

MegaDefense (White Paper)

Introduction: MegaDefense™ is a natural supplement comprised of a micronized blend of six certified organic, non-GMO medicinal mushrooms (*Agaricus blazei*, *Lentinula edodes*, *Grifola frondosa*, *Coriolus versicolor*, *Ganoderma lucidum* and *Cordyceps sinensis*).

This product is classified as a dietary supplement under US-FDA guidelines.

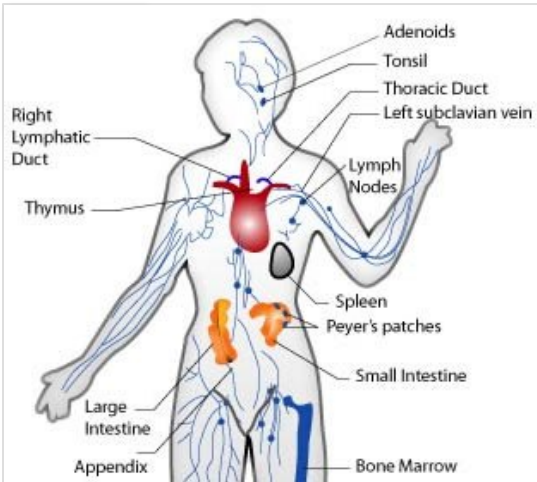
This monograph will outline the following:

- Immune system overview
- Improving immune system function
- An overview of medicinal mushrooms
- Full spectrum chemistries
- IM6 Full Spectrum Immune Complex Overview
 - Clinical activity of *Agaricus blazei*.
 - Clinical activity of *Lentinula edodes*.
 - Clinical activity of *Grifola frondosa*.
 - Clinical activity of *Coriolus versicolor*.
 - Clinical activity of *Ganoderma lucidum*.
 - Clinical activity of *Cordyceps sinensis*.

Keywords: antigen, antibody, phagocytes, lymphocytes, neutrophil, *medicinal mushroom*, *Agaricus blazei*, *Lentinula exodes*, *Grifola frondosa*, *Coriolus versicolor*, *Ganoderma lucidum*, *Cordyceps sinensis*, *immune system*, *leukocytes*, *NK*,

About the Immune System

The immune system is the body's defense against infectious organisms and harmful or toxic compounds. The basic function of the immune system is to attack organisms and substances that invade the body's systems through a series of steps called the "immune response".



This system involves a network of cells, tissues and organs that all work together to protect the body. Immune system cells are called "white blood cells" (**leukocytes**). These come in two basic types that combine to seek out and destroy disease-causing organisms or substances. The two basic types of leukocytes are:

1. **Phagocytes:** cells that absorb and destroy invading organisms
2. **Lymphocytes:** cells that allow the body to remember and recognize previous invaders and help the body destroy them (creation of antibodies)

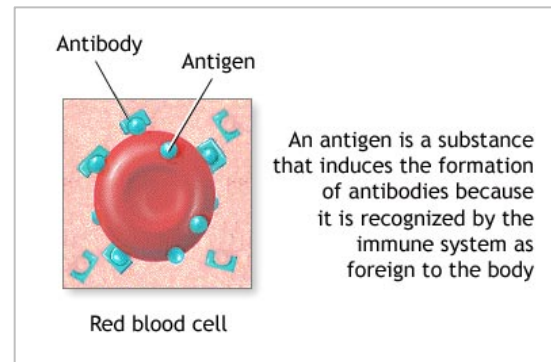
A number of different cells are considered phagocytes. The most common type is the **neutrophil**, which primarily fights bacteria. When looking for evidence of a bacterial infection, a physician may order a blood test to verify an increased number of neutrophils triggered by the infection.

There are several other types of phagocytes, each with their own specific function to make sure that the body responds appropriately to a specific type of invader.

The two kinds of lymphocytes are **B lymphocytes** and **T lymphocytes**. Lymphocytes are grown in the bone marrow and either mature there into B cells, or migrate to the thymus gland, where they mature into T cells. B lymphocytes and T lymphocytes have separate functions: B lymphocytes function as the body's intelligence system, seeking out their targets and sending defenses to lock onto them. T lymphocytes are like soldiers, destroying invaders that the intelligence system has identified.

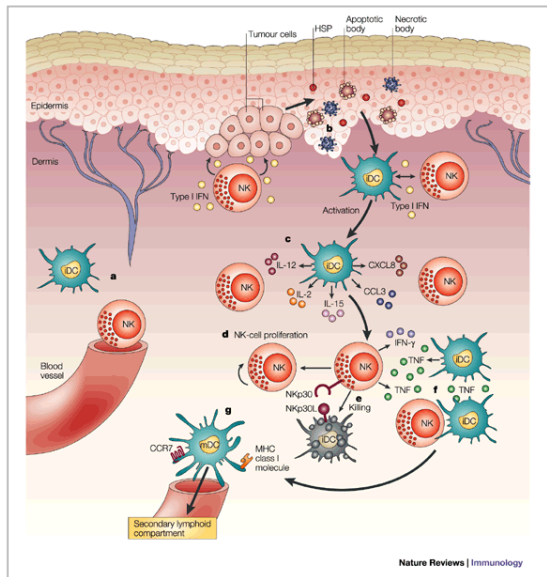
Here's how it all works:

When **antigens** (foreign substances that invade the body) are detected, several types of cells work together to recognize them and respond. These cells trigger the B lymphocytes to produce antibodies, specialized proteins that lock onto specific antigens.



Once antibodies are produced, they continue to exist in a person's body. These can recognize the same antigen at a later time, and allow the immune system to react quickly. As an example, if someone gets sick with a disease like chickenpox, that person typically doesn't get sick from it again. The immune system reaction is so fast; the person never experiences the symptoms of the disease. This is also how immunizations may prevent certain diseases.

An immunization (vaccination) introduces a safe or inactive version of an antigen to the body. This allows the body to produce antibodies that will then protect the person from future attack by the germ or substance that produces that particular disease. Although these antibodies have the ability to recognize an antigen and lock onto it, they cannot destroy the invader. T cells are tagged by antibodies or cells that have been infected or somehow changed. These become specialized hunters for the antigens that match their tagged antibodies.



These T cells are called "**Killer Cells.**" T cells then signal other cells (like phagocytes) to destroy the invader. Antibodies can also neutralize toxins (poisonous or damaging substances) produced by different organisms. Lastly, antibodies can activate the production of **complement** proteins that assist in killing bacteria, viruses or infected cells.

All of these specialized cells, and parts of the immune system, offer the body protection against disease. This protection is called **immunity.**

Improving Immune System Function

While toxins certainly have an influence on immune system health and activity, there are many other factors involved. Genetics play a role and some individuals are prone to either **immuno-suppression** (reduced immune system function) or **hyper-immunity** (an over-active immune system that may cause oxidative stress or an autoimmune reaction). As an example, asthma sufferers are prone to the hyper-immune response that leads to an asthma attack. Medications can also cause immune system dysfunction. Steroids, anti-inflammatory drugs and medications to treat autoimmune diseases will reduce the activity of the immune system and increase the risk for opportunistic infection. As an alternative, there are compounds that function as "immuno-modulators". These compounds act to improve overall immune system function without the risk of a hyper-immune response.

To reiterate, the immune system exists in a delicate balance. It needs to recognize foreign invaders to be able to protect the body, but the reaction needs to be measured. If the immune system over-reacts to a stimulus, it may cause much more damage than the original foreign body may have caused. As an example, an overactive immune system creates damaging free radicals that may increase risk for cancer or heart disease. It may also create inflammation that can cause tissue damage. Lastly, a hyper-immune response may create autoimmunity, where the immune system attacks normal, healthy tissue. Because of these risks, it is vital to create a viable check and balance system to maintain proper immune system health. This may be possible with natural immuno-modulating agents.

Medicinal mushrooms have been used as functional foods for thousands of years and clinically for more than a hundred years. The main constituents of the mushroom cell wall are polysaccharides that have been known to act as immuno-modulators. Specifically, **β-glucans** ("Beta-glucans") have been shown to improve overall immune system health without the risk for hyper-immunity.

Full-Spectrum Chemistries

There is a lot of confusion today in the field of pharmaceutical mushrooms as to what form of mushroom product is the best for use. There are various components of the mushroom, which have been used as separated compounds. Is it the fruit-body, the mycelium or an extract standardized from some particular compound, which is responsible for the mushroom's properties? This question is not as straightforward as it seems.

- **Fruit body.** This is the mushroom seen above the ground. It is the spore-producing portion involved with reproduction. Basically, the fruit body is equivalent to the flower of a plant. Fruit bodies only form in response to some stress from the environment.
- **Mycelium.** This is the growth form of the organism under the ground where all of the life processes occur: growth, feeding, competing for survival and some forms of reproduction.
- **Broth.** In cultivated mushroom products, the mycelium can be grown either by fermentation, in a tank full of liquid "broth", or on a solid substrate of some material that is found in the natural growth condition.

For the production of many mushroom-derived drugs and health supplements, the compounds are extracted not from the mycelium but from the broth in which the mycelium is grown.

As an example, there are a number of pharmaceutical drugs produced from the Shiitake mushroom (*Lentinula edodes*): *lentinan* from the fruit body; *LEM* from the mycelium; and *KS-2* from the residual culture broth, an extracellular compound.

To extract lentinan from Shiitake mushrooms is a pretty straightforward chemical process. But what about another compound present in Shiitake, called eritadenine?

This compound is useful in the treatment of high cholesterol levels, while lentinan is used for the treatment of cancer.

So, what is the more valuable product: the raw, full-spectrum Shiitake or the standardized extract? The answer is neither, or both. It depends on what is hoped to be achieved with the supplement.

For general health-supplement usage, the best product is the one that has the greatest effectiveness over a broad range of potential conditions. In this example, it makes much more sense to use a full spectrum of products—the fruit body, mycelium and broth.

Research has shown that mixed chemistries play a more important role in the effectiveness of how unrelated chemistries might produce specific results. It is a complex form that is still not completely understood but produces clinical results not available with standardized extracts.

Most pharmaceutical mushrooms are utilized as extracts for their most potent and most successful products and formulas. But these are very specific and targeted extracts, made for the particular purpose of concentrating specific compounds.

There are two general categories of bioactive compounds found in pharmaceutical mushrooms:

1. The **polysaccharides**, which comprise most of the medicinal compounds, are soluble in hot water and not in alcohol. The immunostimulant type of action so well known in mushrooms is from this class of compounds. When looking for immunomodulation action, it is advisable to not use alcohol extracts as they will not be effective.
2. The **nucleosides**, another class of compounds, are soluble in non-polar solvents like alcohol and hexane. These compounds are usually smaller in molecular size and are more specific in their bioactivity compared with polysaccharides.

Super Mushroom Blend

It is therapeutically best to utilize a blend of several mushroom species, because "the whole is greater than the sum of its parts." For one thing, it is easier for pathogens in the body to adapt and become resistant to one mushroom than to several. Secondly, each mushroom species has a unique arsenal of anti-infective and immunomodulating agents.

These special agents include:

- Polysaccharides
- Glycoproteins
- Ergosterols
- Triterpenoids

The agents listed above are *precursors* to the more complex compounds, beta glucans. It is the synergy between ALL of these elements that makes mushrooms so medicinally powerful when consumed as a whole food—mycelium included.

Because mushrooms have such powerful immune-boosting effects, it isn't surprising that some have great potential for battling life-threatening conditions. Mushrooms that have been researched for their anti-tumor activity appear to increase the number and activity of killer T and natural killer (NK) lymphocytes, with no toxicity to healthy cells.

Cancer cells are notorious for "hiding" from chemo agents. New research has shown that certain mushroom extracts help chemotherapy drugs better locate and identify cancer cells by "uncloaking them," thereby making chemo more effective.

Medicinal mushrooms are also believed to strengthen the immune system of those undergoing chemotherapy, so cancer patients may get a double benefit.

Research has shown that mushrooms provide a variety of health benefits that may include the following:

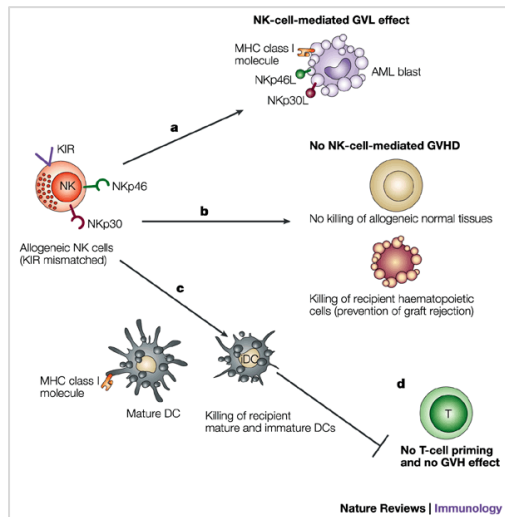
- Increased longevity
- Improved blood flow
- Cholesterol and blood sugar normalization
- Liver protection
- Kidney support
- Anti-viral, antibacterial and antifungal
- Improved respiratory function
- Reduced risk for heart disease
- Decreased platelet aggregation
- Improved blood flow
- Improved skin and hair
- Increased sexual function and athletic ability

A carefully designed blend of medicinal mushrooms may deliver a powerful therapeutic punch, with current research focusing on everything from protection against seasonal colds or flu, all the way to more serious health conditions.

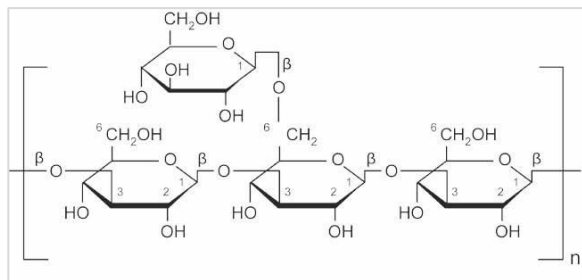
IM6 Full Spectrum Immune Complex Overview

Pure, organic and patent-protected, **IM6 Full Spectrum Immune Complex** is considered to be the most technologically advanced immune blend for use in dietary supplements on the market today. Featuring a combination of more than 200 highly purified, immune-active high molecular heteropolysaccharides and Beta 1,3-1,6 triple right hand helix beta glucans, IM6 is derived from six closely related organisms—100% USDA certified organic, certified kosher, biotech lab cultivated, full spectrum, non-GMO *Agaricus blazei*, *Lentinula edodes*, *Grifola frondosa*, *Coriolus versicolor*, *Ganoderma lucidum* and *Cordyceps sinensis*.

Each of these species offers a slightly different polysaccharide structure, which activates many more types of immune cells than just simple beta glucans do. While yeast-based beta glucans activate only Natural Killer (NK) cells, research shows **IM6 Full Spectrum Immune Complex** activates all 260 different classes of immune cells including: NK cells, T cells, macrophages and many others.



IM6 Full Spectrum Immune Complex is a combination of both water-soluble heteropolysaccharide and high molecular weight non-soluble triple helix beta glucans. It is fully micronized through a proprietary process to a maximum particle size of less than 40 microns, which makes it instantly bioavailable.



These 1,3-1,6 beta-glucans have a range of molecular weight from less than 20 kD to over 2,000 kD, and are thought to be effective in activating a wide range of immune responses. A tremendous body of reference work exists, indicating over 800 different species of higher basidiomycetes fungi

(mushrooms) contain immune-modulating and anti-tumor polysaccharide compounds with this tertiary structure.

This has led to the development of a number of drugs of the Lentinan class. These drugs are widely used (primarily in Asia) as adjuncts in the treatment of cancer.

Prior to the introduction **IM6 Full Spectrum Immune Complex**, all the mushroom-derived polysaccharide immune modulators brought to market have been derived from a single species of fungi, consisting of only a single molecular weight polysaccharide with single tertiary structure, which indicates the probable attachment to only single immune-triggering receptors at the cellular level.

However, recent advances in immune science have revealed a wide range of different cellular receptors, each of which attach to different structural types and sizes of polysaccharide molecules. This multi-receptor, multi-structure binding indicates multiple mechanism of action in the triggering of immune responses, which is much more complex than was previously thought.

While it has been known since the 1970's that Natural Killer (NK) cells were activated by polysaccharide triggers, it is now believed that most, if not all, of the different classes of immune cells are activated or triggered by the attachment of either pure polysaccharides or protein-bound polysaccharide molecules to receptors found at the cell surface such as CR3, LacCer, Dectin-1 and other activation receptors.

It is this multi-receptor activation pathway that led to the development of **IM6 Full Spectrum Immune Complex**, which contains over 200 different immune-active polysaccharide structures. This complex polysaccharide formulation is thought to activate the full range of immune response in the human body.

The species of fungi from which these polysaccharide immune compounds are derived are:

Agaricus blazei, *Lentinula edodes*, *Grifola frondosa*, *Ganoderma lucidum*, *Trametes (Coriolus) versicolor*, and *Cordyceps sinensis*.

We will explore some of the history, benefits and research available for each of the six medicinal mushrooms featured in **IM6 Full Spectrum Immune Complex** in the pages that follow.

Background of *Agaricus Blazei* (Sun) Mushroom

Agaricus blazei (*A blazei*) is known in Brazil as the sun mushroom, in Japan as himematsutake, agarikusutake or kawarihiratake and in China as Ji Song Rong. It was brought to Japan in the 1970s due to its beneficial health effects, which included the prevention of: diabetes, hyperlipidemia, arteriosclerosis and chronic hepatitis^{1,2}. Nowadays, it is widely utilized in Oriental countries as an edible mushroom. Considered as a functional food (functional food is a part of an everyday diet and is reduce the risk of chronic disease beyond the widely accepted nutritional effects), it is vastly utilized in traditional medicine in the form of a medicinal extract for the prevention and treatment of cancer³.

In general, the total composition of the mushroom is water (90%), protein (2–40%), carbohydrates (1–55%), fiber (3–32%) and ash (8–10%). The ash content is made up mainly of salts, as well as metals like calcium and magnesium. Among the carbohydrates are notably some biologically active polysaccharides, present in the basidiocarp and/or mycelium, such as the β -glucans ("Beta-glucans") which have attracted the attention of investigators⁴.

RESEARCH: A recent study suggests that *Agaricus* extract has estrogen-like activity and may help prevent atherosclerosis via dual roles in cell signaling, macrophage development suppression and endothelial cell recovery from vascular damage⁵. A major constituent of *Agaricus*, ergosterol, was found to inhibit tumor growth in mice via direct inhibition

of tumor-induced angiogenesis⁶. Other studies demonstrated that polysaccharides present in *Agaricus* extract caused activation of macrophages or natural killer cells⁷ and induced cytotoxic T-lymphocyte activity in tumor-bearing mice. Specifically, activation of natural killer cells was mediated through IL-12-induced IFN-gamma expression⁸. Both aqueous and organic extracts of *Agaricus* offered protection to cells exposed to methyl methanesulphonate, a mutagenic agent. The stimulus produced by linoleic acid on beta-DNA polymerase, an enzyme involved in repair mechanism following exposure of DNA to alkylating agents, is thought responsible for such an effect⁹. Furthermore, *Agaricus* extract stimulates caspase 3 activation and reduces telomerase activity¹⁰ possibly through regulation of Akt signaling thereby inducing apoptosis in cancer cell lines. Blazeispirol A, produced by *Agaricus* fermentation, causes both caspase-dependent and -independent cell death in human Hep 3B cells¹¹. Agaritine, a hydrazine-containing constituent exhibits anti-tumor activity toward U937 leukemic cells mediated through apoptosis¹².

Background of *Lentinula Edodes* (Shiitake) Mushroom

Shiitake, an edible mushroom indigenous to East Asia, is cultivated worldwide for its purported health benefits. The fresh and dried forms of the mushroom are commonly used in East Asian cooking. It is also valued as a medicinal mushroom. Shiitake is popular in many countries around the world and is commonly found in supermarkets and Asian grocery stores.

Lentinan ([1,3] beta-D-glucan), a polysaccharide isolated from shiitake, is thought to be responsible for many of the mushroom's beneficial effects. An injectable form of lentinan is used for cancer treatment in some countries, but it has not been evaluated in large studies.

RESEARCH: In vitro studies conducted with lentinan have indicated its anticancer effects in colon cancer cells¹³; these effects may result from its ability to suppress cytochrome P450 1A enzymes that are known to metabolize pro-carcinogens to active forms¹⁴.

Lentin, the protein component of shiitake, has been shown to exert antifungal properties, as well as inhibiting the proliferation of leukemic cells, and suppressing the activity of HIV-1 reverse transcriptase¹⁵.

Studies of shiitake extracts suggest antiproliferative¹⁶, immunostimulatory¹⁷, hepatoprotective¹⁸, antimutagenic¹⁹, and anticaries²⁰ effects in vitro and in mice. But a clinical trial failed to show any benefit of an oral shiitake extract in the treatment of prostate cancer²¹.

More recently, however, improvements were reported in quality of life and survival with an oral formulation of superfine dispersed lentinan in patients with hepatocellular carcinoma²², gastric cancer²³, colorectal cancer²⁴, and pancreatic cancer²⁵. Larger, well-designed studies are needed to determine whether oral lentinan is superior to the injectable form.

Background of *Grifolia Frondosa* (Maitake) Mushroom

Grifola frondosa is a species of mushroom usually referred to as maitake in Japan, where it's indigenous. The mushroom is one of many recognized medicinal mushrooms in Japan and China, but a majority of Western scientists and doctors believe its health benefits are largely folklore. However, scientific investigation during the last decade in Asia has shown that maitake mushrooms contain many nutrients beneficial for health.

Grifola frondosa has been used in Japan and other Asia countries as a food source and medicine for a few thousand years. It was commonly referred to as

the dancing mushroom in earlier times because people danced for joy when they found some in the wild -- the mushrooms were known to be strongly medicinal, so they were quite valuable.

RESEARCH: In 2009, a phase I/II human trial, conducted by Memorial Sloan-Kettering Cancer Center, showed Maitake could stimulate the immune systems of breast cancer patients²⁶. Small experiments with human cancer patients, have shown Maitake can stimulate immune system cells, like NK cells²⁷. *In vitro* research has also shown Maitake can stimulate immune system cells²⁸. An *in vivo* experiment showed that Maitake could stimulate both the innate immune system and adaptive immune system²⁹.

In vitro research has shown Maitake can induce apoptosis in cancer cell lines (human prostatic cancer cells, Hep 3B cells, SGC-7901 cells, murine skin carcinoma cells) as well as inhibit the growth of various types of cancer cells (canine cancer cells, bladder cancer cells). Small studies with human cancer patients, revealed a portion of the Maitake mushroom, known as the "Maitake D-fraction", possess anti-cancer activity. *In vitro* research demonstrated the mushroom has potential anti-metastatic properties³⁰⁻³⁵. In 1997, the U.S. Food and Drug Administration (FDA) approved an Investigational New Drug Application for a portion of the mushroom.

Research has shown Maitake has a hypoglycemic effect, and may be beneficial for the management of diabetes^{36,37}. The reason Maitake lowers blood sugar is due to the fact the mushroom naturally contains an alpha glucosidase inhibitor³⁸.

Maitake contains antioxidants and may partially inhibit the enzyme cyclooxygenase³⁹. An experiment showed that an extract of Maitake inhibited angiogenesis via inhibition of the vascular endothelial growth factor (VEGF)⁴⁰.

Lys-N is a unique protease found in Maitake. Lys-N is used for proteomics experiments due to its protein cleavage specificity⁴¹.

Background of *Coriolus Versicolor* (Turkey Tail) Mushroom

Coriolus versicolor is a mushroom used in traditional Asian herbal remedies. Two substances extracted from the mushroom, polysaccharide K (PSK) and polysaccharide-peptide (PSP), are being studied as possible complementary cancer treatments. *Verisicolor* polysaccharide (VPS), another extract from the mushroom that is sold as a dietary supplement in the United States, is also being studied.

Coriolus versicolor has been a component of traditional Asian medicine for centuries. In the 1980s, the Japanese government approved the use of PSK for treating several types of cancer. In Japan, PSK is a best-selling anti-cancer drug where it is currently used as a cancer treatment along with surgery, chemotherapy, and radiation therapy. PSP was discovered more recently and has been studied mainly in China.

Coriolus versicolor is thought to be a biological response modifier. The proteoglycan constituents are responsible for its immunostimulant and anticancer activities.

RESEARCH: Many different mechanisms of action have been proposed for the activity of these components. PSK has been found to induce cytokine expression in human peripheral blood mononuclear cells *in vitro*. In another studies, PSP, as well as *Coriolus* extract, selectively induced apoptosis of human promyelocytic leukemia HL-60 cells^{42,43}. It also increased apoptotic cell death in cells that had been treated with the chemotherapeutic agent, camptothecin. In these cells, PSP reduced cellular proliferation, inhibited cell progression through both the S and G2 phases of DNA replication, reduced 3H - thymidine uptake, and prolonged DNA synthesis time⁴⁴. An additional *in vitro* study showed that a medicinal mushroom blend that included *Coriolus Versicolor* inhibited cell proliferation and induced cell cycle arrest at the G2/M phase in the invasive human breast cancer cell line MDA-MB-231⁴⁵. DNA-

microarray analysis indicated that the mushroom extract inhibited the expression of cell cycle regulatory genes and suppressed metastatic behavior through the inhibition of cell adhesion, cell migration, and cell invasion . The inhibition of metastatic behavior was linked to the suppression of urokinase plasminogen activator (uPA)⁴⁶. PSP has also been shown to inhibit the interaction between HIV-1 gp120 and CD4 receptor, HIV-1 transcriptase activity, and glycohydrolase enzyme activity associated with viral glycosylation⁴⁷.

Researchers have found that PSK, one of the substances that can be extracted from *Coriolus versicolor*, has several anti-cancer properties. In some animal studies, it slows the spread of cancer cells. PSK also appears to have some immune system–boosting properties in people undergoing chemotherapy and may lessen some side effects of chemotherapy and radiation therapy⁴⁸. PSK is also believed to be a strong anti-oxidant, a compound that blocks the action of free radicals, activated oxygen molecules that can damage cells⁴⁹.

More than 2 dozen human studies of PSK have been reviewed by experts at the University of Texas MD Anderson Cancer Center. Almost all of these studies were done in Japan and focused on cancer of the esophagus, stomach, colon, or breast. Most of them found that people with cancer were helped by PSK. People who received PSK with other treatments, such as surgery, chemotherapy, or radiation therapy, generally had longer periods of time without disease and had increased survival rates compared with patients who received only standard treatment. Side effects from PSK in these studies were very mild. Smaller studies have suggested PSK may not be as effective against liver cancer or leukemia⁵⁰⁻⁵³.

Background of *Ganoderma Lucidum* (Reishi) Mushroom

Usually known as *Reishi* or *Ling zhi*, *Ganoderma Lucidum* is one of the highest ranked medicines in Chinese medicine and has extended to usage in Japanese and Korean medicine as well as having some prevalence in the West.

Its mechanisms are diverse, but are usually localized around moderating the immune system (reducing its activity when overstimulated, increasing its effects when deficient) and proliferating the immune system at the same time, increasing the amount of active cells and thus the potential for their effects.

Ganoderma also possesses anti-oxidative effects, and can act on a few other systems such as aldose reductase (which can help with diabetic symptoms) and 5-alpha reductase (which can help with prostate cancer risk). Due to these effects paired with the modulation of the immune system, *Ganoderma Lucidum* shows promise in being *therapeutic* for insulin resistance, prostate cancer risk, and a variety of conditions correlated with metabolic syndrome.

It is also well known and touted for its anti-cancer effects, which are secondary to both potentiating the immune system (usually through activation of natural killer cells, and increasing tumor necrosis factor-alpha) and also some other mechanisms that allow *Ganoderma* to be synergistic within itself in reducing tumor growth and reducing the chance of metastasis.

Although it awaits replication in more trials, it shows promise in a wide variety of cancer-related and therapeutic goals; *Reishi* has demonstrated efficacy as an adjunct therapy (taken alongside other medications) for breast cancer, hepatitis, fatigue syndrome and prostate cancer in human trials so far.

RESEARCH: Derived from the cap and stem of the mushroom, *reishi* mushroom is used as an immunestimulant by patients with HIV and cancer. The active constituents are thought to include both beta-glucan polysaccharides and triterpenes⁵⁴. Extracts of *reishi* can stimulate macrophages, alter

the levels of TNF and interleukins^{55,56}, inhibit platelet aggregation⁵⁷.

Clinical studies indicate that *Reishi* extracts improve lower urinary tract symptoms (LUTS) in men^{58,59}, exert mild antidiabetic effects and may improve dyslipidaemia⁶⁰.

In vitro and animal studies indicate that *reishi* has chemopreventive effects⁶¹, alleviates chemotherapy-induced nausea⁶², enhances the efficacy of radiotherapy⁶³, and increases the sensitivity of ovarian cancer cells to cisplatin⁶⁴. It was also effective in preventing cisplatin-induced nephrotoxicity⁶⁵.

In small clinical studies, *reishi* increased plasma antioxidant capacity⁶⁶, and enhanced immune responses in advance-stage cancer patients⁶⁷. Remission of hepatocellular carcinoma (HCC) has been reported in a few cases⁶⁸.

Background of *Cordyceps Sinensis* (Catepillar) Mushroom

The *Cordyceps* mushrooms have a long history as medicinal fungi. The earliest clear record is a Tibetan medical text authored by Zurkhar Nyamnyi Dorje in the 15th Century outlining the tonic propensities of *Yartsa gunbu* (*Cordyceps sinensis* renamed now to *Ophiocordyceps sinensis*), especially as an aphrodisiac⁶⁹. Modern scientific studies have confirmed and expanded on the findings of traditional Chinese medicine, that the *Cordyceps* fungus has a multitude of health benefits. As with the other medicinal mushrooms previously mentioned, *Cordyceps sinensis* contains extremely high levels of polysaccharides - especially beta-glucans as well as antioxidants and a unique nucleoside known as Cordycepin⁷⁰.

Cordycepin (3'-deoxyadenosine) is a derivative of the nucleoside adenosine, differing from the latter by the absence of oxygen in the 3' position of its ribose part. Because cordycepin is similar to adenosine, some enzymes cannot discriminate between the

two. Therefore, it can participate in certain biochemical reactions (for example, be incorporated into an RNA molecule, thus causing the premature termination of certain RNA or protein synthesis). This may be a probable mechanism for the antiviral properties of *Cordyceps sinensis*.

RESEARCH: In traditional Chinese medicine (TCM), the main use of Cordyceps has been in the treatment of asthma and other bronchial conditions⁷¹. Studies have shown that Cordyceps may be effective against tuberculosis⁷², leprosy and human leukemia⁷³.

Cordyceps has been shown to provide many health benefits in clinical studies as well as in vivo analyses.

The best-known medicinal action of Cordyceps is in the increase of physical stamina. In 1993, the Chinese National Games brought this mushroom to the attention of the world's sporting authorities. A group of nine women athletes who had been taking Cordyceps shattered nine world records. Clinical research has shown that Cordyceps use increased cellular bio-energy, ATP (adenosine triphosphate)⁷⁴. Increased synthesis of ATP and faster energy recovery have been reported. It would seem that Cordyceps improves the internal balance mechanism, thus making the utilization of oxygen more efficient. These properties may account for the overall physical enhancement, the extra endurance and the anti-fatigue effects that been reported in humans using Cordyceps.

Several scientific studies have demonstrated the benefits of Cordyceps sinensis in alleviating the symptoms of various respiratory illnesses including chronic bronchitis and asthma⁷¹.

Numerous studies have demonstrated the benefits of Cordyceps sinensis in treating heart rhythm disturbances such as cardiac arrhythmia and chronic heart failure^{75,76}.

As with the other medicinal mushrooms, Cordyceps has been found to enhance "natural killer" (NK) cell activity, thus increasing T-cell production and acting

as an immunomodulatory agent⁷⁷. Extracts of Cordyceps sinensis have also shown promise in studies of liver disease⁷⁸, numerous cancers^{73,79-81} and sexual dysfunction⁸².

co-factors and polysaccharides. These quench free radicals through electron donation or electron acceptance. Again, there are two completely different mechanisms that provide the same benefit - creating a synergistic effect.

Anti-Mutagenesis.

Several studies have shown the effects of clinoptilolite on cancer cell lines and in tumors both in vivo and in vitro^{103,104}. This is primarily considered to be caused by the induction of apoptosis and the zeolite's activation of the p21 tumor suppression gene¹⁰². Additionally, the zeolite acts to balance the body's pH^{95,96} and may create an inhospitable environment for cancer cell growth as systemic alkalinity is maintained. Mushroom extracts have been studied almost exclusively for their effects against cancer cell growth^{1,6,7,10,12,13,16,21-26,30-35,42-46,51,61-65,67,68,73,79-81}. The mechanism involved in this case is through immune system activation and immuno-modulation. The expected synergies result in a powerful immuno-modulating agent that reduces the risk of mutagenesis.

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