ZMUNITY Product Overview

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Introduction: ZMUNITY is a natural supplement comprised of micronized, activated zeolite (clinoptilolite) and a micronized blend of seven certified organic, non-GMO medicinal mushrooms (*Agaricus blazei, Lentinula edodes, Grifola frondosa, Trametes versicolor, Ganoderma lucidum, Cordyceps militaris* and *Cordyceps sinensis*).

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

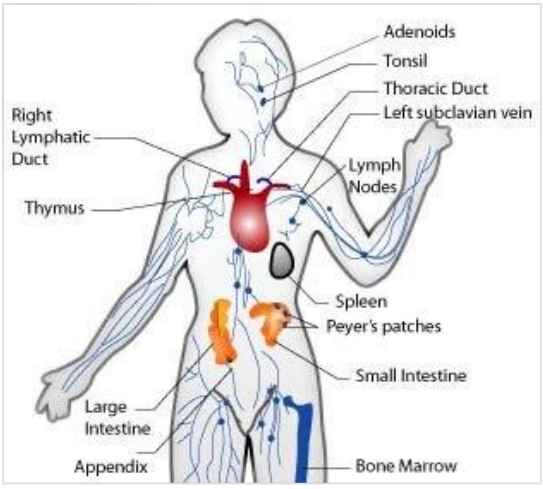
This monograph will outline the following:

- Immune system overview
- Affects of toxins on the immune system
- Methods of detoxification
- Improving immune system function
- An overview of medicinal mushrooms
- Full spectrum chemistries
- IAS Full Spectrum Mushroom Complex Overview
    - Clinical activity of *Agaricus blazei.*
    - Clinical activity of *Lentinula edodes.*
    - Clinical activity of *Grifola frondosa.*
    - Clinical activity of Trametes *versicolor.*
    - Clinical activity of *Ganoderma lucidum.*
    - Clinical activity of *Cordyceps sinensis & Cordyceps militaris.*
- An overview of clinoptilolite.
- The synergies between the activity of the blend of medicinal mushrooms and zeolite.
- Unpublished clinical data on the research underway.

Keywords: antigen, antibody, phagocytes, lymphocytes, neutrophil, *medicinal mushroom, Agaricus blazei, Lentinula exodes, Grifola frondosa, Trametes versicolor, Ganoderma lucidum, Cordyceps sinensis, Cordyceps militaris, immune system, leukocytes, NK, natural killers, detox, chelation, zeolite, clinoptilolite.*

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)

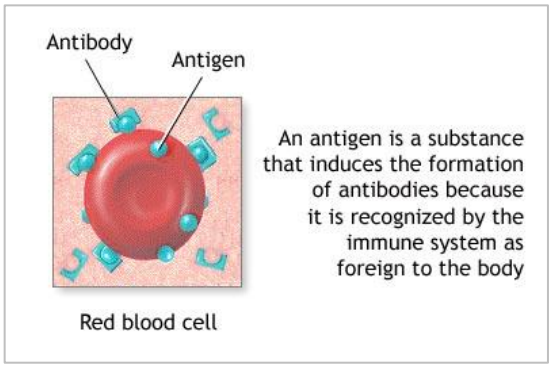
A number of different cells are considered phagocytes. The most common type is the **neutrophil**, which primarily fights bacteria. When looking for evidence of a bacterial infection, a physician may order a blood test to verify an increased number of neutrophils triggered by the infection.

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.

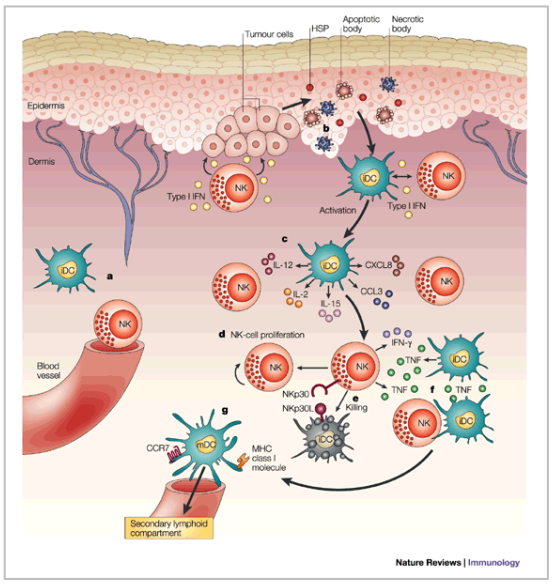
Here's how it all works:

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**.

Toxins Inhibit Immune System Function

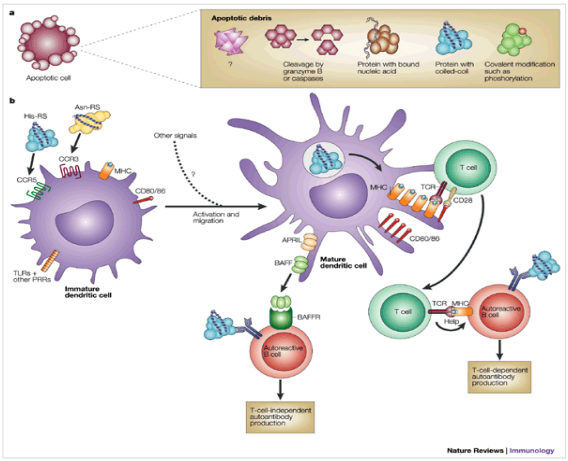
The toxic effects of some metals, such as lead and arsenic, have been recognized for hundreds of years. There has been continuing medical and political concern over the increasing contamination of the environment by heavy metals. Because lead or other metals are so widely utilized in everyday life, they have the potential to pose a continuous risk for human and animal health.

Heavy metals seem to interact with the immune system in antigen non-specific fashion. In most cases, the heavy metals compete with “good” metals in the function of metalloproteins and metalloenzymes. The good metals are essential to health because nature integrated them into human biochemistry—the size and charge of the essential metals integrate with the peptides, proteins and enzymes they are components of, allowing the biomolecules to fold properly and take on the form (3-dimensional structure) and function necessary to support life.

Heavy metals are smaller, higher charged ions that insert into these precisely folded peptides, proteins and enzymes, displace the essential metals and, simply because they are the wrong size and charge, change the 3-dimensional structure of the biomolecule, which alters both form and function. In doing so, the activity of those compounds are altered, decreased or completely inhibited.

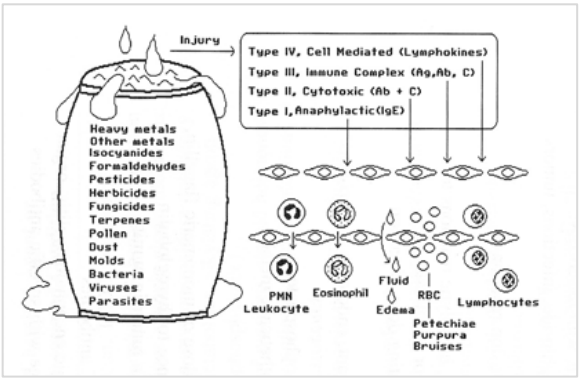
These metals exert direct toxicity to compounds of the immune system, which can either lead to malfunctioning of the system as a whole or to the disruption of the regulatory systems, which may give rise to exaggerated responses. The interaction of heavy metals with the immune system, which may lead to immunosuppression or immunodysregulation, may have consequences of allergy or autoimmunity, whereas autoimmunity or allergy induced by heavy metals may often result in the malfunctioning immune system.

Additionally, these heavy metal-containing compounds may also become targets of the immune response, in essence telling the B cells to create antibodies against natural compounds. These are called "autoantibodies" and can lead to autoimmune diseases like Multiple Sclerosis (MS) and Rheumatoid Arthritis (RA).



Methods of Detoxification

The body has a variety of mechanisms for dealing with toxicity, but the current total load exceeds the body's ability to adapt. When the body fails to break down or remove these toxins, the only other way to deal with them is through sequestration. The body will try to deposit these compounds into tissue to minimize their potential damage. For example, lead may be sequestered into bone, displacing calcium and increasing the risk of osteoporosis. The overall load of these toxins is sometimes called the "body burden".



A high body burden has been implicated in the following:

- *Immunotoxicity* – leading to asthma, allergies, cancers and chronic disease;
- *Neurotoxicity* – leading to cognition impairment, memory loss as well as sensory and motor dysfunction;
- *Endocrine toxicity* – leading to reproductive issues, loss of libido and metabolic impairment.

Aside from limiting exposure, everyone should be actively aiding their bodies in the elimination of these toxins. Most programs for detoxification focus on the body's ability to excrete, either through perspiration or digestive elimination.

Saunas, which have been used to promote perspiration, can also lead to dehydration and electrolyte imbalance. "Natural" or "herbal" laxatives or diuretics are used to increase elimination through urination and fecal wasting. These include the ubiquitous colon cleanse products. By helping our bodies to remove waste quickly, it may aid in lowering the body burden over time.

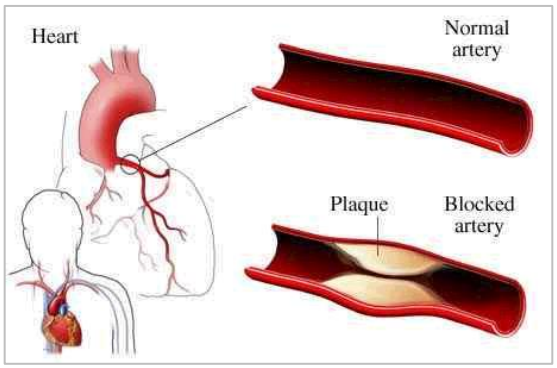
The problems associated with this form of detoxification include: dehydration, dependence and dumping. Any increase in fluid elimination may lead to dehydration and loss of electrolytes. It is important to drink plenty of water and maintain hydration during any detoxification program. Additionally, many diuretics and laxatives may create a dependence for the user.

The body becomes used to the aid in wasting and may cease to function normally without it. As an example, patients abusing natural laxatives may experience severe constipation when discontinuing their use. Lastly, the increase in wasting may facilitate the rapid removal of sequestered toxins from tissues. This is sometimes known as "dumping" and can lead to the side effects of detoxification, sometimes known as a "healing crisis" or "dumping syndrome". It's important to detox slowly in this fashion to prevent these issues.

Chelation

A more direct method for removing toxic compounds is chelation therapy, especially for the removal of heavy metals. The term **chelation** (pronounced “key-layshun”) comes from the Greek word *chele,* which means “claw,” referring to the way the negatively charged chemicals used in this process grab onto positively charged metal molecules (ions).

The first commercially available chelating agent was a chemical called ethylene diamine tetraacetic acid (EDTA), which has a molecular structure that actually resembles a clawed hand.



Chelating agents are substances that can chemically bond with toxic minerals, metals, and chemicals within the body. The proposed goal of chelation therapy is to remove harmful substances from the body by having a chelating agent form a complex with the toxic substance and allow the body to remove that complex using its natural mechanisms of waste product removal. In essence, a chelating agent encircles a mineral or metal ion and carries it out of the body via urine and feces.

Classic chelation may not be well-tolerated in some people. It tends to be expensive and is usually supplied intravenously, which is certainly inconvenient. Additionally, chelating agents tend to be non-specific and may remove healthy metals (calcium, magnesium, etc..) as well as toxic metals. Lastly, most chelators may cause a host of unwanted side effects, including: headaches, local skin irritation, nausea or stomach upset, diarrhea, feeling like fainting, extreme fatigue, fever, cramps and pain in the joints. Most of these side effects can be linked to dehydration or electrolyte imbalance caused by the chelating agent.

The newest research centers on the use of the mineral zeolite ‘clinoptilolite’. When properly micronized and activated, the zeolite effectively attracts and traps small, highly-charged particles that fit into the pores and channels of the zeolite cage. This includes heavy metals (lead, cadmium, mercury, etc.), nitrosamines and environmental pollutants.

Understand that this is a passive process – when the zeolite is in close proximity to these compounds, they will be drawn to the zeolite and either absorbed into the cage or adsorbed onto the surface of the zeolite. Once trapped by the zeolite, these toxins are easily removed from the body.

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:

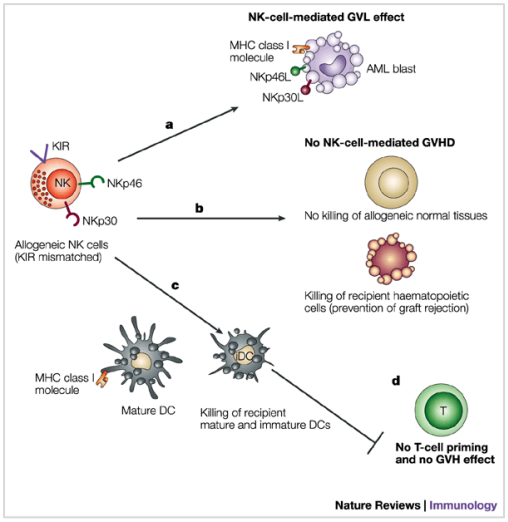
- Increased longevity
- Improved blood flow
- Cholesterol and blood sugar normalization
- Liver protection
- Kidney support
- Anti-viral, antibacterial and antifungal
- Improved respiratory function
- Reduced risk for heart disease
- Decreased platelet aggregation
- Improved blood flow
- Improved skin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

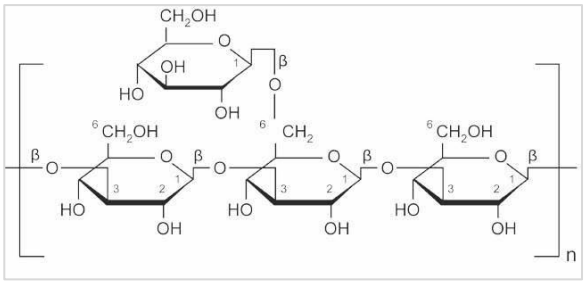
IAS Full Spectrum Mushroom Complex Overview

Pure, organic and patent-protected, **IAS Full Spectrum Mushroom 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, IAS is derived from seven closely related organisms—100% USDA certified organic, certified kosher, biotech lab cultivated, full spectrum, non-GMO *Agaricus blazei, Lentinula edodes, Grifola frondosa, Trametes versicolor, Ganoderma lucidum Cordyceps militaris* and *Cordyceps sinensis*.

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



IAS Full Spectrum Mushroom 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 basidiomyces 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 **IAS Full Spectrum Mushroom 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 IAS Full Spectrum Mushroom 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 versicolor, Cordyceps militaris* and *Cordyceps sinensis*.

We will explore some of the history, benefits and research available for each of the seven medicinal mushrooms featured in **IAS Full Spectrum Mushroom 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 cancer[3].

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 investigators[4].

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 damage[16]. A major constituent of Agaricus, ergosterol, was found to inhibit tumor growth in mice via direct inhibition of tumor-induced angiogenesis[6]. Other studies demonstrated that polysaccharides present in

Agaricus extract caused activation of macrophages[5] or natural killer cells[17] and induced cytotoxic T-lymphocyte activity in tumor-bearing mice. Specifically, activation of natural killer cells was mediated through IL-12-induced IFN-gamma expression[18]. 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 effect[19]. Furthermore, Agaricus extract stimulates caspase 3 activation and reduces telomerase activity[19] possibly through regulation of Akt signaling[20] 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 cells[21]. Agaritine, a hydrazine-containing constituent exhibits anti-tumor activity toward U937 leukemic cells mediated through apoptosis[22].

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 cells;[1] these effects may result from its ability to suppress cytochrome P450 1A enzymes that are known to metabolize pro-carcinogens to active forms.[2]

Lentin, the protein component of shiitake, exerts antifungal properties, inhibits proliferation of leukemic cells, and suppresses the activity of HIV-1 reverse transcriptase.[3]

Studies of shiitake extracts suggest antiproliferative,[4] immunostimulatory,[4] hepatoprotective,[5] antimutagenic,[6] and anticaries[7] 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 cancer.[8]

More recently, however, improvements were reported in quality of life and survival with an oral formulation of superfine dispersed lentinan in patients with hepatocellular carcinoma,[9] gastric cancer,[10] colorectal cancer,[11] and pancreatic cancer.[12] 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 patients.[2] Small experiments with human cancer patients, have shown Maitake can stimulate immune system cells, like NK cells.[3][4] *In vitro* research has also shown Maitake can stimulate immune system cells.[5] An *in vivo* experiment showed that Maitake could stimulate both the innate immune system and adaptive immune system.[6]

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)[7][8][9][10] as well as inhibit the growth of various types of cancer cells (canine cancer cells, bladder cancer cells).[11][12][13] Small studies with human cancer patients, revealed a portion of the Maitake mushroom, known as the "Maitake D-fraction", possess anti-cancer activity.[14][15] *In vitro* research demonstrated the mushroom has potential anti-metastatic properties.[16] In 1997, the U.S. Food and Drug Administration (FDA) approved an Investigational New Drug Application for a portion of the mushroom.[17]

Research has shown Maitake has a hypoglycemic effect, and may be beneficial for the management of diabetes.[18][19][20][21][22][23] The reason Maitake lowers blood sugar is due to the fact the mushroom naturally contains an alpha glucosidase inhibitor.[24]

Maitake contains antioxidants and may partially inhibit the enzyme cyclooxygenase.[25] An experiment showed that an extract of Maitake inhibited angiogenesis via inhibition of the vascular endothelial growth factor (VEGF).[26]

Lys-N is a unique protease found in Maitake.[27] Lys-N is used for proteomics experiments due to its protein cleavage specificity.[28]

Background of *Trametes Versicolor (Turkey Tail)* Mushroom

Trametes 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. A polysaccharide is a carbohydrate formed by a large number of sugar molecule

Trametes 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.

Trametes 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. PSK has been found to induce cytokine expression in human peripheral blood mononuclear cells in vitro. In another studies, PSP, as well as Trametes extract, selectively induced apoptosis of human promyelocytic leukemia HL-60 cells (13) (23). It also increased apoptotic cell death in cells that had been treated with 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 time (14). An additional in vitro study showed that a medicinal mushroom blend that included Trametes Versicolor inhibited cell proliferation and induced cell cycle arrest at the G2/M phase in the invasive human breast cancer cell line MDA-MB-231 (15). 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) [15]. 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 glycosylation [16].

Several animal studies report of synergism between PSK and biologic therapies, including a concanavalin A-bound L1210 vaccine and the IgG2a monoclonal antibody against human colon cancer cells [17]. PSP induces cytokine production and T-cell proliferation and prevents immune suppression due to cyclophosphamide in animal models. Peritoneal macrophages isolated from mice that were fed PSP show increased production of reactive nitrogen intermediates, superoxide anions, and tumor necrosis factor [18]. PSP also shows analgesic activity in mouse models [19]. Non-small cell lung cancer patients have increased leukocyte and neutrophil counts, and increased serum IgG and IgM after consumption of PSP [6]. Healthy volunteers as well as breast cancer patients who used a formula containing Trametes and Salvia were found to have elevated counts of T-helper lymphocytes (CD4+), high ratio of CD4+/CD8+), and elevated absolute counts of B-lymphocytes [7] [8]. TNF-alpha and IL-8 gene expression were also found to be significantly induced after PSK administration in healthy volunteers and gastric cancer patients, although individual response varied [20

Researchers have found that PSK, one of the substances that can be extracted from *Trametes 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 therapy. 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 cells.

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 leukemia.

The effects of PSP are less well known. While some early Chinese studies of PSP have reportedly shown it may help protect the immune system from the effects of cancer treatment, most studies published in medical journals thus far have been in cell cultures or animals. These types of studies can suggest possible helpful effects, but they do not provide proof that such effects can be achieved in humans. Studies in animals have suggested that PSP may slow the growth of lung cancer and sarcoma, and may help make radiation therapy more effective in treating certain brain tumors. One small study in humans found that lung cancer patients taking PSP seemed to maintain their health longer than those who did not take PSP, although they did not get better and did not report improvement in cancer-related

Background of *Ganoderma Lucidum (Reshi)* 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 redutase (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; it 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 triterpenes [(1)]. Extracts of reishi can stimulate macrophages, alter the levels of TNF and interleukins [(2)] [(3)] [(4)] [(5)], inhibit platelet aggregation [(11)] [(12)].

Clinical studies indicate that Reishi extracts improve lower urinary tract symptoms (LUTS) in men [(9)] [(10)(20)], exert mild antidiabetic effects and may improve dyslipidaemia [(29)].

In vitro and animal studies indicate that reishi has chemopreventive effects [(21)], alleviates chemotherapy-induced nausea [(13)], enhances the efficacy of radiotherapy [(22)], and increases the sensitivity of ovarian cancer cells to cisplatin [(27)]. It was also effective in preventing cisplatin-induced nephrotoxicity [(28)].

In small clinical studies, reishi increased plasma antioxidant capacity [(6)] [(7)], and enhanced immune responses in advance-stage cancer patients [(8)]. Remission of hepatocellular carcinoma (HCC) has been reported in a few cases [(23)]. However, further research is needed to establish use of reishi as an anticancer agent [(30)].

Mechanism of action: 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 triterpenes [(1)]. Extracts of reishi can stimulate macrophages, alter the levels of TNF and interleukins [(2)] [(3)] [(4)] [(5)], inhibit platelet aggregation [(11)] [(12)].

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responses in advance-stage cancer patients [8]. Remission of hepatocellular carcinoma (HCC) has been reported in a few cases [23]. However, further research is needed to establish use of reishi as an anticancer agent [30].

Background of *Cordyceps (Sinensis (Catepillar)* & *Militaris*) 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 aphrodisiac.[2] Although there are often-repeated claims of thousands of years of use in traditional Chinese medicine, so far no clear textual source has surfaced.

Cordyceps sinensis is a new generation of mushroom being used by the pharmaceutical industry and also as a dietary supplement amongst more informed consumers seeking alternatives to the more conventional treatments for cancer and AIDS as well as a wide range of other health and immune system issues.

These medicinal mushrooms are extremely high in both beta-glucans, which have been shown to be useful in cancer therapies, and polysaccharides. Polysaccharides are long sugar chains with many oxygen sections within them. As the body breaks down these sugars, the oxygen molecules are released and absorbed on a cellular level. We know that all forms of cancer cannot exist in an oxygen-rich environment and that without proper oxygen levels the body is left to fall into degenerative states that encourage cancer, heart disease, immune disorders and diabetes, and also allow many viral diseases such as hepatitis C, Lyme's disease and many others to flourish in Tibet.

Cordyceps sinensis increases ATP (adenosine triphosphate) levels in the body by almost 28 per cent. ATP is the body's energy supply source—the body's battery, so to speak—and is required for all enzyme processes. It is also now believed that ATP is where cold-fusion ("Brown's gas") processes occur in the body on a molecular level. Although the concept of molecular-level cold fusion is not the subject of this article, I believe this is the root of biological energy exchanges, which will be explored in future writings. The impact on the energy state alone would make this mushroom a true superfood, but there is much more to be shared.

Modern scientific studies have confirmed and expanded on the findings of traditional Chinese medicine, that the Cordyceps fungus has a multitude of health benefits and can treat a wide range of illnesses.What makes Cordyceps important for use with cancer is that it contains beta-glucans and polysaccharides.

As the sugars break down, the numerous oxygen molecules are released on a cellular level, the result being that cancerous materials present are immediately destroyed. Cordycepin, one of the target compounds (nucleosides), inhibits the DNA repair mechanism and is probably responsible for its antiviral (HIV) effects

RESEARCH: The medicinal properties of Cordyceps are remarkable. In traditional Chinese medicine (TCM), the main use of Cordyceps has been in the treatment of asthma and other bronchial conditions. Modern research now confirms the efficacy of these ancient uses. Much of what is known in the western world about Cordyceps sinensis is due to the work of Dr Georges Halpern, a physician and professor emeritus with the University of Hong Kong and the author of several books about Cordyceps.

One of the highlights of modern research has been the discovery of new antibiotics in this mushroom. One of these, cordycepin, is very effective against all sorts of bacteria that have developed, or are developing, resistance toother, more common antibiotics (such as penicillin, a fungus product!).

Cordyceps is especially effective against tuberculosis, leprosy and human leukaemia, as shown in many trials in China, Japan and elsewhere.

Some additional health benefits of Cordyceps are outlined below.

- *Enhances physical stamina*
  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.

  There have been many reports of amazing improvements in performance in various sports due to the intake of Cordyceps.

  There has even been talk of banning Cordyceps from sporting events because it may give an unfair advantage to those who can get it! Most professional athletes who use it now are unwilling to admit that they do, due to the possibility that some sporting authority will outlaw its use. In the other direction, the Canadian Olympic Committee has taken an official stand on Cordyceps, ruling that it is allowed in professional competition.

  Clinical research has shown that Cordyceps use increased cellular bio-energy—ATP (adenosine triphosphate)—by as much as 55 per cent. 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 are seen in humans using Cordyceps.

- *Improves respiratory function*
  Several scientific studies have demonstrated the benefits of Cordyceps sinensis in alleviating the symptoms of various respiratory illnesses including chronic bronchitis and asthma.

- *Increases oxygen absorption*
  In a double-blind, placebo controlled study with 30 elderly volunteers, Cordyceps was shown to improve significantly the maximum amount of oxygen these people were able to assimilate.

  Chinese studies of cardiovascular illnesses have shown that ethanol extracts of Cordyceps mycelia and Cordyceps fermentation solutions caused a change in the biological action that allowed for an increase in cellular oxygen absorption by up to 40 percent. In addition, studies have shown the effect of these compounds in relieving chronic obstructive pulmonary disease.

- *Improves heart function*
  Numerous studies have demonstrated the benefits of Cordyceps sinensis in treating heart rhythm disturbances such as cardiac arrhythmia and chronic heart failure.

- *Helps maintain healthy cholesterol levels*
  Four studies have demonstrated that Cordyceps sinensis helped to lower total cholesterol by 10–21 percent and triglycerides (neutral fats) by 9–26 per cent, and at the same time helped to increase HDL ("good") cholesterol by 27–30 per cent.

  One of the highlights of modern research has been the discovery of new antibiotics in this mushroom.

- *Improves liver functions*
  Cordyceps sinensis has been shown to improve liver functions as well as help with

cirrhosis, sub-chronic and chronic hepatitis and related liver diseases which are more prevalent than most people think.

The liver is the living filter of the body, cleaning the blood and all other fluids of impurities. There is no way for you to survive, much less feel healthy, without a functioning liver.

Clinical trials with Cordyceps supplement involving 33 patients with hepatitis B and eight patients with cirrhosis of the liver showed a 71.9 percent improvement on the thymol turbidity test and a 78.6 percent improvement on the SGPT test. These are enzyme tests showing changes in liver functions.

- *Improves kidney disease*
  A Chinese study has shown a 51 percent improvement in chronic kidney disease after only one month of dietary supplementation with Cordyceps.

- *Reduces tumor size*
  Several clinical studies with cancer patients have been conducted in China and Japan, using a therapeutic dose of 6.0 grams of Cordyceps per day.

  In one study with 50 lung cancer patients who were administered Cordyceps in conjunction with chemotherapy, tumors reduced in size in 46 percent of patients. A study involving cancer patients with various types of tumors found that Cordyceps sinensis extract (6.0 grams/day for over two months) improved subjective symptoms in the majority of patients.

  White blood cell counts were maintained and tumour size was significantly reduced in about half of the patients.

  Researchers in Japan reported that Cordyceps enhances the general reactivity of the immune system in individuals with cancer. To discover this, they subcutaneously injected mice with cancerous (lymphoma) cells and then orally administered Cordyceps. This led to a reduction of tumor size and prolonged life. Cordyceps also improved the antibody responses in these studies

- *Enhances immunity and T-cell production*
  Cordyceps has been found to enhance "natural killer" (NK) cell activity, thus increasing T-cell production which results in expanded muscle mass. Muscle power is improved with the building of young, healthy cells. Cordyceps effectively recharges the protective army of NK cells. The body's ability to fight infections and tumours depends on the availability of NK cells. These are essential as the first line of defense for maintenance of the body's protection mechanism, commonly known as the immune system.

  Several scientific studies of Cordyceps have especially focused on NK cells and Cordyceps' effect on them as they relate to cancer formation. One in vitro study demonstrated that Cordyceps significantly enhances NK cell activity in normal individuals as well as leukaemiastricken people.

  In a Chinese study, published in the Chinese *Journal of Integrated Traditional and Western Medicine*, natural Cordyceps enhanced the NK cell activity of normal patients by 74 percent and increased the NK activity of leukaemia patients by 400 percent. Similar improvements of NK cell activities were found in large melanoma tumors.

- *Assists symptoms of aging*
  Clinical research in controlled studies has revealed that elderly patients suffering from fatigue and senility related symptoms reported relief in these areas after using Cordyceps for 30 days. Their fatigue was reduced by 92 percent, their feeling of cold by 89 per cent and their dizziness by 83 percent. Patients with respiratory/ breathing problems felt physically stronger and some individuals were able to jog up to 600 feet (183 metres).

- *Protects against free radical damage*
  Several studies have shown that Cordyceps sinensis gave protection against the damage caused by free radicals and had powerful anti-oxidant properties.

- *Helps discomfort from tired legs*
  Various studies have shown that Cordyceps sinensis improved the flow of blood in the body by relaxing the smooth muscles of the blood vessels and allowing them to expand, and also enhanced the functioning of the heart and lungs. Cordyceps therefore prevents or reduces the contraction of blood vessels which interferes with blood flow in the legs—the main cause of tired legs.

- *Improves sexual function*
  Three separate Chinese double-blind, placebo controlled studies with over 200 men with "reduced libido and other sexual problems" showed remarkably similar results. On average, 64 per cent of the Cordyceps-users reported significant improvement at the conclusion of the experimental period compared with 24 percent of the placebo group.

  In another double-blind, placebo-controlled study conducted with 21 elderly women with similar complaints, 90 percent reported improvements of their condition following the use of Cordyceps, compared with none in the control group.

  Researchers in Japan reported that Cordyceps enhances the general reactivity of the immune system in individuals with cancer, Cordyceps has been shown to improve libido and quality of life in men and women, fight infertility and increase sperm count and survival. Clinical studies involving 189 male and female patients with decreased libido and desire showed improvement of symptoms in 66 per cent of cases. A double-blind study conducted by the Institute of Materia Medica in Beijing showed an 86 percent improvement in female libido and desire. The most dramatic physical proof came from a fertility study involving 22 males which showed that, after eight weeks of taking a Cordyceps supplement, their sperm count increased by 33 per cent, their incidence of sperm malformations decreased by 29 per cent and their sperm survival rate increased by 79 percent

- *Reverses HIV*
  In a study in 2004 in Ghana, 3,000 early-stage HIV patients were given a formula with Cordyceps sinensis as a primary ingredient. Beyond anyone's wildest dreams, at the end of six months all 3,000 patients showed "no presence in their blood of HIV". When an HIV–AIDS patient took the Immune-Assist drug for cancer, their clinical picture improved dramatically in regard to the HIV infection.

Immune Function, Anti-cancer; Response and DNA Repair

It has long been understood that the beta-glucan compounds found in many species of mushroom significantly enhance immune function. This class of compounds is the most widely prescribed class of anticancer

medications in the world. The pharmaceutical drugs lentinan, SK and grifolan are examples of these compounds.

There is evidence of another mechanism at play in the Cordyceps anti-tumour response besides the wellknown immune modulation triggered by the polysaccharide compounds. It is related to the structure of at least some of the altered nucleosides found in Cordyceps, exemplified by the cordycepin compound (3'-deoxyadenosine).

This is a molecule almost identical to normal adenosine, with the exception that it is lacking an oxygen atom on the ribose portion of the molecule atthe 3' position.

The same lack of this 3' oxygen can be seen in other Cordyceps compounds such as dideoxyadenosine. The lack of oxygen at this particular position is thought to be important in a very specific way. The structure of DNA depends on this oxygen to create the bond between adjacent nucleosides. This bond is between the 3' and the 5' positions on the ribose portions of the nucleosides, effectively forming the "ladder structure" that holds the DNA together.

In the replication of any cell, the first step is the separation of the DNA molecule down the middle, like unzipping, between the pairs of complementary nucleosides.

The next step is the insertion, one at a time, of new complement nucleosides. These form hydrogen bonds between the complement pairs and phosphate–sugar bonds between the 3' and 5' positions at the outside edge of the molecule, which is the ribose portion.

The synthesis of the new DNA molecules proceeds with the sequential insertion of new complement nucleosides one at a time into the newly forming DNA molecule until the original strand of DNA is replicated twice, each of these strands being an exact copy of the original and forming the genetic code for a new generation of cells.

This synthesis continues to proceed with the insertion of each new nucleoside, unless a 3'-deoxyadenosine (cordycepin) molecule is pulled in.

When this happens, there is no oxygen present at that vital position to form the 3'–5' bond, and the replication of the new DNA molecule stops. Once the DNA synthesis stops, the cell cannot continue to divide and no new cell is formed. (In normal mammalian cells, this insertion of the de-oxygenated adenosine is of little importance, as healthy cells have an inherent DNA repair mechanism.)

When this sort of error occurs, the altered nucleoside (the cordycepin) is removed from the string of nucleosides and a new segment of adenosine is inserted. However, by their very nature, cancer cells have lost this DNA repair mechanism. (If they could correct their DNA errors, they would not be cancer cells.)

Most bacteria and all viruses (including the human immunodeficiency virus, HIV) lack this DNA repair mechanism.

There is evidence of another mechanism at play in the Cordyceps anti-tumor response besides the well-known immune modulation triggered by the polysaccharide compound significant anti-tumor response.

For example, a normal healthy breast tissue cell has an average life span of about 10 days, after which it reproduces and a new cell is formed. But breast cancer cells multiply much more quickly than healthy cells, reproducing on average every 20 minutes. This means that breast cancer cells replicate about 750 times more quickly than the surrounding healthy tissue. If the cordycepin were equally toxic to both types of cells, it would be killing off the cancer cells 750 times faster than the healthy cells.

But because of that DNA repair mechanism in the healthy cells, cordycepin appears not to interfere with the healthy cell replication, and the tumour-cell kill rate is actually much higher than the 750:1 ratio.

- The same sort of DNA interruption mechanism is also responsible for the anti-tu0ur effects of some other chemotherapy agents. This same mechanism of DNA synthesis inhibition is probably the mechanism responsible for the antiviral effects seen with cordycepin.

Background of clinoptilolite

Zeolites are a family of crystalline aluminosilicate minerals. The first zeolite was described in 1756 by Cronstedt, a Swedish mineralogist who coined the name from two Greek words meaning 'boiling stones', referring to the evolution of steam when the rock is heated. About fifty different natural zeolites are now known and more than one hundred and fifty have been synthesized for specific applications such as industrial catalysis or as detergent builders.

Clinoptilolite is a naturally occurring zeolite, formed by the devitrification (ie the conversion of glassy material to crystalline material) of volcanic ash in lake and marine waters millions of years ago. It is the most researched of all zeolites and is widely regarded as the most useful. In common with other zeolites, clinoptilolite has a cage-like structure consisting of SiO_4 and AlO_4 tetrahedra joined by shared oxygen atoms. The negative charges of the

AlO_4 units are balanced by the presence of exchangeable cations - notably calcium, magnesium, sodium, potassium and iron. These ions can be readily displaced by other substances, for example heavy metals (mercury, lead, cadmium, etc..) and ammonium ions.

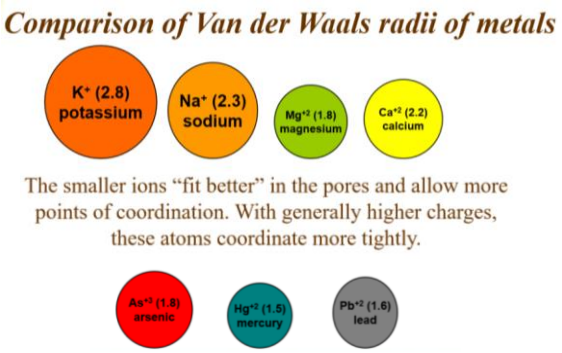
This phenomenon is known as cationic exchange, and it is the very high cationic exchange capacity of clinoptilolite which provides many of its useful properties. Clinoptilolite is currently used in diverse applications such as drinking water purification, air filtration, plant fertilizer and as an animal feed additive. Many studies have shown that clinoptilolite absorbs toxins created by molds in animal feeds, as well as enhancing nutrient absorption by cattle, pigs, lambs and other animals. In the United States, clinoptilolite falls under the category of sodium aluminosilicate and has GRAS (Generally Recognized as Safe) status used primarily as an anti-caking agent (Code of Federal Regulations, Title 21, Section 182.2727).

Because of its cage-like structure and negative charge, clinoptilolite has the ability to draw to itself and trap within itself positively charged heavy metals and other toxic substances. The zeolite in the ZMUNITY attracts and traps small, highly-charged particles that fit into the pores and channels of the zeolite cage.

Whereas most chelating agents used for detoxification are non-specific, only relying on charge for binding potential, the clinoptilolite seems to be highly specific for the toxic heavy metals. Research has shown that the smaller the diameter of the metal and the higher the charge of the metal, the greater the affinity it has for the activated zeolite. Higher charges simply increase the strength of binding with higher binding characteristics. The small size allows for deeper access into the zeolite pores with more points of coordination (attachment). Larger atoms do not fit into the zeolite cage as well and so are more easily exchanged for higher-affinity metals. As an example of this phenomenon, arsenic has a charge of +3 and an atomic radius of approximately 1.8 angstroms, while potassium has a charge of only +1 and an atomic radius of approximately 2.8 angstroms. The arsenic binds with very high affinity for the zeolite while the potassium has no affinity whatsoever.

The metals that are toxic to humans are toxic *because* they are smaller atoms that carry a higher positive charge and can easily displace the essential electrolytes, which tend to be larger and have less charge density. These essential ions are not essential *because* they are larger or "weaker", they are essential because nature integrated them into human biochemistry - the size and charge of the essential metals integrate with the peptides, proteins and enzymes they are components of, allowing the biomolecules to fold properly and take on the form and function necessary to support life.

The smaller, higher charged ions insert into these precisely folded peptides, proteins and enzymes, displace the essential metals and, simply because they are the wrong size and charge, change the 3-dimensional structure of the biomolecule which alters both form and function. Size and charge, in this case, are simply circumstantial to activity. The zeolite in the ZMUNITY preferentially binds smaller, more charge-dense ions. That is the primary characteristic for which it was selected for use in the product. Metals with a smaller size and a higher charge will bind with greater affinity for the zeolite. The smaller size allows for deeper penetration into the zeolite cage. Additionally, the smaller size allows for more points of coordination with the zeolite. In other words, more of the surface of a small atom will be held directly by the zeolite. The higher charge allows for a tighter bond simply because of charge-to-charge interactions. Consider the example of refrigerator magnets to illustrate this point. A weak magnet will not stick well to the side of a refrigerator and will not even hold one piece of paper. This is like a metal with a low charge trying to be held by the high negative charge of the zeolite. A strong magnet can hold many pieces of paper to the refrigerator and is hard to remove because of its strong interaction. This is similar to a metal with a high positive charge that will bind very strongly to the high negative charge of the zeolite cage. As we stated previously, all of the metals that are good for us (magnesium, calcium, potassium, etc..) tend to be large with lower charges. All of the metals that are toxic (mercury, lead, arsenic, etc..) tend to be smaller with higher positive charges.



The clinoptilolite binds a variety of toxins. This includes heavy metals (Lead, Cadmium, Mercury, etc..), nitrosamines and others. Cationic exchange is an entirely passive process – when the zeolite is in close proximity to these high-affinity compounds, they will be drawn to the zeolite and either absorbed into the cage or adsorbed onto the surface of the zeolite. There is no chemical activity in this process. The zeolite will not be drawn to compounds in an effort to 'rip' metals away from them. In other words, the zeolite will not pull metals that are sequestered inside tissue or bone. If, on the other hand, the tissue has already released free metals into the system, the zeolite will have the ability to trap and remove it.

Uniqueness of the zeolite contained in *ZMUNITY*

Research conducted in the development of the Cell Defender found that there were two major obstacles in using natural clinoptilolite as a dietary supplement and oral chelator.

- First, the average particle size of mined clinoptilolite is 40-250 microns. Particles in this size range are far too large to allow for absorption from the digestive tract into the bloodstream. Therefore, every zeolite that had been used previously would be primarily a digestive cleanser. In order to

utilize the zeolite as a systemic detoxifier, the crystals would have to be reduced in size to less than 2 microns.

- The second issue is one of activity. Natural zeolites act as filters in nature, absorbing a variety of toxins that surround the minesite. Clinoptilolite analyzed from the minesite contains heavy metals, volatile organic compounds (VOCs) and other high-affinity toxins that, in essence, take up space in the crystal – thus limiting its potential to detoxify by reducing its available surface area.

To remedy these issues, the product is manufactured in two distinct steps: *Micronization* and *Activation*.

Micronization

The zeolite mineral used in Cell Defender is reduced in size mechanically, prior to the activation process, to a size of 0.39 to 5 microns. This does not destroy the properties of the molecule. To the contrary, reducing the particle size increases access to the charged "cages" that would otherwise be unusable. For instance, a micron-sized particle has millions of "pores" available to bind heavy metals and other toxins. The small size of the particle permits diffusion deep within itself, allowing access to the inner "cages" that would be inaccessible in a larger particle due to limitations in diffusion distance. Most importantly, the structure of the individual "cages", and therefore the ability to sequester heavy metals and other toxins, is unaffected.

Consider this: If a five-carat diamond is broken into five one-carat diamonds, the structure of each one-carat diamond is exactly like that of the original five-carat diamond, only smaller. And if that one-carat diamond were pulverized into dust, each resulting, tiny piece of diamond would have the same structure and properties of the original five-carat diamond. The Silicon-Oxygen bonds in the zeolite are even more thermodynamically stable, i.e. are stronger, than the Carbon-Carbon bonds of the diamond. It would take a concerted effort and extreme amounts of energy to reduce the zeolite to particles that no longer possessed the characteristic "cage" structure and therefore the ability to sequester toxic metal ions. Nature required over 1000^{o}C and tremendous pressures to create a zeolite. The conditions used to activate Clinoptilolite, the zeolite used in Cell Defender, are insufficient to dehydrate the mineral or alter its physical characteristics.

Micronization of the zeolite also allows for uptake into the bloodstream from the digestive tract.

Many compounds (minerals and pharmaceuticals/nutraceuticals) are absorbed in the gut that are in this size range. For example: sucrose molecules greater that 2 microns are absorbed through the gut; several sugar-coated proteins (biopharma oral preps designed to prevent digestion in the stomach prior to absorption) are in the 3-5 micron range and are easily absorbed; albuterol sulfate has an average particle size of 4 microns and is absorbed through the lung mucosa (which has similar permeability to the gut mucosa); pharmaceutical preparations of the immunosuppressant, cyclosporin, consist of particles 2-4 microns in size. In short, the concept of absorbing a particle that is sub-0.5 to 5 microns is generally well established. Additionally, preliminary studies done on human volunteers taking the Cell Defender chronically have demonstrated the presence of clinoptilolite in the serum at concentrations greater than 1ng/dL.

Activation

Cell Defender is manufactured under a closely-guarded, proprietary process. The primary goal of this process is to remove the toxins naturally present in the mineral. Just as it does in the body, zeolite absorbs metal ions and other toxins that filter through it as it sits in the ground waiting to be mined. The toxins that the mineral absorbs prior to being mined do not make it dangerous, *per se*, as zeolite sequesters these toxins very well. The zeolite is simply less effective. For instance, if the particle has ten thousand "cages" and five thousand are

already full before it is mined, the particle will not be as effective when introduced as a supplement as a particle with all ten thousand “cages” available. Cell Defender undergoes an ‘activation process’ that forces the removal of all these toxins. This process removes all extraneous metals and empties out the zeolite cage - therefore removing any toxins that were found with the zeolite and 'activating' the molecule to be at its most effective. Understand that the zeolite molecule is, for all practical purposes, indestructible.

Heat up to 900º Fahrenheit will not crack the molecule and it can be frozen in solution and defrosted without any change in activity. It is also amphoteric – meaning that it exists just as well in an acidic or a basic environment. The zeolite is activated in a very weak acid under high temperature conditions. This does not break the zeolite down; it simply forces the evacuation of stored toxins in the zeolite cage. For purposes of activation, heat is added to the system *only* to increase the bond resonance within the structure of the cage, effectively “loosening the grip” of the zeolite, promoting a more complete exchange of the naturally occurring toxic metal ions with more beneficial ones. Being positively charged and thus absorbed by the zeolite, Calcium and Magnesium are used to exchange for the toxins.

These healthy metals migrate back into the zeolite and help stabilize the molecule. After ingestion, they easily undergo cationic exchange with metals that are higher in the affinity scale of the zeolite (i.e. Mercury, Lead, Cadmium, etc..). Without this process, other zeolite products must contain toxins and heavy metals as part of the zeolite cage. Additionally, without a heat process or some preservative, they must contain bacterial and fungal contamination.

Cell Defender is the only zeolite formulation that is micronized and activated.

Synergies of IAS & Cell Defender - Claims and Benefits

The concept of synergistic benefits takes into account that two or more substances work together so that their total effect is greater than the sum of their individual benefits. In biochemistry, this is usually a result of substances having similar benefits that are created through different mechanisms of action. Because the mechanisms are isolated from each other, their benefits can be maximized and usually results in synergy. When examining the synergies between the IAS Mushrooms and the activated zeolite, it is simple to note several distinct claims with differing mechanism to support those claims.

<u>Both products act as immuno-modulators</u>.

The zeolite does not stimulate the immune system, but allows it to function optimally by removing toxins, viruses, yeasts, bacteria, and fungi which can depress immune function and interfere with hormones[6]. Additionally, heavy metals have been indicated in the inhibition or down-regulation of zinc finger proteins[7]. These proteins are necessary for proper cell division and immune system response. The zeolite has been indicated in stabilizing zinc finger protein activation through the removal of inhibitory toxic heavy metals. As noted previously, the IAS Mushrooms modulate the immune system by cellular signaling. This increases T-Cell activation without creating a hyper-immune response[8]. These provide several different mechanisms to activate and stabilize immune system function.

<u>Both products provide superior antioxidant protection.</u>

Clinoptilolite is considered to act as an antioxidant through a simple mechanism of the capture and removal of small, oxidative compounds[9,11]. The IAS Mushrooms function as an antioxidant because of its constituent antioxidant compounds, which include co-factors and polysaccharides. These quench free radicals through electron donation or electron

acceptance[10]. 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[11,12]. This is primarily considered to be caused by the induction of apoptosis and the zeolite's activation of the p21 tumor suppression gene[13]. Additionally, the zeolite acts to balance the body's pH and may create an inhospitable environment for cancer cell growth as systemic alkalinity is maintained. Agaricus extracts have been studied almost exclusively for their effects against cancer cell growth[1,14-20]. The mechanism involved in this case is through immune system activation and immuno-modulation[21]. The expected synergies result in a powerful immuno-modulating agent that reduces the risk of mutagenesis.

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