

Functional Mushrooms

By Dr. Chris, PharmD

INTRODUCTION

Mushrooms have always been a mysterious and fascinating species. They have been around far longer than the animal kingdom, and humans have been utilizing their unique properties for thousands of years. From East Asia to Europe and North America, different cultures have discovered the medicinal and therapeutic benefits of functional mushrooms. These mysterious fungi have the power to thrive in the harshest environments and contain chemicals that are active in humans, making them a valuable addition to our daily wellness routines. Despite their long history of use, we have only just begun to uncover the secrets of these fascinating creatures.

The Inner Structure of Mushrooms: A Closer Look at the Different Parts of a Mushroom

Understanding the anatomy of mushrooms can be challenging due to the diverse range of mushroom species. As members of the fungi kingdom, mushrooms are distinct organisms that require energy and reproduction but possess unique structures to support these needs. The visible mushroom, also known as the fruiting body, is only a small aspect of the organism's overall anatomy. The majority of the fungus, including the mycelial networks that can expand for miles, is located beneath the surface.^{47,48}

What is the Fruiting Body of a Fungus?

The fruiting body, or mushroom, is the part of the fungus that is visible and often consumed. However, it is only a small portion of the overall anatomy of a mushroom. Beneath the surface, there are intricate networks of hyphae that make up the mycelium. The mushroom, also known as the sporophore, is composed of a cap and stem and serves the primary purpose of spreading spores at the end of its life cycle, allowing for the continuation of the fungal organism.⁴⁹

Mushrooms have 4 primary structures:^{50,51,52}

1. Cap

- The anatomy of mushrooms can vary greatly, with different shapes, sizes, and colors. The most recognizable form of mushroom anatomy includes a cap and stem. The cap, also known as the pileus, is the top part of the mushroom that holds the gills or pores. They can come in different shapes, sizes, and textures, such as smooth or covered with scales or teeth. The shape of the cap is unique to each species and can assist in identifying the mushroom. In its early stages, the cap can be evenly rounded and then expand as it matures.
- The physical appearance of mushrooms can vary greatly, with some having a cap and stem while others, like lion's mane mushrooms, having unique characteristics such as "teeth" or shaggy hair-like structures. These structures, known as scales, form a hard-shelled protection for the fungi and can appear in various shapes and sizes. They are often found on the cap but can also be present on the stem, and can be useful in identifying different species of mushrooms. Additionally, scales can appear as a result of cracking as the cap expands during growth, or can be seen when the mushroom is still immature.

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2. Cap underside

- The gills, also known as lamellae, are a key feature of the mushroom's anatomy that are responsible for producing and releasing spores. They are located beneath the cap of many common mushrooms and can be used for identification. Due to their distinct characteristics, they can be used to differentiate between edible and poisonous mushrooms. The gills are thin-walled structures that surround the stem of the mushroom and are typically found in clusters. They are composed of two layers, the lamellae which reach from the stem to the edge, and the lamellulae which are shorter gills that don't reach the stem. Not all mushrooms have lamellulae, which can also be a distinguishing characteristic.
- Mushrooms can have various structures on their undersides that are used for spore production. Ridged mushrooms, have structures that resemble gills but are actually ridges that cannot be easily detached from the cap. Examples of mushrooms that possess ridges include Chanterelle mushrooms and Gomphus clavatus, commonly known as pig's ears mushrooms. These characteristics can aid in identifying different mushroom species.
- Mushrooms also have the option of having pores instead of gills as their spore-producing structure. Pores are small, sponge-like openings that release spores, and they can be found on the underside of the mushroom cap. These pores lead to tubes within the cap, and as the spores mature, they fall out of the tubes and into their environment through these openings. Pore characteristics such as color, size, pattern, and quantity can be used to identify the species of the mushroom.
- Some mushrooms, such as lion's mane and hedgehog mushrooms, possess teeth or spines that hang from the mushroom cap or stem, which can aid in identifying the species. These teeth, which can be a few millimeters to a few centimeters long, are less common than other features such as gills or pores, making them useful in identifying the mushroom species. Additionally, some mushrooms have false gills, called ridges, which can be distinguished from true gills by attempting to detach them from the mushroom.

3. Spores

- The reproductive cells responsible for fungi reproduction are known as spores. Similar to the way in which plants require seeds for reproduction, mushrooms require spores. The spores, which can be found on the underside of the mushroom cap, within the gills or pores, can be thought of as the "seeds" of the mushroom, while the visible mushroom is considered the "fruit."

4. Stem

- The stem, or stipe, of a mushroom is the structure that supports the cap and the spores it contains. This part of the mushroom typically takes on a cylindrical shape and is strong and durable. The stem is also often equipped with an annulus or vulva, which serves to protect the spores during the development process.

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What is Mycelium?^{54,55}

Mycelium, a complex network of hyphae, is an integral but often unseen aspect of mushroom anatomy. Its primary role is to absorb nutrients and water. The growth of mushrooms is contingent on favorable environmental conditions, and mycelium can survive for extended periods without producing mushrooms. It is important to note that while all mushrooms originate from mycelium, not all mycelium will produce mushrooms.

Medicinal Parts of Mushrooms^{54,55}

The medicinal properties of mushrooms are attributed to the presence of specific compounds, particularly polysaccharides, such as beta-glucans. These compounds have been found to have a positive impact on the immune system, blood sugar levels, and energy levels. These benefits are commonly found in mushrooms such as reishi, lion's mane, cordyceps, turkey tail, and chaga.

It is important to consider the beta-glucan content when selecting a mushroom supplement, as this compound is responsible for many of the health benefits associated with mushrooms. To ensure that a supplement is of the highest quality, it should be made from only the fruiting body of the mushroom and not include any of the mycelium or grain substrate in which it grows. Unfortunately, some manufacturers include these elements in their supplements, resulting in a product that has little to no actual mushrooms and is instead full of unnecessary filler.

What Is Beta-D-Glucan?^{55,56,57}

When considering the use of medicinal mushrooms as a supplement, it is important to consider the presence of several polysaccharides, to include beta-d-glucans. This polysaccharide has been the subject of numerous studies, and there is a significant amount of scientific evidence supporting its benefits. Over 80 clinical studies have shown positive results for the use of beta-d-glucans. Some brands focus solely on this and standardized dosing, however, when natural ingredients are included, it is not standardized as nature produces this at different levels in different mushrooms leaving us with a variable amount.

To gain an understanding of beta-d-glucan, it is important to first define polysaccharides. Polysaccharides are complex carbohydrate structures composed of a chain of simple sugar molecules. They play a supportive role in cells or tissues and are used as an energy reserve. Examples of common polysaccharides include cellulose, glucose, and fructose. Beta-d-glucan, the most prevalent polysaccharide found in the cell walls of mushrooms, is a specific type of polysaccharide.

How Beta-D-Glucan Works Inside Your Body⁵⁸

When considering the use of medical mushrooms in one's daily regimen, the presence and concentration of beta-d-glucans should be considered. Beta-d-glucans are a type of polysaccharide, which are complex carbohydrate molecules. They are known to act as Biological Response Modifiers (BRM), which can help to regulate the immune system by either increasing or decreasing its response. However, the effects of beta-d-glucans on the immune system can vary depending on the shape,

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complexity, solubility, size, and method of extraction used. A two-phase method should be utilized to ensure all beneficial compounds are pulled for dual potency purposes. This is required to first remove polar compounds using water as a carrier then alcohol to extract the remaining non-polar compounds. The first phase is similar to making tea in hot water. The second uses the remaining fruiting bodies that are then processed with alcohol to ensure that the beneficial compounds are all collected.

The beta-d-glucans found in mushrooms are believed to act as pathogen-associated molecular patterns (PAMPs) that interact with pattern-recognition receptors (PRRs) in the immune system. Upon consumption, beta-d-glucan is absorbed by the intestines and binds to fungal receptors on immune cells, which break it down into smaller polysaccharides. These smaller polysaccharides are then transported to the spleen, bone marrow, and lymph tissues, where they can enhance the ability of natural killer cells and other immune system cells to direct resources to specific areas of the body.

Mycelium vs Fruiting Body^{49,50,51}

In the field of mycology, a mushroom is known as the fruiting body of a fungal organism, specifically basidiomycetes, with the exception of cordyceps mushroom which belongs to the ascomycete group. The life cycle of these fungi comprises of three main stages: spores, mycelium, and mushroom. Spores are present in the air and under suitable conditions, they germinate and grow into branching filaments called hyphae. As the hyphae continue to grow, they fuse together to form mycelium, which is an underground network that expands by feeding on organic plant matter. This is the vegetative stage of the organism, during which mycelium produces enzymes to break down the plant material in its growth radius, recycling it into beneficial compounds that return to the soil. In nature, mycelium forms large networks by breaking down wood, logs, leaves, and other plant matter. The plant matter on which fungi feed is commonly referred to as the substrate, and mycelium becomes entwined in it, creating an inseparable mass of substrate and mycelium.

It is important to note that the term "mushroom" refers to the reproductive structure, or fruiting body, of a fungal organism known as a basidiomycete, with the exception of the cordyceps mushroom which is an organism known as an ascomycete. The spores of the basidiomycete can germinate and grow into branching filaments called hyphae, which will eventually fuse together to form mycelium. Mycelium, the underground network that feeds off of organic plant matter, is considered the vegetative stage of the organism. Under appropriate conditions, the mycelium will produce a mushroom which will produce spores that allow for the formation of new mycelial networks and the spread of the fungus. It is important to differentiate between the terms "mushroom" and "mycelium" as they are not interchangeable.

Mushrooms and their Impact on Hormonal Health in Women

Mushrooms May Help Balance Hormones⁵⁹

It is crucial to understand that hormonal imbalances can affect women of all ages, not just those going through menopause or postmenopause. This is because hormones interact and work together to maintain a state of balance, or homeostasis, in the body. To date, researchers have identified over 50 hormones present in the human body, a few examples being:

- Estrogen

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- Testosterone
- Insulin
- Thyroid hormones
- Progesterone
- Antidiuretic hormone
- Cortisol

Mushrooms May Help With PCOS And Fertility^{59,60,61}

Polycystic Ovarian Syndrome (PCOS) is a prevalent condition among women, characterized by elevated androgen levels and alterations in insulin sensitivity. These high levels of androgens may impede ovulation, result in the formation of cysts, and cause additional symptoms such as excessive facial hair growth.

There has been growing interest in the use of anti-androgen compounds derived from plants and fungi as an alternative therapy to traditional medications. These compounds can inhibit or reduce the effects of hormones like testosterone.

A study by Fujita and colleagues evaluated the activity of different mushroom species on the enzyme 5-alpha-reductase. This enzyme converts testosterone to dihydrotestosterone, an androgen that plays a role in the development of masculine characteristics. The study found that reishi had the most significant inhibitory activity against 5-alpha-reductase among the 19 species tested, suggesting that it may assist in maintaining a balanced hormonal state.

Reishi for Stress-Related Fertility Issues⁵⁹

Chronic stress and other factors, such as obesity and hormonal imbalance, can significantly increase the risk of infertility. However, research suggests that incorporating reishi mushrooms into one's diet may help mitigate these risks. It is important to note that stress can manifest in various forms, including, but not limited to, pro-inflammatory foods, financial challenges, relationships, and lack of sleep.

Adaptogens, such as reishi mushrooms, can assist in regulating the body's response to stress and maintaining equilibrium. Studies suggest that reishi can influence the endocrine glands involved in stress hormone production, potentially promoting balance in the levels of these hormones. Additionally, reishi has been shown to improve sleep quality.

Hericium erinaceus – Lions Mane – The Focus Mushroom

INGREDIENT BACKGROUND^{1,2,3}

Hericium erinaceus, also known as lion's mane mushroom, monkey's head mushroom, hedgehog mushroom, satyr's beard, pom pom, bearded tooth, and Yamabushitake. It is a mushroom with both

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edible and medicinal properties. Lion's Mane is an edible fungus with a long history of use in Chinese medicine. It contains important nutrients like β -glucan polysaccharides, which have immune-modulating, and cholesterol-lowering effects, as well as antioxidant and neuroprotective properties. This mushroom has been shown to have therapeutic effects on various diseases, including Alzheimer's disease, immune disorders, and various types of cancer. It appears that different active molecules in this mushroom have different effects on different organs and diseases through different mechanisms. There are therapeutic effects on various diseases that affect multiple physiological systems, including the nervous system, digestive system, circulatory system, and immune system.

EFFICACY/APPLICATIONS^{4,5,6,121}

The consumption of edible mushrooms, such as Lion's Mane, may have potential benefits for slowing the progression of neurological disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, multiple sclerosis, and motor neuron disease. These mushrooms contain a variety of bioactive compounds, including hericenones A, B, C, D, E, F, G, and H, which are aromatic compounds found in the fruiting bodies of Lion's Mane. Research has shown that these compounds have a strong ability to stimulate the production of nerve growth factor, which is essential for the growth, maintenance, and survival of nerve cells in the brain and peripheral nervous system. Additionally, hericene A has been found to significantly boost the production of BDNF and its downstream pathways, leading to improved learning and memory. Lion's Mane contains a variety of other secondary metabolites, such as polyphenols, acids, terpenoids, alkaloids, sesquiterpenes, lactones, sterols, and metal chelating agents, which have medicinal properties and have been used to treat these disorders.

These mushrooms also contain a range of vitamins, including B1, B2, B12, C, D, and E. Lion's Mane has also been shown to have anti-aging effects, promoting the growth of nerve fibers, stimulating the production of nerve growth factor, and improving cognitive function by reducing anxiety and improving sleep quality. It also has a positive impact on neuroinflammation by improving antioxidant function, mitochondrial function, and anti-apoptosis.

SAFETY/ABSORPTION/METABOLISM^{7,8,9}

Toxicology studies in rats suggest that doses up to 5g/kg bodyweight are safe in rats when given as MUNOPHIL, which is a combination of lion's mane and Panax Ginseng. The percentage of this compound by weight that is lion's mane was not listed. There has been one case study of a 63 year old man who suffered acute respiratory failure, and the excess lymphocytes in his lungs showed high reactivity to lion's mane daily for 4 months in dosages commonly bought. The connection between the two, when rated, is seen as a 'probably' connection. As a dietary supplement, take one 500mg Lion's Mane Mushroom 8:1 Extract Capsule 1-2 times daily.

Inonotus obliquus – Chaga – The Skin Mushroom

INGREDIENT BACKGROUND^{10,11,12}

Chaga, or *Inonotus obliquus*, is a mushroom that is frequently taken as a dietary supplement. It is a fungus that has a charcoal-like appearance and thrives on the trunks of birch trees, often remaining on the same trunk for up to 80 years. It has been used for medicinal purposes for centuries and is frequently touted as a cure-all in alternative medicine, claiming to treat a wide range of conditions from cancer to gastrointestinal diseases. However, it's important to note that these claims are primarily based on laboratory studies and animal research, with only one human study being conducted. While there is

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some evidence that Chaga may have positive effects on the immune system and cancer prevention, further research in human subjects is necessary to validate these claims.

EFFICACY/APPLICATIONS^{13,14,15,122}

Chaga is a mushroom that contains a diverse array of potentially beneficial chemical compounds, including polyphenols, melanin, triterpenoids, and polysaccharides. Among these compounds, polysaccharides are the most extensively researched. Currently, laboratory-based research suggests that Chaga may have a variety of positive effects. Cancer research has shown Chaga to have anti-cancer properties in both laboratory and animal-based studies, inhibiting cancer cell replication and stimulating anti-cancer activity in the immune system. In addition, Chaga has been found to inhibit virus replication in laboratory studies, specifically in feline viruses, herpes simplex, and hepatitis C. Furthermore, polysaccharides present in Chaga have been found to reduce markers of oxidative stress and inflammation in laboratory studies. Additionally, it has been demonstrated that Chaga can reduce fatigue, improve gut, and treat skin condition like psoriasis.

SAFETY/ABSORPTION/METABOLISM^{16,17,18}

It is important to note that Chaga, although a mushroom, does not contain any psychoactive compounds. However, the safety data for Chaga is limited and the main concern is that it contains high levels of oxalate, a compound commonly found in plants that can cause kidney stones. Despite anecdotal evidence suggesting that Chaga is relatively safe, there have been two reported cases of oxalate-induced kidney disease resulting from long-term consumption of Chaga. In one case, a 49-year-old man developed end-stage renal disease after consuming Chaga daily for five years, although he had also consumed more than double the recommended manufacturer dose. Another case study reported that a 72-year-old woman with liver cancer developed oxalate-induced kidney disease after consuming 4-5 teaspoons of Chaga daily for six months. Chaga is a type of mushroom that is sold as a dried extract. It is believed to have health benefits, but there have been a couple of reports of people getting kidney stones after taking it. Some studies have shown that Chaga has high levels of oxalate, which can be harmful to the kidneys. Because of this, it is important to talk to your doctor before taking Chaga if you have any kidney problems.

Cordyceps – The Athlete Mushroom

INGREDIENT BACKGROUND^{19,20,21,22}

Cordyceps sinensis (CS) is a fungal parasite found on the larvae of Lepidoptera. During late autumn, the fungus infects the caterpillar and gradually consumes its host. By early summer of the following year, the fungal infestation has killed the caterpillar and the fruiting body emerges from its head. Due to this unique life cycle, it is known as the "winter-worm, summer-plant" in Chinese. CS has been used as a herbal tonic in traditional Chinese medicine to treat a wide range of illnesses in the Orient. This mushroom belongs to the phylum Ascomycoea, the sub-phylum Ascomycotina, and the class Clavicipitaceae, which are generally considered to have medicinal properties.

There are multiple species of *Cordyceps*, with the most commonly used species being *Sinensis*, which has been shown to contain the bioactive compound Cordycepin (3'-deoxyadenosine). This compound is also present in *Cordyceps Militaris* and *Cordyceps Kyushuensis*. *Cordyceps* has been shown to possess a potent anti-oxidative effect, although its potency can vary greatly from sample to sample.

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The anti-oxidative effects of Cordyceps are primarily attributed to its polysaccharide content, and the potency is similar between the mycelium and the fruiting body of the mushroom.

EFFICACY/APPLICATIONS^{23,24,25,26,123}

Cordyceps is a functional mushroom that not only provides low-calorie nutrition but also contains a variety of beneficial compounds such as amino acids, vitamins and minerals. The mushroom contains cordycepin and other bioactive compounds that provide a range of benefits. One of its most notable benefits comes from its prebiotic fiber content which supports the digestive system and promotes a healthy gut microbiome.

Cordyceps has been shown to improve oxygen consumption and support cardiovascular and respiratory health. Studies have demonstrated that consuming cordyceps for 28 days during high-intensity exercise improves both aerobic and anaerobic performance, and increases oxygen consumption and blood lactate levels. Additionally, Cordyceps has been found to enhance endurance and recovery by increasing the availability of oxygen to exercising muscles, which in turn enhances the production of adenosine triphosphate (ATP) which provides cellular energy to the body. In addition, Cordyceps are currently being researched for its potential effects on testosterone levels in aging males. While preliminary findings suggest that it may improve conditions such as late onset hypogonadism and benign prostatic hyperplasia, further studies are necessary to fully understand the specific components and mechanisms of action that contribute to these effects.

Furthermore, cordyceps has been found to support immune function by modulating the immune system and promoting gut health due to its polysaccharide content. As an adaptogenic mushroom, cordyceps helps the body to react appropriately when challenged by infection or inflammation, by maintaining balance in the body.

SAFETY/ABSORPTION/METABOLISM^{27,28,29}

Cordyceps has been studied in human trials with a dosage range of 250-3,000mg per day, either as a single dose or divided into multiple doses taken with meals. However, it is currently unclear if this is the optimal dosage and some research has yielded inconclusive results. Additionally, there is currently a lack of safety data for Cordyceps in human studies. Despite this, a long history of use in Traditional Chinese Medicine suggests that Cordyceps is non-toxic. In fact, the Chinese government has approved Cordyceps CS-4 for use in hospitals and recognizes it as a safe, natural drug.

Lingzhi, Ganoderma lingzhi – Reishi – The Rest & Relaxation Mushroom

INGREDIENT BACKGROUND^{30,31}

Ganoderma lucidum, also known as Reishi or Lingzhi, is a mushroom with a long history of promoting health and longevity in Asian countries such as China and Japan. It is a large, dark mushroom with a glossy exterior and woody texture. The Latin word lucidus, meaning "shiny" or "brilliant," refers to the varnished appearance of the surface of the mushroom. In China, it is referred to as lingzhi and is considered to be the "herb of spiritual potency," symbolizing success, well-being, divine power, and longevity. In Japan, it is known as reishi or mannentake. Often referred to as the "Mushroom of Immortality," studies have extensively examined the effects of Ganoderma lucidum on overall well-

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being, including cardiovascular health, energy and stamina, immune system function, and overall vitality. It is believed to help in maintaining a healthy stress response and calming nerves.

EFFICACY/APPLICATIONS^{32,33,34}

Ganoderma lucidum has been shown to have anti-oxidative effects when consumed as a supplement. It has also been found to have a therapeutic effect on insulin resistance, reduce the risk of prostate cancer, and help to treat a variety of conditions associated with metabolic syndrome.

The Lingzhi mushroom is particularly known for its anti-cancer properties. It has been found to activate natural killer cells, increasing their activity and the body's ability to fight tumors. Supplementing with *Ganoderma lucidum* has been found to reduce the chances of metastasis, which is when cancer spreads to other parts of the body. *Ganoderma lucidum* has a variety of mechanisms, but they are primarily focused on modulating the immune system. The Lingzhi mushroom is able to reduce immune system activity when it is overstimulated and bolster the immune system when it is weakened. In general, *Ganoderma lucidum* has been found to increase the number of active immune system cells. Though further research is needed to confirm these effects, *Ganoderma lucidum* has shown promise boost the immune system, increase strength and stamina, and lower cholesterol.

SAFETY/ABSORPTION/METABOLISM^{35,36,37}

The standard dosage of *Ganoderma lucidum* depends on the form of the supplement being consumed. A general *Ganoderma lucidum* extract does not differentiate between the triterpenoids and polysaccharides present in the mushroom, which make up the ethanolic and water-soluble extracts respectively. The standard dose for the basic extract is 1.44g to 5.2g, with the most popular dose being 5.2g taken in three doses of 1,800mg. The standard dosage for the ethanolic extract is 6mg, while the water-soluble extract should be dosed similarly to the basic extract. It's worth noting that the basic extract is essentially dehydrated mushroom powder, which makes it about 10 times as potent as the actual mushroom. This means that 5g of extract is equivalent to about 50g of whole mushroom. A study of 1.44g of Reishi extract (equivalent to 13.2g of fresh mushroom) consumed for 28 days showed no toxicological signs of blood, liver or cardiac parameters. A non-significant beneficial trend was noted in this study for cardiac parameters (Triglycerides, HDL-C, LDL-C).

Trametes versicolor - Turkey Tail

INGREDIENT BACKGROUND^{38,39,40}

Turkey tail, also known as *Trametes versicolor* or *Coriolus versicolor*, is a mushroom found growing on dead hardwood trees throughout the world. Despite its name, it is completely vegan and does not contain any animal parts. The mushroom is known for its distinctive layered stripes of brown, tan, gray, and white which can be quite striking. In Japan, it is called "kawaritake" or "cloud mushroom" due to its resemblance to swirling clouds. In many Asian cultures, turkey tail is believed to symbolize longevity, health, spiritual attunement and infinity.

In Chinese culture, it is known as Tun Zhi and has been used for centuries by practitioners of Traditional Chinese Medicine as an immunomodulator that supports immune function and helps fight infections. Many people brew it into a tea to clear dampness, increase energy, and strengthen the lungs, stomach and spleen. Its ability to support the health of both an underactive and overactive immune system is unique and has long been valued by traditional medicine practitioners.

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EFFICACY/APPLICATIONS^{40,41,42}

Turkey tail is one of the most extensively researched functional mushrooms, known for its natural polysaccharides, such as polysaccharide K (PSK) and polysaccharide peptide (PSP). These protein-bound polysaccharides help to support a healthy immune response and manage inflammation at the cellular level. It also contains a wide range of natural compounds that help to improve stamina and support gut health, which in turn positively impacts the immune system. Turkey tail is rich in antioxidants, including powerful flavonoids and more than 35 phenols, that help to manage inflammation and stimulate the release of immune-supportive compounds. It also contains prebiotics, which nourish the beneficial bacteria in the gut and help to restore a balance of good flora in the gastrointestinal tract, supporting improved digestion and a healthy immune response.

SAFETY/ABSORPTION/METABOLISM^{43,44,45}

The consumption of up to 9 grams of Turkey Tail mushroom daily for a period of 6 months by women with breast cancer has been found to be well-tolerated and without any significant negative side effects. Turkey tail mushroom products have a long history of safe usage in traditional medicine in East Asia and have been found to alleviate side effects associated with chemotherapy in randomized controlled trials. However, it should be noted that the effectiveness of the mushroom may vary depending on the preparation used.

Grifola frondose - Maitake

INGREDIENT BACKGROUND⁶⁴

The mushroom commonly known as "Maitake" in Japanese translates to "dancing mushroom", so named due to the joyous reactions of those who discovered it in the wild. This mushroom possesses exceptional healing properties and is classified as an adaptogen, which are substances that aid the body in coping with stress and restoring balance to various bodily systems. While it can be used for culinary purposes, it is primarily utilized for its medicinal properties.

Maitake mushrooms are found growing in the wild in certain regions of Japan, China, and North America, specifically at the base of Oak, Elm, and Maple trees. While it can be cultivated, it typically does not thrive as well as it does in its natural habitat. The mushroom is typically available during the autumn months.

Although maitake mushrooms have been utilized in traditional medicine in Japan and China for thousands of years, it has only recently gained popularity in the United States over the past two decades. It is widely praised for its potential to promote health, vitality, and longevity.

EFFICACY/APPLICATIONS^{65,66,67,68}

Maitake extracts are commonly available as dietary supplements that are marketed to improve immune function and to treat ailments such as AIDS and cancer. The active ingredient in these supplements has been identified as beta 1,6-glucan, a protein-bound polysaccharide.

Preclinical studies have demonstrated various benefits from maitake extract, including protection against parasites, diabetes, and high cholesterol, hypertension, and inflammation. Additionally, it has been shown to have potential in reducing the growth of tumors, enhancing bone marrow colony formation, reducing the toxicity of a specific cancer treatment, and increasing the activity

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of a certain protein that helps the body fight off infections. In animal studies, oral administration of the extract has been found to mature certain cells in the blood, improve the recovery of certain blood cells after injury, and protect against suppression of the immune system caused by a specific chemotherapy drug.

In small studies, some subjects who took maitake extract had regression of tumors or significant improvements in symptoms. In a small number of trials, oral maitake extract was found to have an effect on the immune system in postmenopausal breast cancer patients and enhance the function of certain immune cells in patients with a specific blood disorder.

SAFETY/ABSORPTION/METABOLISM^{69,70}

The consumption of Maitake mushroom is considered to be generally safe for the majority of individuals, however, limited information is available regarding potential side effects. Some individuals have reported experiencing nausea after consuming Maitake mushroom. The most commonly used form of Maitake mushroom is an extract, which is typically taken orally in a dose of 1-1.5 grams per day for a period of up to 2 years. However, there is insufficient reliable data to determine appropriate dosing for other forms of the mushroom.

Shiitake

INGREDIENT BACKGROUND^{71,72}

The earliest known records of shiitake mushroom cultivation date back to the Song Dynasty in China in 1209, making it the oldest known cultivated mushroom. The name "shiitake" originates from the Japanese language, with "shii" referring to the tree it grows on, which is a relative of oak, and "take" meaning mushroom.

In Japan, shiitake cultivation was traditionally achieved by cutting down shii trees and leaning the logs against trees that were already producing shiitake mushrooms or were known to contain shiitake spores. This was a method to inoculate the logs with spores so they could be grown and harvested.

Shiitake mushrooms play a significant role in their ecosystem, acting as decomposers like most fungi. They are able to digest lignin, an organic polymer found in the cell walls of many plants that gives them woody and rigid properties. This enables the mushrooms to decompose trees, clearing deadfall from the forest floor and returning crucial nutrients to the soil.

EFFICACY/APPLICATIONS^{73,74,75,76,77,78}

Lentinan, a polysaccharide isolated from shiitake mushrooms, is believed to be responsible for the beneficial effects associated with shiitake consumption. While research has demonstrated the substance to have anti-cancer properties, it is considered a biological response modifier, meaning it modifies the body's response to a stimulus, rather than having a direct toxic effect on tumor cells. Preclinical studies have shown that shiitake extracts possess immunostimulatory, antiviral, liver-protective, cholesterol-lowering, antiproliferative, cytotoxic, anti-mutagenic, and anti-caries properties.

A randomized trial involving young adults found that consuming shiitake mushrooms for a period of four weeks led to changes in immune function. In patients with advanced gastrointestinal cancer, an oral shiitake mycelial extract was found to decrease the incidence of adverse effects associated with

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chemotherapy, and when used in combination with immunotherapy, it improved the quality of life for cancer patients. However, a polysaccharide/oligosaccharide complex derived from a shiitake extract did not demonstrate effectiveness in the treatment of prostate cancer.

SAFETY/ABSORPTION/METABOLISM^{79,80,81}

The shiitake mushroom has been cultivated and consumed by humans for centuries and is generally considered safe and beneficial to eat. However, some individuals may experience adverse effects, particularly when consuming shiitake mushrooms raw or in large quantities.

One known side effect associated with consumption of raw shiitake mushrooms is shiitake dermatitis, a rash that develops as a reaction to the polysaccharide lentinan, which breaks down when heated. The rash is characterized by severe itching and can spread to various parts of the body. It typically appears within 24 hours of exposure to raw shiitake mushrooms and can last for up to three weeks.

Agaricus bisporus - White Button

INGREDIENT BACKGROUND^{86,87}

White mushrooms, scientifically known as *Agaricus bisporus*, belong to the Fungi kingdom and constitute approximately 90% of mushrooms consumed in the United States. *Agaricus bisporus* can be harvested at various stages of maturity. When they are young and immature, they are referred to as white mushrooms if they have a white color or crimini mushrooms if they have a slight brown hue. When fully grown, they are known as portobello mushrooms, which are larger and darker in color. White mushrooms are also commonly referred to as table, common, button, or champignon mushrooms. They have a small stem, smooth cap, and mild flavor that complements a wide range of dishes. White mushrooms grow on composted soil among a variety of other fungi and bacteria, which play crucial roles in the growth process by breaking down raw materials before the mushrooms can develop.

EFFICACY/APPLICATIONS^{88,89,90,91,92}

White mushrooms contain cancer-fighting properties. It is believed that multiple antioxidant compounds, such as polyphenols, polysaccharides, ergothioneine, glutathione, selenium, and vitamin C, contribute to their potential anti-cancer properties.

These antioxidants work to counter the negative effects of oxidative stress, which can cause cellular damage that accelerates aging and increases the risk of developing heart disease and certain types of cancer. The main phenolic compounds found in white mushrooms are flavonoids and phenolic acids, which have the potential to act both as antioxidants and pro-oxidants. In their role as antioxidants, they aid in cell survival, while as pro-oxidants, they can lead to cell death, preventing tumor growth.

White mushrooms may also promote heart health. *Agaricus* mushroom contains chemicals that might improve the body's use of insulin and decrease insulin resistance in people with type 2 diabetes and cardiovascular diseases. Risk factors for heart disease such as oxidative stress, inflammation, high cholesterol, and high triglyceride levels have been strongly linked to heart disease, and the presence of ergothioneine and beta glucan in white mushrooms may help to reduce this risk.

Beta glucan, a type of soluble fiber, can lower blood cholesterol levels by forming a gel-like substance when digested, which traps triglycerides and cholesterol, preventing their absorption.

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Additionally, research indicates that ergothioneine may help to decrease triglyceride levels after a meal. One study involving 10 men found that consuming either 2 teaspoons (8 grams) or 1 tablespoon (16 grams) of mushroom powder as part of a meal led to a significant reduction in blood triglyceride levels, compared to the control group. The researchers attributed this effect to the powder's ergothioneine content. Furthermore, ergothioneine may inhibit the development of arterial plaque, a risk factor for heart disease that can lead to high blood pressure and stroke.

SAFETY/ABSORPTION/METABOLISM^{93,94,95}

White button mushroom extract supplements are widely used as a dietary supplement, however, the FDA has not established specific guidelines for its use and consumption. These supplements are generally considered safe and do not typically cause significant side effects, with the exception of potential allergic reactions. Some side effects that have been reported from consuming dirty or old whole white button mushrooms include upset stomach, nausea, or diarrhea. These side effects may be intensified by taking more than the recommended dosage. As a dietary supplement, it is recommended to take 1,000 mg (slightly less than 1/2 tsp) once or twice daily. Agaricus mushroom extract seems to be safe for most people when taken for up to 12 weeks. Powdered agaricus seems to be safe for most people when taken for up to 6 months. It should be noted that Agaricus products may cause low blood sugar (hypoglycemia) in some individuals with diabetes, and can also cause itching, nausea, and diarrhea.

Auricularia polytricha - Black Fungus

INGREDIENT BACKGROUND^{97,98}

The black fungus, also known as *Auricularia auricula*, is a highly valued edible mushroom worldwide. It is abundant in various nutrients such as carbohydrates, amino acids, and trace elements. Additionally, it contains several functional compounds including polysaccharides, melanin, polyphenols, and flavonoids. The black fungus has been used as a traditional Chinese medicine for centuries, particularly for the treatment of jaundice and sore throats. Due to its nutrient-rich and pharmacologically active properties, it is considered a valuable ingredient in traditional Chinese medicine. Studies have also revealed its potential in enhancing immunity, reducing inflammation, fighting viruses, preventing blood clots, and inhibiting tumor growth.

EFFICACY/APPLICATIONS^{99,100,101}

The extract of *Auricularia polytricha* has been found to have the ability to absorb glucose and inhibit the activity of alpha-amylase, indicating potential benefits for blood sugar regulation. *Auricularia auricula* and *A. polytricha* have been used in traditional Chinese medicine for centuries to treat hemorrhoids and improve stomach health. Additionally, research has shown that *Auricularia polytricha* has antioxidant and antimicrobial properties against various microorganisms, including *Candida albicans*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

The *Auricularia* species, contain high levels of antioxidants, which have been shown to combat oxidative stress in the body and reduce the risk of inflammation and diseases. Additionally, black fungus contains powerful polyphenol antioxidants and prebiotics, specifically beta-glucans, which promote digestive health, maintain bowel regularity, and enhance the immune response to pathogens. Studies have also shown that black fungus may help lower LDL cholesterol, ultimately reducing the risk of heart

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disease. However, it should be noted that more research is needed to fully understand the effects of black fungus on human health.

SAFETY/ABSORPTION/METABOLISM¹⁰²

Black fungus, also known as *Auricularia* species, is a popular edible mushroom that is generally considered safe to consume when purchased from commercial suppliers. However, it is important to note that it is typically sold in a dried form, and should be soaked before use to soften its texture. Additionally, black fungus should be cooked thoroughly to eliminate any bacteria and remove any residue. Studies have also shown that boiling black fungus may enhance its antioxidant activity. However, it is not recommended to forage for black fungus due to the risk of misidentification or contamination, as wild mushrooms can absorb pollutants from their environment and consuming the wrong mushroom can have serious consequences.

Agaricus subrufescens - Agaricus blazei - Royal Sun

INGREDIENT BACKGROUND¹⁰³

The origins of *Agaricus blazei* Murill are closely tied to the village of Piedade in Brazil's Atlantic rainforest, where it has been used as a traditional remedy for promoting longevity and health. Historically, it was viewed as more than just a food source, and its use for medicinal purposes has been documented in Byzantine medical texts. In the 1960s, researcher Takatoshi Furumoto brought attention to the mushroom, which led to further study of its potential health benefits. Researchers discovered it to be high in immune-modulating compounds such as beta-glucans and proteoglycans, and it has been shown to have anti-infection and anti-tumor effects in animal studies. Efforts were made to cultivate the mushroom globally in the 1970s.

EFFICACY/APPLICATIONS¹⁰⁴

Agaricus blazei Murrill, a mushroom of significant biomedical significance, is rich in a variety of bioactive compounds, many of which are referred to as Biological Response Modifiers (BRMs) that activate the immune system for various defensive functions. The polysaccharides found in *A. brasiliensis* have been known to have anti-cancer, anti-viral, and immunomodulatory effects, along with other substances that may also play a role. Additionally, beta-glucans and their enzymatically hydrolyzed oligosaccharides from *A. brasiliensis* have been shown to have properties that can help reduce high blood sugar, high levels of triglycerides, high cholesterol, and the thickening and hardening of artery walls.

SAFETY/ABSORPTION/METABOLISM¹⁰⁵

Several studies have reported various medicinal benefits of *Agaricus subrufescens*, including anti-cancer, anti-microbial, anti-oxidant, and anti-inflammatory properties. However, there is a lack of information on the toxicological effects of compounds found in this mushroom, as well as on the potential relationship between consuming *Agaricus subrufescens* and the development of certain pathologies. Our research found that strains of *A. subrufescens* from different origins do not appear to be toxic in vivo or in vitro, with some strains showing slight cell growth stimulation at the concentrations tested.

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Flammulina filiformis – Needle Mushroom

INGREDIENT BACKGROUND^{106,107,108}

The enokitake mushroom, scientifically known as *Flammulina filiformis*, is a type of edible fungus belonging to the family Physalacriaceae. It is commonly known as enokitake, winter mushroom, velvet shank, or golden needle mushroom and is widely cultivated in East Asia. It is commonly used in Japanese cuisine, and has been cultivated in China since 800 AD. The mushroom can be grown on various substrates such as sawdust, wheat straw, and paddy straw. Cultivated enokitake mushrooms are typically grown in the dark which results in pale fruit bodies with long and narrow stipes and small caps. However, when exposed to light, it produces more typical, short-stiped, and colored fruitbodies. Enokitake mushrooms are sold fresh and canned, and have a crisp texture. They are commonly used in soups and other dishes in East Asian cuisine.

EFFICACY/APPLICATIONS^{109,110,111,112}

Enoki mushrooms have been found to possess various properties that can promote overall health and well-being. These include the ability to protect against oxidative damage by virtue of their antioxidant compounds such as vitamins C and E, selenium, polysaccharides and polyphenols, which help to remove harmful free radicals and prevent oxidative damage to cells. Additionally, research suggests that certain bioactive compounds present in enoki mushrooms have the potential to inhibit the growth of various types of cancer. The mushroom also plays a role in regulating the immune system, thanks to its bioactive polysaccharides, FVE protein, and ribosome-inactivating protein. Furthermore, the polyphenols present in enoki mushrooms have been found to have the ability to lower bad cholesterol levels, thus reducing the risk of heart diseases such as atherosclerosis.

SAFETY/ABSORPTION/METABOLISM^{113,114,115,116}

It is important to note that there is research suggesting that consuming enokitake mushrooms may have negative effects on muscle health, specifically through increased activity of creatine kinase. It is recommended that further research be conducted to fully understand the potential hazards of consuming this mushroom species before promoting it as a health food. Additionally, individuals with mushroom allergies should avoid enoki mushrooms and be cautious of packaged foods that may contain mushroom extracts. Furthermore, consuming enoki mushrooms raw has been linked to listeriosis, a bacterial infection, and should be avoided to prevent food poisoning.

Pleurotus ostreatus – Oyster Mushroom

INGREDIENT BACKGROUND¹¹⁷

The oyster mushroom, scientifically known as *Pleurotus ostreatus*, is a versatile mushroom known for its mild flavor and licorice-like aroma. It is commonly used in Asian cuisine and can be found growing wild in North America, Europe, and Asia, as well as being commercially cultivated worldwide. The mushroom gets its name from its resemblance to oysters in both appearance and flavor. Oyster mushrooms are saprotrophic, meaning they feed on dead and decaying material such as wood, and can grow up to 10 inches in size, with a cap that ranges in color from white to dark brown. Additionally, it is known to be one of the few carnivorous mushrooms that releases chemical to attract microorganisms and then uses its mycelia to digest them as a means of obtaining nitrogen.

EFFICACY/APPLICATIONS¹¹⁸

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Oyster mushrooms have been found to possess a variety of health benefits, including the ability to lower cholesterol levels, alleviate inflammation, provide a rich source of antioxidants, inhibit cancer growth, and boost brain health. Studies have shown that oyster mushrooms contain compounds that can help reduce total cholesterol levels and triglycerides in rats. They also possess anti-inflammatory properties and are effective at increasing antioxidant levels in the body. Additionally, research suggests that oyster mushrooms may inhibit the growth of certain types of cancer cells. Furthermore, oyster mushrooms are rich in nutrients such as niacin and riboflavin, which have been linked to improved brain function and protection against neurodegenerative diseases and dementia.

SAFETY/ABSORPTION/METABOLISM¹¹⁹

Some studies have suggested that oyster mushroom consumption may have potential negative side effects, such as increased activity of plasma creatine kinase, which can have deleterious effects on both skeletal and cardiac muscle. Additionally, some people may be allergic to oyster mushrooms. It is also important to note that oyster mushrooms have been associated with outbreaks of listeriosis, an infection caused by the bacteria *Listeria monocytogenes*. These bacteria can grow on oyster mushrooms and eating them raw can lead to listeriosis or food poisoning. It is important to ensure proper handling, cooking, and storage of oyster mushrooms to avoid these risks.

CONCLUSION

Mushrooms have been used as medicine for centuries, particularly in Asia, where they have a long history of safe use in treating various illnesses. Today, they are being studied for their potential in treating lung diseases and cancer. These powerful mushrooms are packed with antioxidants, polysaccharides, and other unique compounds that may provide a variety of benefits such as enhancement of cognition, mood-boosting, immune-strengthening, stress-relieving, and anti-aging. Not only are medicinal mushrooms safe to consume, but they are also becoming increasingly popular as a natural addition to anyone's wellness routine. According to Allied Market Research, the global functional mushroom market generated a staggering \$7.98 billion in 2020 and is projected to reach an astonishing \$19.33 billion by 2030. Many big companies have also started to offer medicinal mushroom supplements, which claim to increase energy and support the immune system.⁴³ So, whether you're looking to boost your brain power, elevate your mood, or fortify your immune system, adding medicinal mushrooms to your diet may be a natural and effective way to support your overall health and wellness.

***Disclaimer:**

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