

DR. ANNA SITKOFF, ND

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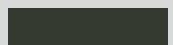
# MEDICINAL MUSHROOMS



 BIOCHEMISTRY - MEDICINAL USES - EXTRACTION METHODS - RECENT  
RESEARCH

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# Who am I?

- Reishi and Roses Blog 2015- present
  - Medicinal mushroom educator 2015 - present
  - Fomitopsis cajanderi research with Olivia Froehlich and Dr. Cynthia Wenner 2017-2019
  - Medicinal Mushrooms chapter in The Textbook of Natural Medicine 5th edition 2019
  - Scientific advisor/ mushroom consultant
  - Graduated from Bastyr University 2020
  - Co-founder of Lucidum Medicinals 2020
  - Currently practicing as a primary care physician in Port Townsend, WA
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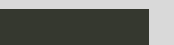
Disclosure statement:  
I am a co-founder of the medicinal  
mushroom company, Lucidum  
Medicinals, and I have worked as the  
scientific advisor for NAMMEX  
(North American Medicinal  
Mushroom Extracts).

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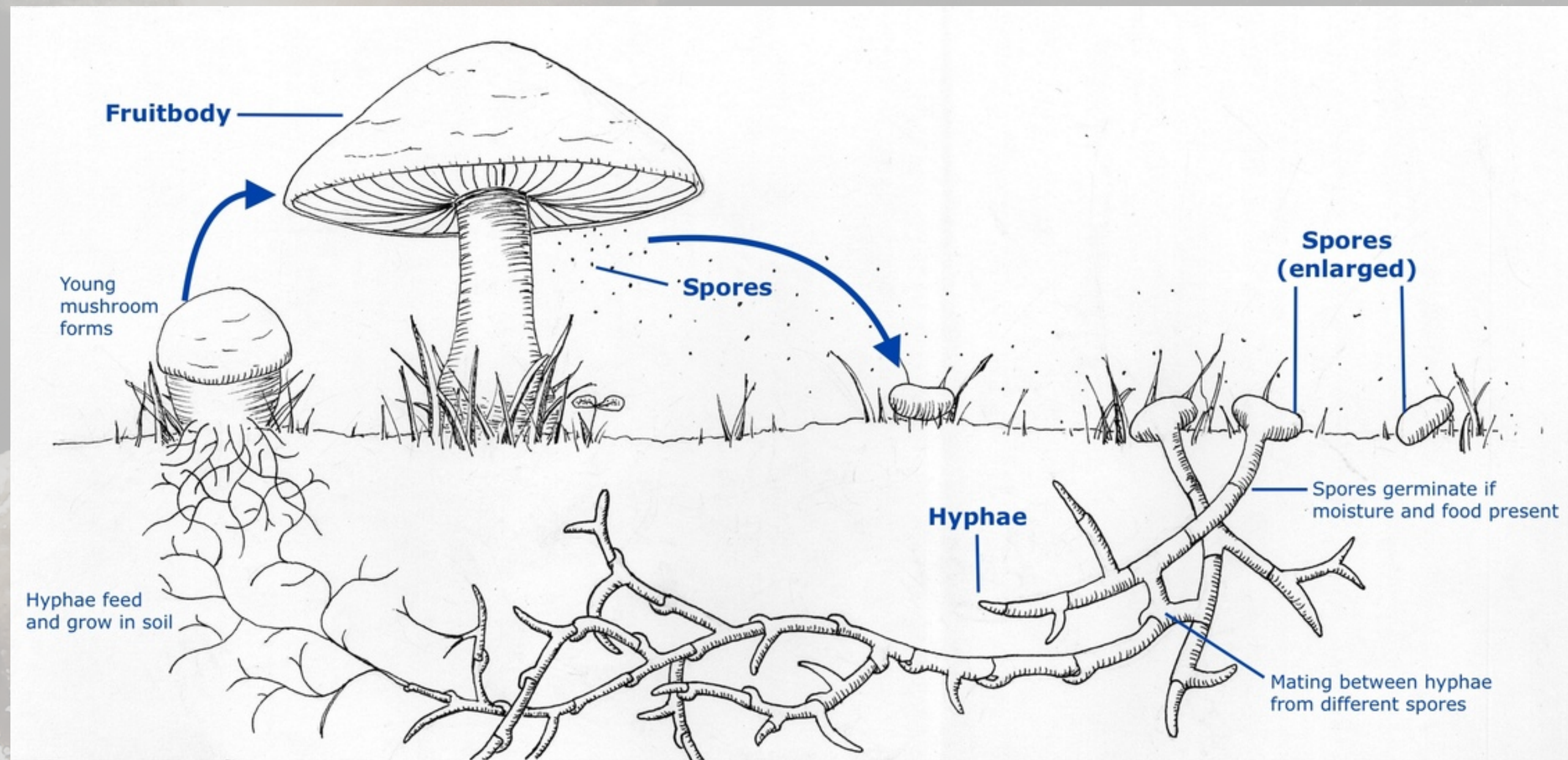
# Outline

- Fungal anatomy
- Ubiquitous mushroom constituents
- Mushroom constituents and human health
- Extraction methods
- Research review of common medicinal mushrooms





# Fungi Life Cycle





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# Mycelium

The mass of interwoven hyphae that forms the vegetative portion of the fungus and is often submerged in another substance like soil, grain or other organic matter.

Like the roots of the fungal organism

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# Myceliated Grain

When grain is used as the substrate the mycelium grows on, the final product is myceliated grain, NOT pure mycelium

**\*\***When extracts are made with myceliated grain, the mycelium is not removed from the grain.



A close-up photograph of a red mushroom with white spots, likely an Amanita muscaria, growing in a field of dry grass. The mushroom has a bright red cap covered in numerous small, white, scaly spots. Its stem is white and appears slightly textured. The background is a soft-focus field of dry, yellowish-brown grass. A thin horizontal line is positioned above the title.

# Mushroom

The fruiting body or macroscopic above ground portion of the greater fungal organism.

A small, solid black horizontal line located in the bottom right corner of the image.



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# Ubiquitous Mushroom Constituents

- Ergosterol
- Polysaccharides ( $\beta$  1,3/1,6-Glucan)
- Terpenes (triterpenes and sesquiterpenes)
- Ergothioneine

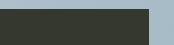


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# Ergosterol

Cholesterol:Humans :: Ergosterol:Mushrooms

- When mushrooms are exposed to UV light, ergosterol is converted to ergocalciferol, or vitamin D<sub>2</sub>.
- Vitamin D<sub>2</sub> is then converted to calcidiol in the liver and eventually calcitriol, our active vitamin D<sub>3</sub>, in the kidneys.
- Ergocalciferol-D<sub>2</sub> is not as bioavailable as D<sub>3</sub>, but can improve vitamin D deficiency PMID: 27192696



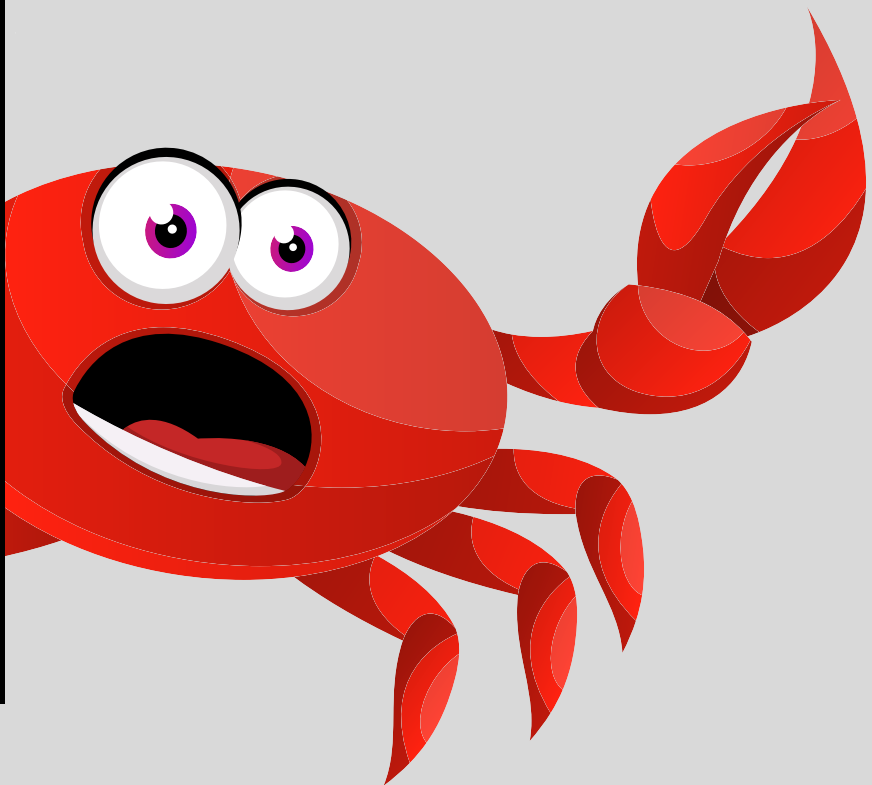


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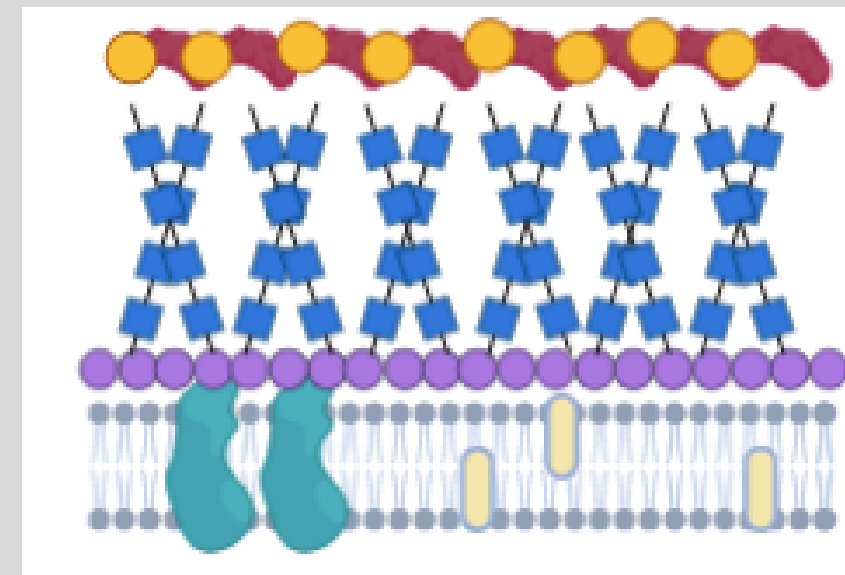
# Polysaccharides ( $\beta$ (1,3/1,6)-glucan)

Long sugar molecules that help to:

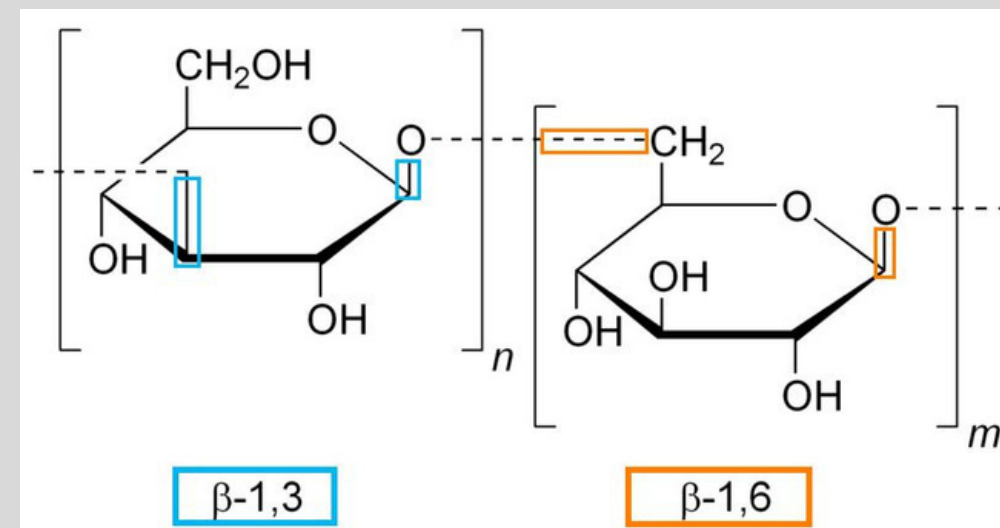
- Modulate the immune response PMID: 26770080
- Regulate blood sugar PMCID: PMC7830770
- Support the microbiome (intestinal and vaginal)  
PMID: 28353071 PMID: 28885559 PMID: 28302110



The mushroom cell wall



Extraction with hot water ,



$\beta$ -glucan



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# Polysaccharides - Immune-modulation

Modulation - stimulate and suppress different aspects of the immune system at the same time.

- Stimulate an anti-viral immune response
- Suppress inflammatory cytokines (chemicals that promote movement in the immune system)



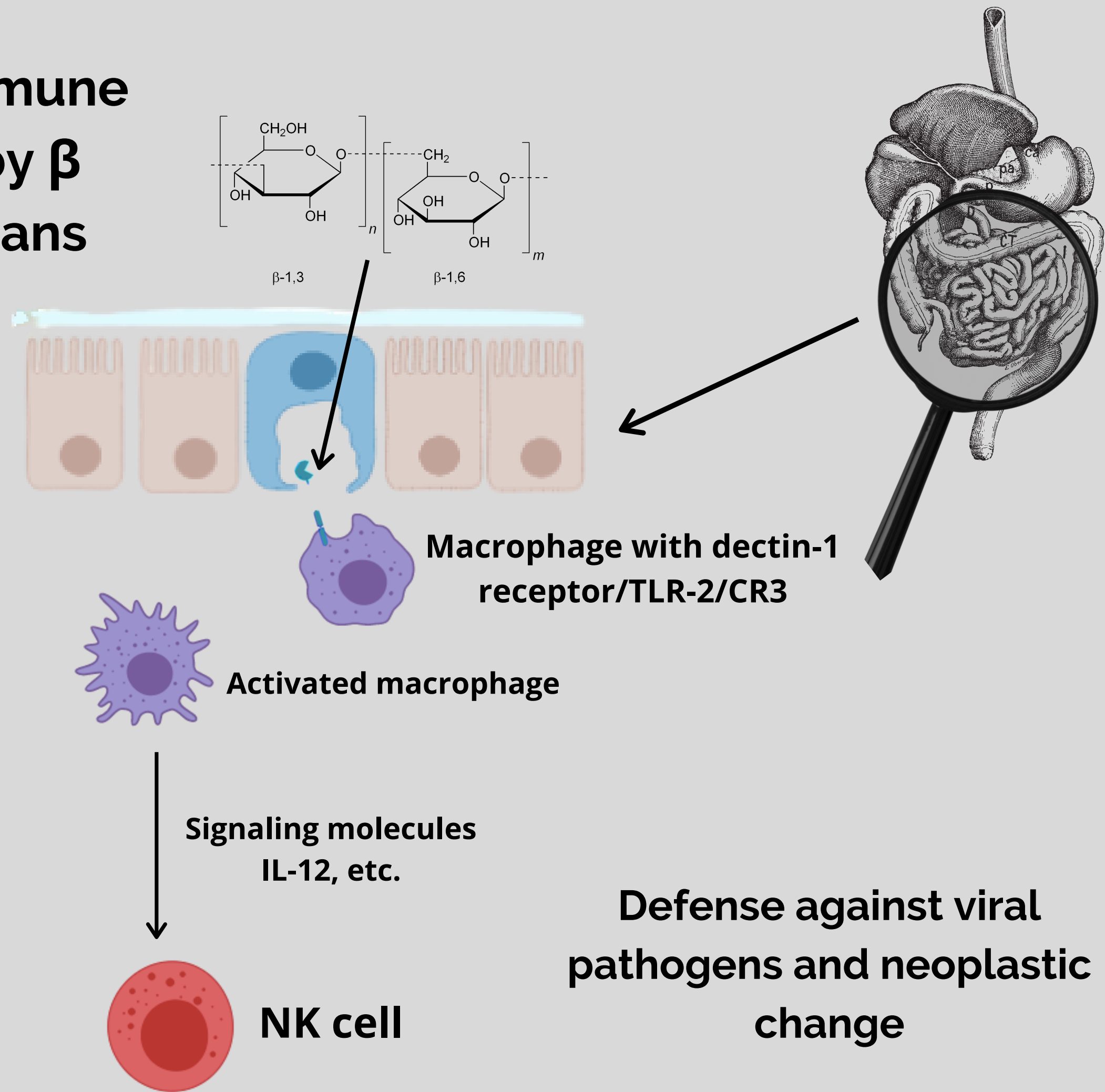
PMID: 26770080



Mushroom	Cytokine response	Immune response (simplified)
<b><i>Grifola frondosa</i></b> <b>(Maitake)</b>	IL-10	Anti-inflammatory
	IL-2, TNF- $\alpha$ , IFN- $\gamma$	Pro-inflammatory
<b><i>Lentinus edodes</i></b> <b>(Shitake)</b>	IL-4, IL-10	Anti-inflammatory
	TNF- $\alpha$ , IL-1	Pro-inflammatory

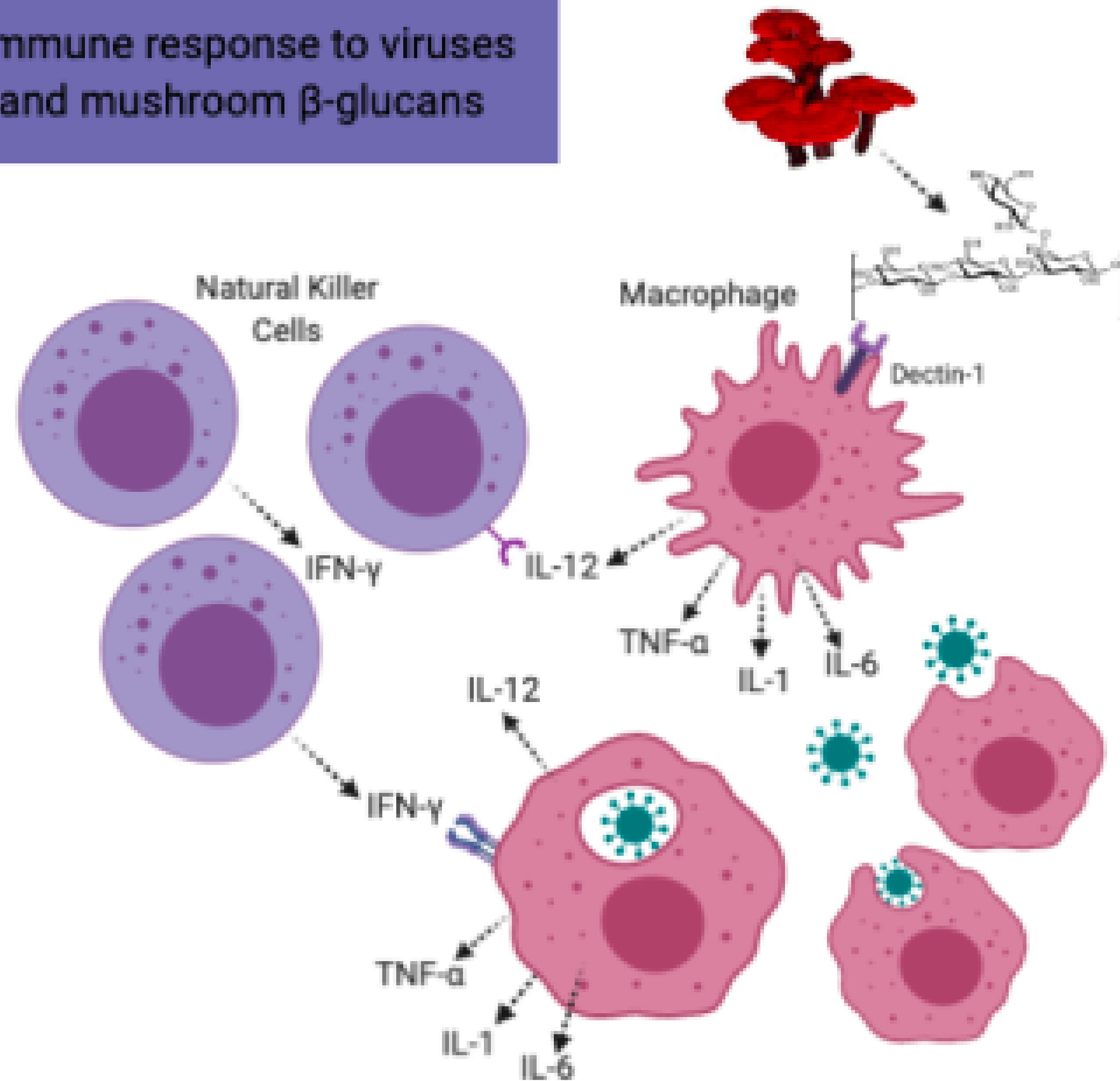


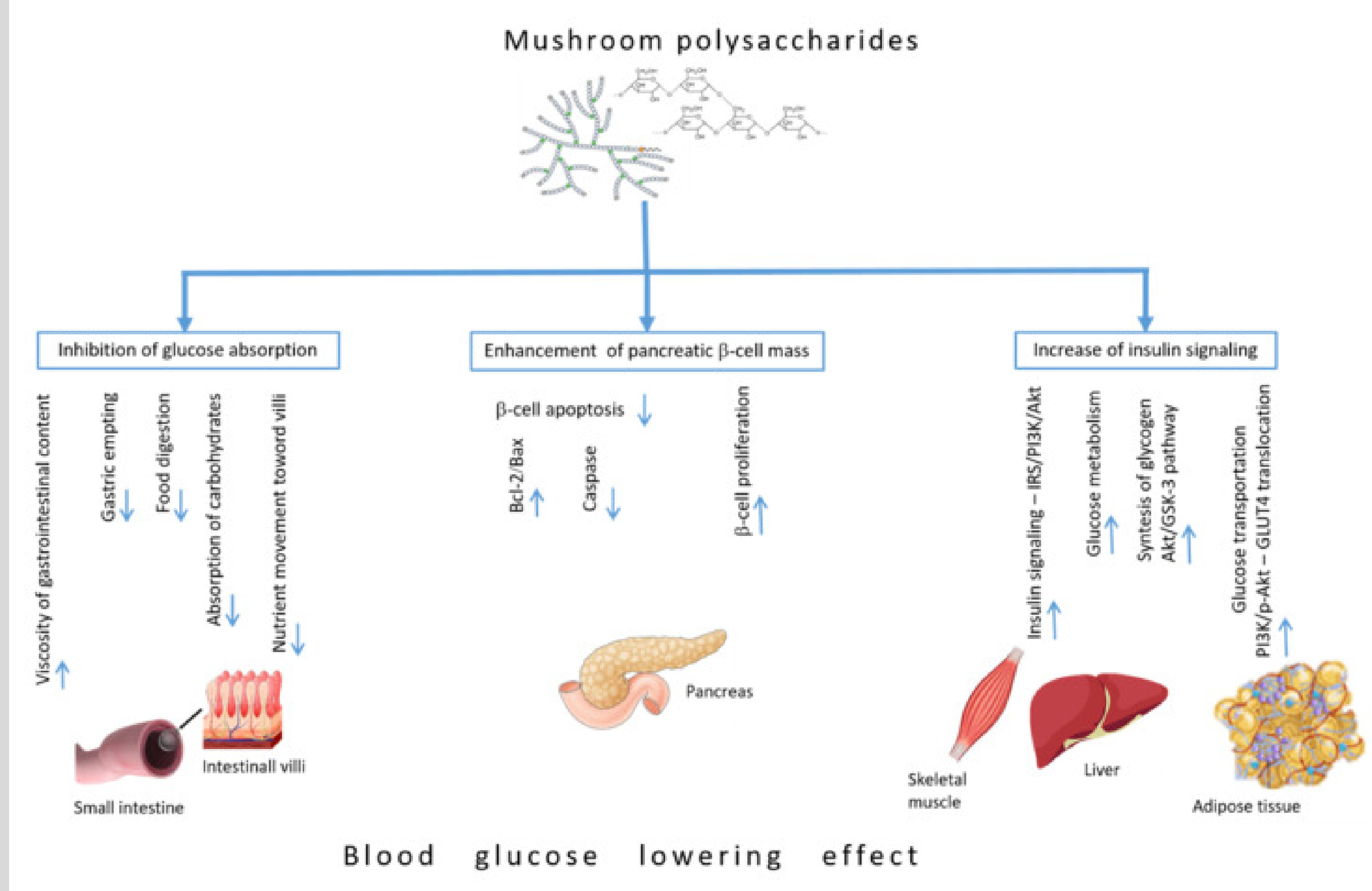
Example of immune stimulation by  $\beta$  (1,3/1,6) glucans





## Immune response to viruses and mushroom $\beta$ -glucans





**Aramabašić Jovanović J, Mihailović M, Uskoković A, Grdović N, Dinić S, Vidaković M. The Effects of Major Mushroom Bioactive Compounds on Mechanisms That Control Blood Glucose Level. J Fungi (Basel). 2021;7(1):58. Published 2021 Jan 16. doi:10.3390/jof7010058**



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# Polysaccharides – Prebiotic

Prebiotics = Food for probiotics

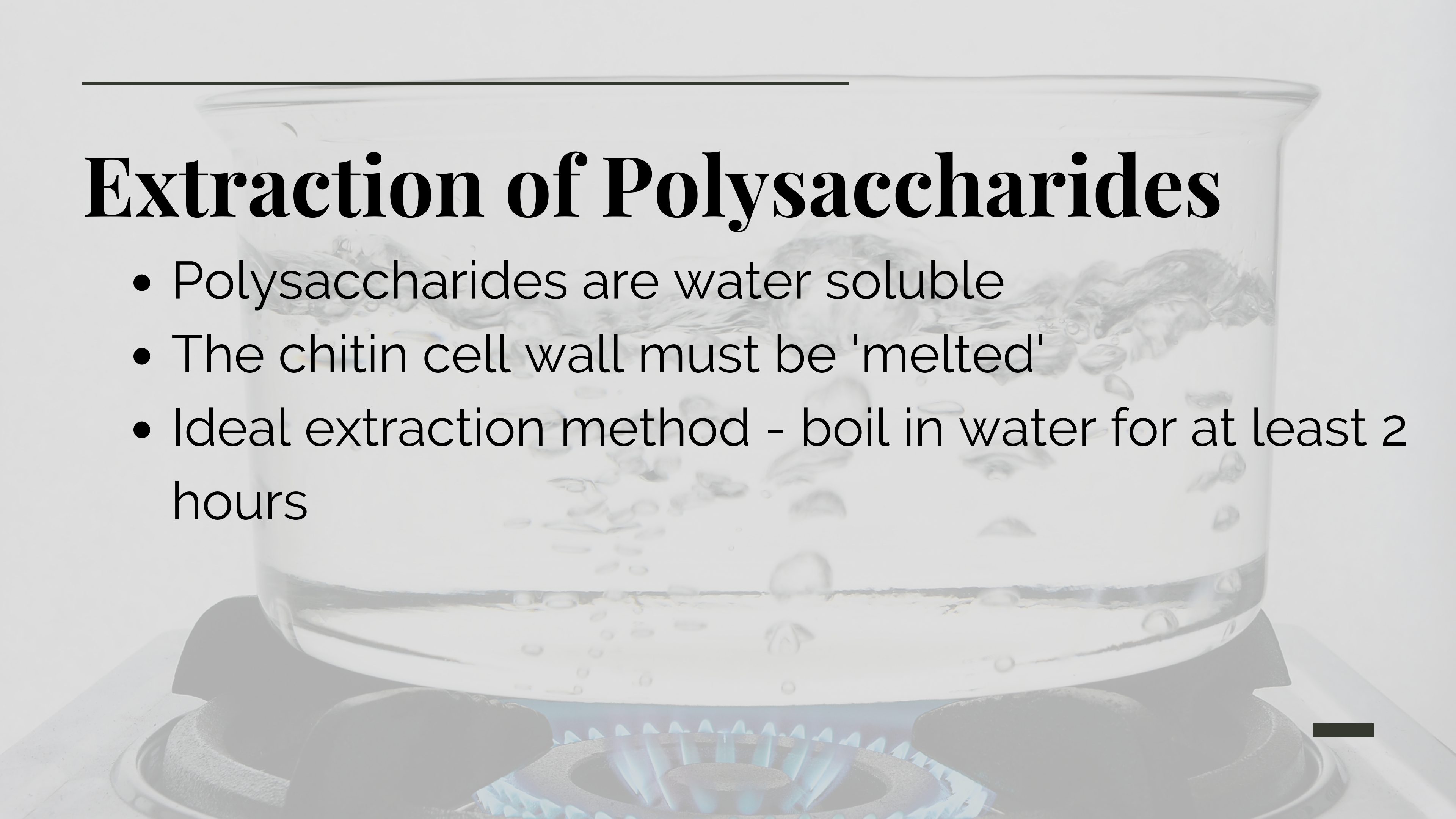
- The more food there is for the probiotics, the more probiotics there will be to compete out the 'bad' bacteria.
  - Polysaccharides from mushrooms increase *Lactobacillus* spp. and *Bifidobacterium* spp. while decreasing other non-beneficial bacteria  
PMID: 28885559
  - Polysaccharide gel made from turkey tail mycelium extracts (PSP) significantly increased *Lactobacillus* species in the vaginal biome  
PMID: 28302110
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# Extraction of Polysaccharides

- Polysaccharides are water soluble
- The chitin cell wall must be 'melted'
- Ideal extraction method - boil in water for at least 2 hours





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# Concentrated Mushroom Syrup

1. Collect mushrooms or purchase dried mushrooms from your local herb shop, slice thin and dry over night
2. Get the dry weight of the mushrooms in grams, then place mushrooms in crockpot or large soup pot and cover with water – so water covers by a few inches
3. let Simmer for a minimum of 2 hours, if using a crockpot it is great to simmer overnight
4. Press out mushrooms from decoction
5. Place aqueous extract (decocted liquid) in smaller soup pot and let simmer – this is where you want to keep a close eye on the process, stirring somewhere in between occasionally to avoid over simmering and burning
6. Simmer down until there is 30mL of extract (if you started with 300g) – the idea is that you have an equivalent of 10g dried mushroom material for every 1mL liquid. – 10:1
7. Take off the heat and add an equal amount of honey – if there is 30mL of extract, you will add 30mL of raw honey and mix thoroughly, now you have a 5:1 concentrated syrup.

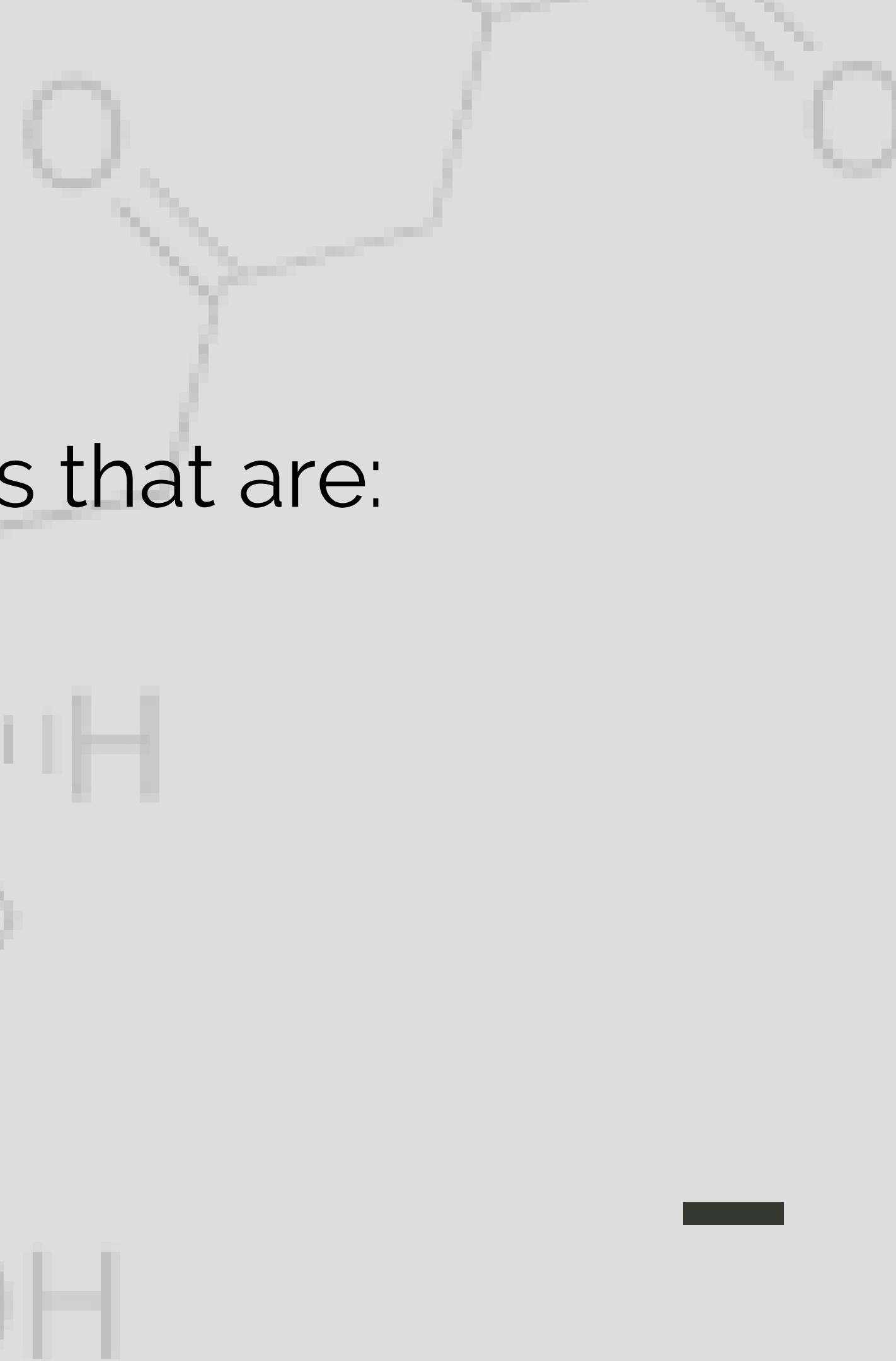


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# Triterpenes

Fat soluble secondary metabolites that are:

- Anti-neoplastic
- Anti-histamine
- Anti-viral
- Bitter



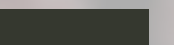


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# Triterpenes - Anti-neoplastic

Lanostane triterpene glycosides (Lanostanoids)

- Secondary metabolites that have been well-researched for their cytotoxic activity on a number of different cancer cell lines in-vitro and in-vivo animal trials.
- Promote apoptosis through G1 cell cycle arrest and P53 induction PMID: 23092389





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# Triterpenes - Anti-histamine

- Decrease type 1 hypersensitivity reactions PMID: 20079412
  - Decrease itchiness and swelling associated with allergy - internal or external

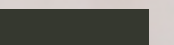




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# Triterpenes – Bitter

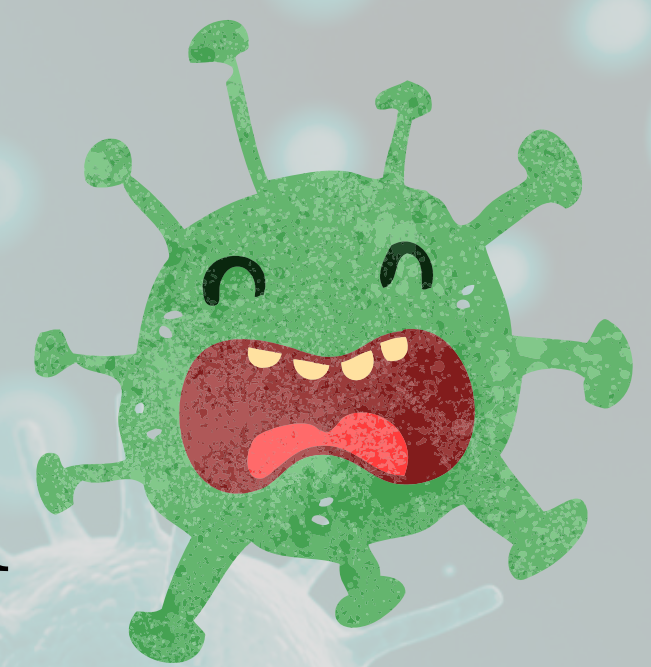
- Bitter receptors in the back of the tongue are innervated by the vagus nerve.
- When the vagus is stimulated from bitters this can bring you into a more relaxed state and support flow of digestive enzymes and stomach acid.





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# Sesquiterpenes - Anti-viral



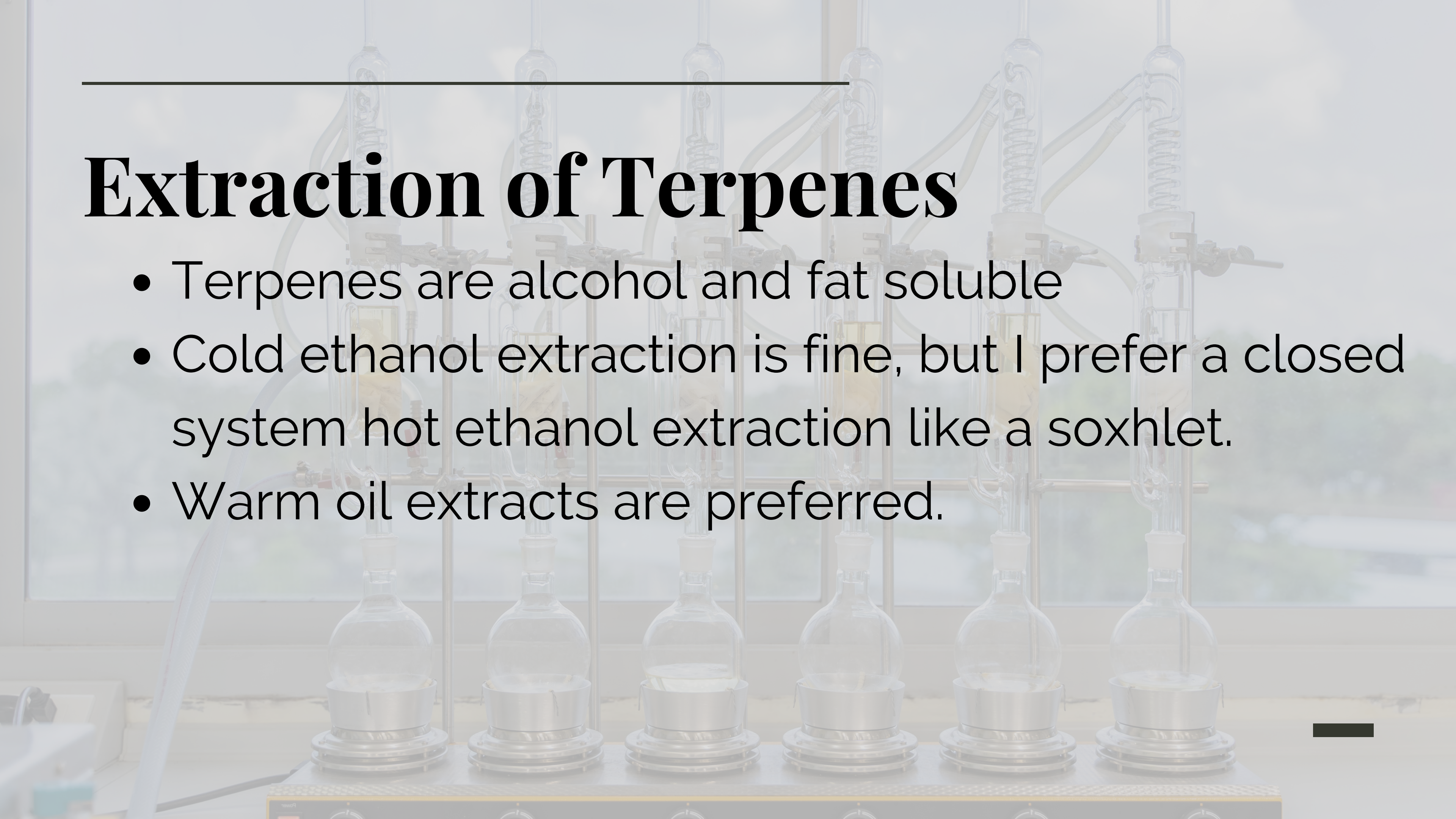
- Specifically from *Cryptoporus volvatus* (cryptic globe fungus) Cryptoporic acid
  - Neuraminidase inhibition
  - If neuraminidase is inhibited, the virus can not leave a cell to then infect other cells
  - Neuraminidase inhibition is the mechanism of action in OTC drugs like Tamiflu.



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# Extraction of Terpenes

- Terpenes are alcohol and fat soluble
- Cold ethanol extraction is fine, but I prefer a closed system hot ethanol extraction like a soxhlet.
- Warm oil extracts are preferred.





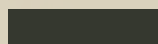
# Hot Ethanol Soxhlet Extraction





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# Mushroom Infused Oil

- In a Crock pot, cover dried mushroom slices with coconut oil or other preferred oil
  - Heat on warm over night
  - Strain out mushrooms from oil using a cheese cloth.
  - Let oil cool and use as a food oil or as a base for body care products.
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# Ergothioneine - The Elusive Amino Acid

Most abundant in oyster mushrooms

- Extremely bioavailable
- Anti-oxidant
  - Used as back-up to glutathione
  - Can be stored in cells for up to one month
- May help to prevent cognitive decline



# Could Ergothioneine Aid in the Treatment of Coronavirus Patients?

Irwin K. Cheah <sup>1,2</sup> and Barry Halliwell <sup>1,2,\*</sup>

<sup>1</sup> Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117596, Singapore; bchickm@nus.edu.sg

<sup>2</sup> Institute of Experimental Medicine, National University of Singapore, Singapore 117596, Singapore

Based on studies in a range of in vitro and in vivo models, ergothioneine has exhibited the ability to modulate inflammation, scavenge free radicals, protect against acute respiratory distress syndrome, prevent endothelial dysfunction, protect against ischemia and reperfusion injury, protect against neuronal damage, counteract iron dysregulation, hinder lung and liver fibrosis, and mitigate damage to the lungs, kidneys, liver, gastrointestinal tract, and testis, amongst many others. When compiled, this evidence suggests that ergothioneine has a potential application in the treatment of the underlying pathology of COVID-19.

patients develop a severe and critical illness, spurred on by excessive inflammation that can lead to respiratory or multiorgan failure. Numerous studies have established the unique array of cytoprotective properties of the dietary amino acid ergothioneine. Based on studies in a range of in vitro and in vivo models, ergothioneine has exhibited the ability to modulate inflammation, scavenge free radicals, protect against acute respiratory distress syndrome, prevent endothelial dysfunction, protect against ischemia and reperfusion injury, protect against neuronal damage, counteract iron dysregulation, hinder lung and liver fibrosis, and mitigate damage to the lungs, kidneys, liver, gastrointestinal tract, and testis, amongst many others. When compiled, this evidence suggests that ergothioneine has a potential application in the treatment of the underlying pathology



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# Comprehensive Extractions

- Mushroom powdered extract
- Double extracts





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# Mushroom Powdered Extract

1. Chop freshly harvested mushroom fruiting body
2. Further grind fruiting body in blender
3. Dehydrate over night
4. Place in pot and cover with water
5. Boil down until there is a thick mushroom slurry
6. Place slurry on dehydrator tray (or oven tray)
7. Dehydrate 12-24 hrs at 110 degrees F (if using oven – use lowest setting possible)
8. Grind down in high speed blender
9. If you desire a less fibrous extract, sift further for a finer powder





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# Double Extract

1. Make a mushroom decoction on stove top, Crock pot, or preferably an Instant pot. I prefer the Instant Pot method because this is a closed system (volatile compounds can't escape) and the process only takes 45 minutes. Instant Pot aqueous extracts seem to have considerably more polysaccharides than other extraction methods.
2. **With soxhlet** - squeeze extract from mushroom marc and set aside. Run soxhlet extractor for up to 8 hours with dried mushroom material and 190 proof alcohol.
  - a. Let cool, and combine ethanol extract with aqueous extract.
3. **Without soxhlet** - add aqueous extract and mushroom marc to large jar. Pour 190 proof alcohol over marc and aqueous extract until alcohol is taking up 30% of volume. Shake well and let sit for 2 weeks.
  - a. After 2 weeks, use a cheese cloth and potato ricer to squeeze out the double extract from the mushroom marc.



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# Common Mushrooms Used as Medicine

- Reishi
- Lion's mane
- Cordyceps
- Turkey tail
- Maitake
- Shiitake
- Oyster
- Chaga
- Tremella





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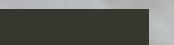
# Reishi

*Ganoderma lucidum*

"Herb of spiritual potency"

A review of human clinical trials

- Anti-viral
- Decreases lower urinary tract symptoms
- Cancer support
- Improves cortisol rhythm in women with chronic fatigue syndrome





# Control of oral human papillomavirus (HPV) by medicinal mushrooms, *Trametes versicolor* and *Ganoderma lucidum*: a preliminary clinical trial

Bruno Donatini <sup>1</sup>

Affiliations + expand

Oral HPV (16 and 18) was eradicated in 88% of patients in the treatment group while HPV was only eradicated in 5% of patients in the control group.

Dose: 400mg/day

Form: Fruiting body powders

Time: 2 months

*versicolor* (TV), *Ganoderma lucidum* (GL), and *Laetiporus sulphureus* (LS), on the clearance of oral human papillomavirus (HPV, serotypes 16 and 18). Among 472 patients who underwent oral swabs for gingivitis, 61 patients were positive for HPV16 or HPV18. Twenty patients were included in group 1 (LS) and 41 patients were included in group 2 (TV+GL) for 2 months. Polymerase chain reaction (PCR) for HPV was performed at inclusion and after 2 months. In group 1, the clearance was equal to 5% after 2 months of treatment. In group 2, the clearance was equal to 88% ( $P < 0.001$ ). The detection of HPV16 or HPV18 could become relevant in routine since positivity is frequent and



# Preliminary study of the applications of *Ganoderma lucidum* in chronic fatigue syndrome

Sukanya Soksawatmakhin and Wjit Boonyahotra

Department of Aging and Rehabilitation, School of Anti-Aging and Regenerative Medicine,  
Mae Fah Luang University, Chiang Rai, Thailand

Reishi supplementation helps to increase low cortisol levels and satisfaction in women with chronic fatigue syndrome

Dose: 2 g, divided into 0.5 g four times a day

Form: *G. lucidum* aqueous extract (form not disclosed)

Time: 12 weeks

Sukanya Soksawatmakhin  
Mae Fah Luang University

Hospital  
38/11-13 Asoke Place  
Building  
Sukhumvit 21  
Bangkok 10110  
Thailand

**E-mail**  
dr.sukunyasok@gmail.com

study on fatigue and quality of life of CFS. A total of 50 volunteers were randomly assigned to receive *G. lucidum* extract or placebo. Each volunteer was asked to respond to SF-12 questionnaires for quality of life and score the levels of fatigue and VAS, before and 4, 8 and 12 weeks after the first dose. Serum cortisol level was measured before and 12 weeks after the first dose. Satisfaction and side effects were also evaluated at the end of the study. In comparison to placebo, a significant increase in



# Effect of an extract of *Ganoderma lucidum* in men with lower urinary tract symptoms: a double-blind, placebo-controlled randomized and dose-ranging study

Masanori Noguchi<sup>1</sup>, Tatsuyuki Kakuma, Katsuro Tomiyasu, Yoshiko Kurita, Hiroko Kukihara, Fumiko Konishi, Shojiro Kawanoto, Kuniyoshi Shimizu, Ryudieiro Kondo, Rei Matsuoka

Affiliations: 1. Sapporo

Reishi improved lower urinary tract symptoms in men - significant improvement in IPSS scores

Dose: .06mg, 6mg, and 60mg/day (6mg was the superior dose)

Form: Fruiting body

Time: 8 weeks

lower urinary tract symptoms (LUTS).

**Methods:** We enrolled male volunteers (> or = 50 years) with an International Prostate Symptom Score (IPSS; questions 1-7) > or = 5 and a prostate-specific antigen (PSA) value < 4 ng/mL. Volunteers were randomized into groups of placebo (n = 12), *G. lucidum* of 0.6 mg (n = 12), 6 mg (n = 12) or 60 mg (n = 14), administered once daily. Efficacy was measured as a change from baseline in IPSS and the peak urine flow rate (Q(max)). Prostate volume and residual urine were estimated by ultrasonography, and blood tests, including PSA levels, were measured at baseline and at the end of the treatment.



## Effects of ganopoly (a Ganoderma lucidum polysaccharide extract) on the immune functions in advanced-stage cancer patients

Yihuai Gao<sup>1</sup>, Shufeng Zhou, Wenqi Jiang, Min Huang, Xihu Dai

Affiliations + expand

PMID: 12916709 DOI: [10.1081/imm-120022979](https://doi.org/10.1081/imm-120022979)

Ganoderma polysaccharides increase cancer specific immune cells in patients with advanced cancer. Significant increase in the mean plasma concentrations of interleukin (IL-2), IL-6, and interferon (IFN)-gamma

Dose: 1800 mg Ganopoly, three times daily orally before meals

Form: Polysaccharide extract

Time: 12 weeks

randomly on the immune function of advanced-stage cancer patients. Thirty-four advanced-stage cancer patients were entered onto this study, and treated with 1800 mg Ganopoly, three times daily orally before meals for 12 weeks. Immune parameters (cytokines, T cell subsets, mitotic response to phytohemagglutinin (PHA) and natural killer activity) were compared between baseline and after 12-week treatment. Thirty patients are assessable for their immune functions. Treatment of Ganopoly for 12 weeks resulted in a significant ( $P < 0.05$ ) increase in the mean plasma concentrations of interleukin (IL-2), IL-6, and interferon (IFN)-gamma, whereas the levels of IL-1 and tumor necrosis factor (TNF-alpha) were significantly ( $P < 0.05$ ) decreased. A marked variability among patients with advanced-stage cancer was observed in the numbers of each lymphocyte subset at baseline. The mean absolute number of CD56+ cells was significantly ( $P < 0.05$ )





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# Lion's mane

*Hericium erinaceus*

A review of the clinical trials

- Mood and memory support
- Gut inflammation
- Nerve repair (only rodent studies thus far)



A DOUBLE-BLIND STUDY ON EFFECTIVENESS OF  
HERICIUM ERINACEUS PERS THERAPY ON CHRONIC  
ATROPHIC GASTRITIS

A PRELIMINARY REPORT

Xu Cai-pu 徐采朴, Liu Wei-wen 刘为纹, Liu Feng-xian 柳风轩, Chen Shou-song 陈寿松

Liao Fu-quan 廖福权, Xu Zhao 徐 钊, Jiang Li-guo 姜利国, Wang Chuan 王 川

and Lu Xiu-hui 吕秀惠

Significant improvement in upper abdominal pain, dysplasia, and an overall reduction in inflammatory infiltration

Dose: 3 tablets (unknown how many grams - my guess is about 1.5g)

Form: Fruiting body

Timing: 3 months (the researches suggest longer treatment of 6 months)

(34 males and 16 females) with age ranging from 50 to 60 years, were randomly divided into two groups: Group I consisted of 25 patients, taking 3 tablets of HEP after each meal and Group II consisted of another 25 patients, taking only placebo in the same manner. The course of the treatment was 3 months. Gastro-

9 patients showed an increase of PAO, with an average of 7.3 mEq/L, while it was only 2.00 mEq/L in the controls.

Table 1. The changes of dysplasia in the two groups after treatment



# Peripheral Nerve Regeneration Following Crush Injury to Rat Peroneal Nerve by Aqueous Extract of Medicinal Mushroom *Hericium erinaceus* (Bull.: Fr) Pers. (Aphyllphoromycetideae)

[Kah-Hui Wong](#), <sup>1, 2</sup>, [Murali Naidu](#), <sup>2</sup> [Pamela David](#), <sup>2</sup> [Mahmood Ameen Abdulla](#), <sup>3</sup> [Noorlidah Abdullah](#), <sup>1</sup> [Umah Rani Kuppusamy](#), <sup>3</sup> and [Vikineswary Sabaratnam](#) <sup>1,\*</sup>

▶ [Author information](#) ▶ [Article notes](#) ▶ [Copyright and License information](#) ▶ [Disclaimer](#)

This article has been corrected. See [Evid Based Complement Alternat Med. 2018; 2018: 9820769](#).

Rats with crushed nerves who received lion's mane mushroom healed much faster than the rats who did not receive the lion's mane.

Dose: 10 or 20 mL/kg (1-2g/day)

Human dose equivalent - 972mg- 1.9g/day for a 60kg person

Form: Fruiting body aqueous extract

Time: 14 days

axotomized peroneal nerve injury in adult female Sprague-Dawley rats by daily oral administration. The aim was to investigate the possible use of this mushroom in the treatment of injured nerve. Functional recovery was assessed in behavioral experiment by walking track analysis. Peroneal functional index (PFI) was determined before surgery and after surgery as rats showed signs of recovery. Histological examinations were performed on peroneal nerve by immunofluorescence staining and neuromuscular junction by combined silver-cholinesterase stain. Analysis of PFI indicated that return of hind limb function occurred earlier in rats of aqueous extract or mecobalamin (positive control) group compared to negative control group. Regeneration of axons and reinnervation of motor endplates in extensor digitorum longus muscle in rats of aqueous extract or mecobalamin group developed better than in negative control group. These data suggest that daily oral administration of aqueous extract of *H. erinaceus* fresh fruiting



# Reduction of depression and anxiety by 4 weeks *Hericium erinaceus* intake

Mayumi Nagano <sup>1</sup>, Kuniyoshi Shimizu, Ryuichiro Kondo, Chickako Hayashi, Daigo Sato,  
Katsuyuki Kitagawa, Koichiro Ohnuki

Affiliations + expand

The women who consumed lion's mane cookies experienced significantly less anxiety and depression compared with the placebo.

Dose: 2g

Form: Fruiting body powder in cookies!

Time: 4 weeks

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



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

Koichiro Mori <sup>1</sup>, Satoshi Inatomi, Kenzi Ouchi, Yoshihito Azumi, Takashi Tsuchida

Affiliations + expand

PMID: 18844328 DOI: [10.1002/ptr.2634](https://doi.org/10.1002/ptr.2634)

Yamabushitake group showed significantly increased scores on a 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

Dose: Four 250mg tablets tid

Form: Fruiting body tablets

Time: 16 weeks

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 0, 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.



Randomized Controlled Trial > Biomed Res. 2019;40(4):125-131.

doi: 10.2220/biomedres.40.125.

## Improvement of cognitive functions by oral intake of *Hericium erinaceus*

Yuusuke Saitsu<sup>1</sup>, Akemi Nishide<sup>2</sup>, Kenji Kikushima<sup>3</sup>, Kunivoshi Shimizu<sup>4</sup>, Koichiro Ohnuki<sup>1</sup>

Affiliations + expand

The lion's mane group showed significant improvement in the mini mental status examination after 12 weeks

Dose: 3.2g daily

Form: Fruiting body capsules

Time: 12 weeks

blind, placebo-controlled parallel-group comparative study to evaluate the improvement of the cognitive functions by taking supplements containing fruiting body of *H. erinaceus* for 12 weeks.

We performed three kinds of tests: Mini Mental State Examination (MMSE), Benton visual retention test, and Standard verbal paired-associate learning test (S-PA). MMSE alone showed that oral intake of *H. erinaceus* significantly improved cognitive functions and prevented from the deterioration. We speculate that various chemical compounds, including hericenones, in the mushroom have multiple effects to the brain neural networks and improve cognitive functions. Oral intake of *H. erinaceus* is safe and convenient method for dementia prevention so far.



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# Cordyceps

*(Ophio)Cordyceps spp.*

A review of the clinical trials

- Anti-viral
- Endurance
- Kidney support





# Cordyceps militaris Enhances Cell-Mediated Immunity in Healthy Korean Men

Ho Joon Kang<sup>1</sup>, Hyun Wook Baik<sup>1</sup>, Sang Jung Kim<sup>1</sup>, Seong Gyu Lee<sup>2</sup>, Hong Yup Ahn<sup>3</sup>,  
Ju Sang Park<sup>1</sup>, Sang Jong Park<sup>1</sup>, Eun Jeong Jang<sup>1</sup>, Sang Woon Park<sup>1</sup>, Jin Young Choi<sup>1</sup>,  
Ji Hee Sung<sup>1</sup>, Seung Min Lee<sup>1</sup>

Affiliations + expand

PMID: 26284906 DOI: 10.1089/jmf.2014.3350

## Abstract

*Cordyceps militaris* is a mushroom traditionally used for diverse pharmaceutical purposes in East

After 4 weeks of treatment with cordyceps, there was a significant increase in anti-viral immunity (NK cells, IFN- $\gamma$ , and IL-2) compared to the control group

Dose: 1.5g/day (2 375mg bid)

Form: Cultivated fruiting body

Time: 4 Weeks

cytokine cluster (interferon [IFN]- $\gamma$ , interleukin [IL]-12, IL-2, and tumor necrosis factor [TNF]- $\alpha$ )

were measured, along with stability test, at weeks 0, 2, and 4. The *C. militaris* group showed a

statistically significant greater increase in NK200 ( $P = .0010$ ), lymphocyte PI ( $P \leq .0001$ ), IL-2 ( $P =$

$.0096$ ), and IFN- $\gamma$  ( $P = .0126$ ), compared with the basal level, than the placebo group. There was no

statistically significant adverse reaction. *C. militaris* enhanced the NK cell activity and lymphocyte

proliferation and partially increased Th1 cytokine secretion. Therefore, *C. militaris* is safe and

effective for enhancing cell-mediated immunity of healthy male adults.



# Improving Training Condition Assessment in Endurance Cyclists: Effects of *Ganoderma lucidum* and *Ophiocordyceps sinensis* Dietary Supplementation

Athletes supplementing with cordyceps and reishi mushrooms had significantly more free radical scavenging activity after a race than the placebo group. These results could be an indication that these mushrooms are also beneficial for recovery following endurance exercise.

Dose: OCS 1335mg and GL 1170mg

Form: Cordyceps sinensis mycelium and Ganoderma lucidum 'pure extract'

Time: 3 months



Epub 2016 Dec 21.

# Efficacy of *Cordyceps sinensis* as an adjunctive treatment in kidney transplant patients: A systematic-review and meta-analysis

Bee Yean Ong<sup>1</sup> Zariah Aziz<sup>2</sup>

Chronic kidney disease patients who took the cordyceps-based immunosuppressant therapy had significantly lower biomarkers related to kidney disease as well as lower infection rates

Dose: 3-12g/day

Form: Unknown

Time: 6-12 months

**Objectives:** *Cordyceps sinensis* (cordyceps) is a fungus used in traditional Chinese medicine as adjuvant immunosuppressive agent in patients with kidney transplant. This review evaluates current evidence on the efficacy and safety of natural and fermented cordyceps preparations in patients with kidney transplant.



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# Turkey tail

## *Trametes versicolor*

- Immune modulation
  - Constituents extracted from turkey tail mycelium (PSK and PSP) increase anti-viral and anti-tumor specific immunity.
  - The majority of research done on turkey tail is actually on PSK and PSP.
- Prebiotic
  - Constituents extracted from turkey tail mycelium (PSP) promote a healthy vaginal and gut microbiome. PMID: 25006989



# Clinical Studies of Immunomodulatory Activities of Yunzhi-Danshen in Patients with Nasopharyngeal Carcinoma

YI XI BAO, Ph.D.,<sup>1,2,4\*</sup> CHUN KWOK WONG, Ph.D.,<sup>2\*</sup> SING FAI LEUNG, M.D.,<sup>3</sup>  
ANTHONY TAK CHEUNG CHAN, M.D.,<sup>3</sup> POK WAI LI, B.Sc.,<sup>2</sup> ELIZA LAI YI WONG, Ph.D.,<sup>1</sup>  
PING CHUNG LEUNG, M.D.,<sup>1</sup> KWOK PUI FUNG, Ph.D.,<sup>1</sup> YI BING YIN, M.D.,<sup>4</sup>  
and CHRISTOPHER WAI KEI LAM, Ph.D.<sup>2</sup>

## ABSTRACT

**Objectives:** Nasopharyngeal carcinoma (NPC) is a prevalent tumor in Hong Kong. The immune system of such patients could be adversely affected during the course of conventional chemotherapy or radiotherapy. We

Turkey tail in combination with red sage root had immunomodulatory effects in patients with nasopharyngeal carcinoma and improved white blood cells while they underwent radiotherapy. Dose: Yunzhi and Danshen; each capsule contained 0.30 g of Yunzhi and 0.12 g of Danshen. Twelve capsules were taken orally daily. (3.6g Yunzhi and 1.44g Danshen)

Form: Fruiting body extract with red sage root

Time: 16 weeks

tumor necrosis factor receptor 2 was measured by enzyme-linked immunosorbent assay (ELISA). *Ex vivo* production of tumor necrosis factor- $\alpha$ , interleukin (IL)-6, and IL-10 in the whole blood assay culture supernatant was measured by ELISA.

**Results:** The decreases in percentage and absolute count of T lymphocytes in the TCM group were less than those in the placebo group after they took the capsules for 16 weeks (both  $p < 0.05$ ). Furthermore, the decreases in absolute count of T suppressor cells plus cytotoxic T lymphocytes, and T helper cells in the TCM group were significantly lower than those in the placebo group after they took the capsules for 16 weeks (both  $p < 0.05$ ).

**Conclusion:** These results suggest that Yunzhi-Danshen can exert an immunomodulating effect in alleviat-



## Research Article

# Phase 1 Clinical Trial of *Trametes versicolor* in Women with Breast Cancer

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Cynthia A. Wenner,<sup>2</sup> Juliette Gay,<sup>1</sup> Amy Putiri,<sup>2</sup> and Leanna J. Standish<sup>2</sup>

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Results indicated increases in lymphocyte counts (doses of 6 and 9 g/day), increased functional activity of natural killer cells (dose of 6 g/day), and increased numbers of CD8<sup>+</sup> T cells along with CD19<sup>+</sup> B cells

Dose: 6g

Form: Freeze-dried myceliated grain

Time: Changes seen at 2, 4, and 6 weeks

for 6 weeks after recent completion of radiotherapy. Eleven participants were recruited and nine women completed the study. Each cohort was comprised of three participants given one of three doses of *Tv* (3, 6, or 9 grams). Immune data was collected pre- and postradiation, at 3 on-treatment time points and after a 3-week washout. **Results.** Nine adverse events were reported (7 mild, 1 moderate, and 1 severe), suggesting that *Tv* was well tolerated. Immunological results indicated trends in (1) increased lymphocyte counts at 6 and 9 grams/day; (2) increased natural killer cell functional activity at 6 grams/day; (3) dose-related increases in CD8<sup>+</sup> T cells and CD19<sup>+</sup> B cells, but not CD4<sup>+</sup> T cells or CD16<sup>+</sup>56<sup>+</sup> NK cells. **Conclusion.** These findings show that up to 9 grams/day of a *Tv* preparation is safe and tolerable in women with breast cancer in the postprimary treatment setting. This *Tv* preparation may improve immune status in immunocompromised breast cancer patients following standard primary oncologic treatment.



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# Maitake

*Grifola frondosa*

A review of the clinical trials

- Blood sugar regulation
- Immune modulation





## Maitake Mushroom (*Grifola frondosa*) Extract Induces Ovulation in Patients with Polycystic Ovary Syndrome: A Possible Monotherapy and a Combination Therapy After Failure with First-Line Clomiphene Citrate

Ju-Fung Chen, MD, PhD,<sup>1</sup> Kunihiko Tominaga, MD, DPH, PhD,<sup>2</sup> Toshiaki Sato, MD, PhD,<sup>3</sup>  
Hideo Anzai, BS, BS, RPh,<sup>4</sup> and Ryo Matsuoka, MD, PhD<sup>5</sup>

The ovulation rates were 76.9% for the Maitake patients and 93.5% for the CC patients, while combination therapy increased the ovulation rate to 87%. "The present study suggests that maitake alone may induce ovulation in PCOS patients and may be useful as an adjunct therapy for patients who failed first-line CC treatment."

Dose: 18mg MSX + 250mg of dried maitake, 3 tablets tid

162mg MSX + 2.25g dried maitake/day

Form: MSX and fruiting body

Time: 3 months

**Results:** Twenty-six (26) patients in the MSX group and 31 in the CC group were evaluated for ovulation. The ovulation rates for MSX and CC were as follows: 76.9% (20/26) and 93.5% (29/31), respectively by the patients (MSX) and 41.7% (22/53) and 60.0% (50/83), respectively, by the cycles ( $p = 0.0006$ ). In the combination therapy, 7 of 7 patients who failed in MSX monotherapy and 6 of 8 patients who failed in CC monotherapy showed ovulation.



# A phase I/II trial of a polysaccharide extract from *Grifola frondosa* (Maitake mushroom) in breast cancer patients: immunological effects

Gary Deng · Hong Lin · Andrew Seidman · Monica Fornier · Gabriella D'Andrea · Kathleen Wesa · Simon Yeung · Susanna Cunningham-Rundles · Andrew J. Vickers · Barrie Cassileth

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© Springer-Verlag 2009

## Abstract

Oral administration of a polysaccharide extract from maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood

Dose: 5 mg/kg bid

Form: Polysaccharide extract from fruiting body

Time: 3 weeks

treatment, were enrolled sequentially in five cohorts. Maitake liquid extract was taken orally at 0.1, 0.5, 1.5, 3, or 5 mg/kg twice daily for 3 weeks. Peripheral blood was collected at days -7, 0 (prior to the first dosing), 7, 14, and 21 for ex vivo analyses. The primary endpoints were safety and tolerability.

G. Deng (✉) · K. Wesa · S. Yeung · B. Cassileth  
Integrative Medicine Service,

**Results** No dose-limiting toxicity was encountered. Two

compared with both high and low doses.

**Conclusions** Oral administration of a polysaccharide extract from maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood. Cancer patients should be made aware of the fact that botanical agents produce more complex effects than assumed, and may depress as well as enhance immune function.



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# Shiitake

*lentinula edodes*

A review of the clinical trials

- Immune modulation





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

Xiaoshuang Dai <sup>1</sup>, Joy M Stanilka <sup>1</sup>, Cheryl A Rowe <sup>1</sup>, Elizabethe A Esteves <sup>2</sup>, Carmelo Nieves Jr <sup>1</sup>, Samuel J Spaiser <sup>1</sup>, Mary C Christman <sup>3</sup>, Bobbi Langkamp-Henken <sup>1</sup>, Susan S Percival <sup>1</sup>

Affiliations + expand

PMID: 25999155 DOI: 10.1093/ajcn/87.3.572.1.2014.050001

Eating the Shiitake for four weeks led to increased proliferation of anti-viral immune cells, decreased inflammation markers and increased immuno-modulating cytokines

Dose: 5g and 10g

Form: Dried mushrooms

Time: 4 weeks

...whether L. edodes consumption would improve 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



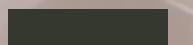
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# Oyster

## *Pleurotus ostreatus*

A review of the clinical trials

- Respiratory support and anti-allergic (decreases eosinophilia)
- High in ergothioneine!
- Lowers cholesterol
- Topical creams help to relieve atopic dermatitis





# Preventive effect of pleuran (β-glucan from Pleurotus ostreatus) in children with recurrent respiratory tract infections- open-label prospective study.

Jaroslav Pasnik<sup>1</sup>, Agnieszka Ślemp<sup>2</sup>, Agnieszka Cywinska-Bernas<sup>1</sup>, Krzysztof Zeman<sup>1</sup> and Milos Jesenak<sup>3</sup>

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There are multiple studies that have shown children treated with pleuran (polysaccharide from oyster mushroom) experienced a significant reduction in the frequency of recurrent respiratory tract infections and missed less days of school.

Dose: 10 mg of pleuran and 10 mg of vitamin C in 1 mL of syrup) per 5 kg of body weight every morning on empty stomach

Form: Pleuran + vitamin C syrup

Time: 3 months

syrup containing pleuran (insoluble β-glucan isolated from Pleurotus ostreatus) on general respiratory morbidity comparing previous year with the same season during the study. Results: Supplementation of pleuran (10 mg/kg) significantly decreased the total number of respiratory tract infections during the treatment and subsequent follow-up period compared to the same period of the previous year ( $4.18 \pm 2.132$  vs.  $8.71 \pm 1.89$ ;  $p < 0.001$ ). In detail, the number of various types of respiratory tract infections (otitis, laryngitis, bronchitis and flu) was also significantly reduced ( $p < 0.01$  for all subtypes of infections). Moreover, a reduction in the number of day-off in kindergarten and school was also noticed. The syrup was well tolerated and no serious adverse effects were observed. Conclusion: Our study supports the use of pleuran in the complementary treatment and preventions of RRTIs in children. β-glucans seem to be an effective and safe tool in the management of RRTIs.



## Effect of the Intake of Oyster Mushrooms (*Pleurotus ostreatus*) on Cardiometabolic Parameters—A Systematic Review of Clinical Trials

[Lisa Dicks](#) and [Sabine Ellinger](#)\*

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This article has been [cited by](#) other articles in PMC.

### Abstract

Cardiometabolic diseases are a leading global health challenge. Their incidence as well as progression is

Standardized blood concentrations of lipid parameters and oxidized LDLs were measured at baseline and after 21 days. Treatment with oyster mushroom soup decreased both triacylglycerol and oxidized low density lipoprotein levels significantly

Dose: 30g/day

Form: Whole dried oyster mushrooms in soup

Time: 3 weeks

high or unclear due to methodological weaknesses and/or inadequate reporting. Thus, *P. ostreatus* intake may improve cardiometabolic health, but evidence for this is low. Hence, further clinical trials with an adequate study design are warranted to validate these suggestions.

**Keywords:** edible mushrooms, *Pleurotus ostreatus*, oyster mushrooms, cardiometabolic health, glucose metabolism, lipids, blood pressure, postprandial, chronic intake, human intervention studies



# $\beta$ -Glucan-based cream (containing pleuran isolated from pleurotus ostreatus) in supportive treatment of mild-to-moderate atopic dermatitis

Milos Jesenak <sup>1</sup>, Slavomir Urbancek <sup>2</sup>, Juraj Majtan <sup>3 4</sup>, Peter Banovcin <sup>1</sup>, Jana Hercogova <sup>5</sup>

Affiliations + expand

PMID: 26654776 DOI: [10.3109/09546634.2015.1117565](https://doi.org/10.3109/09546634.2015.1117565)

## Abstract

**Background:** Atopic dermatitis (AD) is one of the most common chronic inflammatory skin

The patients applied the cream on one segment of the body with atopic dermatitis and a standard emollient on another atopic dermatitis segment. On the application site there was a significant decrease in the number of days and severity of atopic dermatitis.

Dose: 2-3 applications daily

Form: Pleuran based cream

Time: benefits were seen within a few days

side, significant decline in the number of days with AD exacerbation and its severity was observed. Moreover, the subjects experienced decline of pruritus on the  $\beta$ -glucan half of the body (VAS score: 1.00 vs. 1.50,  $p < 0.001$ ). During the study, the continual and significant decline of EASI scores on the site of  $\beta$ -glucan application was observed (V4: 1.57 vs. 1.85,  $p < 0.001$ ). The preparation was in general well tolerated.

**Conclusions:** This is the first study evaluating and confirming the potential use of  $\beta$ -glucan-based cream as a supportive complementary therapy of atopic dermatitis.



A low-angle photograph of a tree trunk and its branches with green and yellowing leaves against a bright sky. The image is semi-transparent, allowing text to be overlaid.

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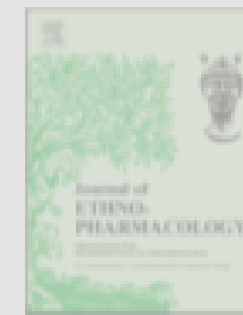
# Chaga

## *Inonotus obliquus*

A review of the clinical trials

- Psoriasis and GI inflammation





Review

Medicinal Plants of the Russian Pharmacopoeia; their history and applications



Alexander N. Shikov<sup>a,\*</sup>, Olga N. Pozharitskaya<sup>a</sup>, Valery G. Makarov<sup>a</sup>, Hildebert Wagner<sup>b</sup>, Rob Verpoorte<sup>c</sup>, Michael Heinrich<sup>d</sup>

<sup>a</sup> Institute of Pharmacy, Pharmaceutical Biology, Ludwig Maximilian University, D - 81377 Munich, Germany

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<sup>d</sup> Research Cluster Biodiversity and Medicines, Centre for Pharmacognosy and Phytotherapy, UCL School of Pharmacy, University of London

Chaga extract was administered three times a day 20–30 minutes before meals. Psoriatic rashes were significantly improved after three months of regular intake, and extensive psoriasis was completely cured in 16 patients.

Dose: 100mL 6 times daily

Form: Chaga paste (10g/100ml water)

Time: 3–5 months

discovery of novel leads for drug development.

Conclusion: The review highlights the therapeutic potential of these Russian phytopharmaceuticals but also highlights cases where concern has been raised about product safety and tolerability, which would



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# Tremella

*Tremella spp.*

A review of the clinical trials

- Cognitive impairment





## Efficacy and Safety of *Tremella fuciformis* in Individuals with Subjective Cognitive Impairment: A Randomized Controlled Trial

Soonhyun Ban,<sup>1</sup> Suji L. Lee,<sup>1</sup> Hyeonseok S. Jeong,<sup>2</sup> Soo Mee Lim,<sup>3</sup> Shinwon Park,<sup>1</sup>  
Young Sun Hong,<sup>3</sup> and Jieun E. Kim<sup>1</sup>

<sup>1</sup>*Department of Brain and Cognitive Sciences, Division of Convergence, Scranton College,  
Ewha Womans University, Seoul, Korea*

There was significant improvement with short term memory and executive performance in the high dose treatment group. *T. fuciformis* supplementation was also associated with increases in grey matter volumes of several brain regions

Dose: 1200mg daily - 2 capsules tid

Form: Fruiting body

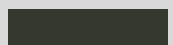
Time: 8 weeks

memory complaint questionnaire compared with those in the placebo group. There were also significantly greater improvements in short-term memory and executive functions in the TF group relative to the placebo group. Exploratory analysis demonstrated that there were significant group-by-visit interactions on the left precuneus, right supramarginal gyrus, right middle frontal gyrus, and right postcentral gyrus at corrected  $P < .05$ . Overall frequency of adverse events did not differ among high-dose TF (40.4%), low-dose TF (35.1%), and placebo groups (41.4%). The current findings suggest that TF could be safely administered to relieve subjective memory complaints and enhance cognition in individuals with SCI.



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**Mushrooms in combination  
may be superior to individual  
mushrooms for immune  
support**





# Synergistic immuno-modulatory activity in human macrophages of a medicinal mushroom formulation consisting of Reishi, Shiitake and Maitake

Brody Mallard <sup>1</sup>, David N Leach <sup>2 3</sup>, Hans Wohlmuth <sup>2 3 4</sup>, Joe Tiralongo <sup>1</sup>

Affiliations + expand

PMID: 31697749 PMCID: [PMC6837746](#) DOI: [10.1371/journal.pone.0224740](#)

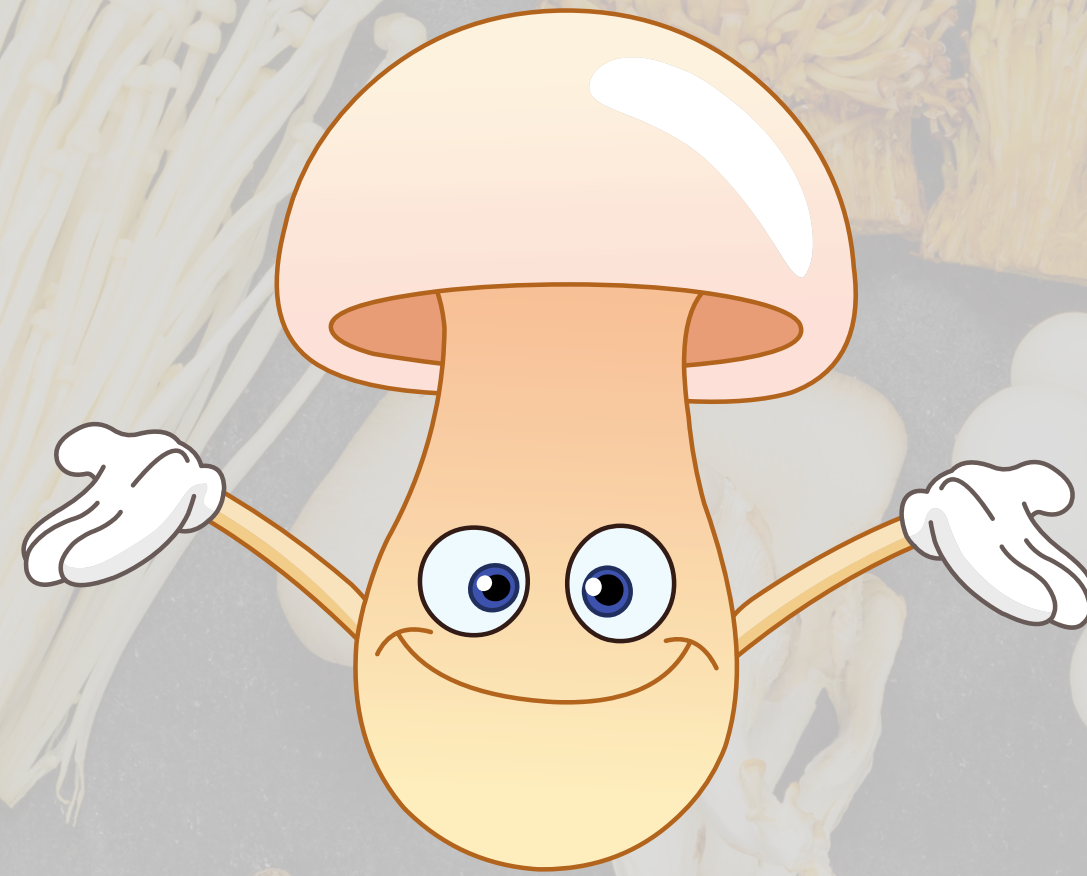
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## Abstract

A key characteristic of mushroom polysaccharides that elicit an immunomodulatory response is that they are rich in  $\beta$ -glucans and low in  $\alpha$ -glucans. In this study we analysed nine commercially available preparations from three mushroom species, Reishi (*Ganoderma lucidum*), Shiitake (*Lentinula edodes*) and Maitake (*Grifola frondosa*), for  $\beta$ - and  $\alpha$ -glucan content. Based on  $\beta$ - and  $\alpha$ -glucan content we selected three extracts to combine into a formula and evaluated the ability of the individual extracts and formula to impact on the expression of cytokines IL-1 $\alpha$ , IL-6, IL-10 and TNF- $\alpha$  in human macrophages with and without LPS stimulation. The majority of mushroom extracts and the formula were found to be highly potent immuno-stimulators possessing EC50 values lower than 100  $\mu$ g/mL. Interestingly the mushroom formula had lower EC50 values in TNF- $\alpha$  expression from LPS stimulated macrophages compared to the individual extracts, suggesting a potential synergistic effect of the mushroom formula. A response additivity graph and curve-shift analysis illustrated that indeed the mushroom formula exhibited an immuno-stimulatory synergistic effect on the expression of the majority of cytokines evaluated in both LPS stimulated and non-stimulated human macrophages, with IL-10 having an antagonistic response. This study represents the first report of a synergistic immuno-modulatory response in human macrophages elicited from a mushroom formula rationally derived from  $\beta$ - and  $\alpha$ -glucan content.



To nerd out more about medicinal mushrooms, check out my blog:  
[reishiandroses.com](https://reishiandroses.com)



Questions?

