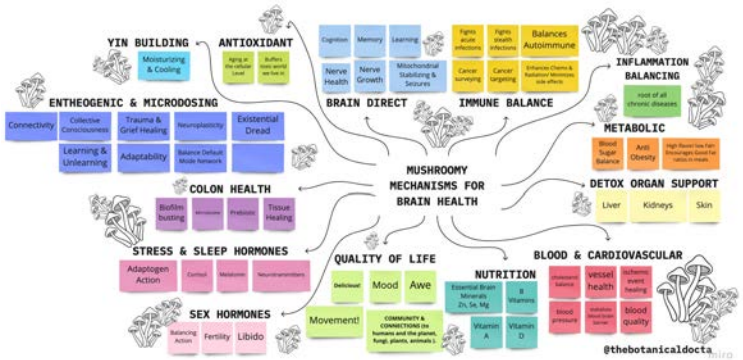
Resihi 6 to 12 grams daily

Lion's Mane: 25-50grams daily
250-750mg used in trials for cognitive function. 3-5g used in clinical trials, 5g fruiting body in soup. 500mg/kg.

Phellinus linteus: 30grams daily dried, if polysaccharide extract 2-3g/day is common.

Shiitake: 6–16 grams; fresh-about 90 grams

Doses from Christopher Hobbs Medicinal Mushrooms III, drugs.com medication database and the Chinese pharmacopoeia



All of our medicinal mushrooms are going to touch on these mechanisms—due to shared basic polysaccharides, antioxidants, minerals, triterpenoids and vitamins.

Of course there are some nuances to it and specific indications but in general they ALL will help brain health.

María Sabina Magdalena García
known as the "priestess of mushrooms,"

Likely the most famous Mexican healer to have ever lived. Her history and reputation led her to **serve as a bridge between the mystical and ritual worlds of her people, and the mystical exploration of the Western world.**
Born into the Mazatec ethnic group in **1894**, she came from a small town called Huautla de Jiménez, in the Sierra de Oaxaca, located in southern Mexico. Her father's family had already included several shamans. From a very young age, contact with them brought her closer to the region's traditional ceremonies, which included the intake of hallucinogenic mushrooms (know as "**holy children**") as a method of contact with divinity. She first tried the mushrooms at the age of eight. It's said that she intuitively developed a knowledge of the rituals and their healing power which, in her culture, was attributed to these mushrooms.
Among the Mazatec people, the most common healing method since prior to the colonial period, was the ritual intake of fungi of a species called Mexican Psilocybe and which grow only in a particular mountain range. When visited by someone with some physical or spiritual condition, **Sabina served as a guide on the patient's journey to, and return from, spiritual realms (along with a cure for the illness). To Sabina, mushrooms were an instrument for connecting dimensions and realities that happen in parallel. Because of their peculiarity, intensity, and various reports of effectiveness, Sabina's healing sessions became very popular in the Mexico of the early 1950s.**
Sabina's total dedication to the healing practice began around the middle of her life during that same decade. Her healing ceremonies with fungi included Mazatec chants, tobacco smoke, mezcal consumption, and ointments extracted from medicinal plants. Such rituals were made at night, for it was at this hour that healer was accompanied and guided by the stars to the kingdoms of the afterlife.
Over time, the story of María Sabina, her fame, and her mystery, caught the attention of media and personalities from many parts of the world and from other disciplines. **One of the first was an American, Robert Gordon Wasson, an economist by profession, best known for his studies in ethnobotany (the interaction between humans and plants). These he made with his wife, Valentina Pavlovna Guercken.** Among their various interests was the use of hallucinogenic plants in the rituals of ethnic groups from different parts of the world. Their interest led the couple to visit the Mazatec Sierra on several occasions, and here they heard of the famous healer from Huautla.
In 1955, Wasson and his wife convinced Sabina to receive them. Guided by her, they conducted several "veladas" (vigils) with the fungi, and they documented the entire experience in photos and recordings. They also obtained research samples of the fungi used in the sessions. Two years later, in 1957, an article written by Wasson was published in Life magazine. The text, accompanied by the images, described the research and chronicled the couple's experiences with Sabina. After its publication, visits by people from all over the world to the healer only multiplied. She was famous. In 1968, Wasson published the book The Wondrous Mushroom: Mycolatry in Mesoamerica in which he revealed in detail the fruits of his mycological and anthropological research in Mexico. Within this text, the main character is Sabina. At the time in the United States, the hippie movement –ever interested in psychedelia and its accompanying mystique– was at its cusp. This influenced the book's enormous popularity.
Domestic and foreign visits increased still further. Many of these visitors were interested purely in psychedelic recreational pursuits. They obviated the history of the ancient practices, and lost respect for the culture and religion of the Mazatec people. This displeased members of Sabina's community who argued that she was profiting from their tradition. Huautla de Jiménez was now constantly receiving national and foreign media figures, tourists, artists, intellectuals, anthropologists, researchers, and celebrities. **Among them, one might find Aldous Huxley, Alejandro Jodorowski, Carlos Castaneda, Albert Hofmann, John Lennon and Walt Disney.**

Full story: www.faena.com/aleph/maria-sabina-a-mostfascinating-mystical-healer

Artist: Rosenfeld Rafti
MushWomb Medicine

"Heal yourself with the light of the sun and the rays of the moon. With the sound of the river and the waterfall. With the swaying of the sea and the fluttering of birds. Heal yourself with mint, neem, and eucalyptus. Sweeten with lavender, rosemary, and chamomile. Hug yourself with the cocoa bean and a hint of cinnamon. Put love in tea instead of sugar and drink it looking at the stars. Heal yourself with the kisses that the wind gives you and the hugs of the rain. Stand strong with your bare feet on the ground and with everything that comes from it. Be smarter every day by listening to your intuition, looking at the world with your forehead. Jump, dance, sing, so that you live happier. Heal yourself, with beautiful love, and always remember,
You are the medicine."
-María Sabina-
Mexican curandera, medicine woman and poet.

Eat more mushrooms!