

Code: FE1933 - 90 vegetable capsules



Exclusive combination of 6 highly concentrated medicinal mushrooms (8:1 extract) that act in synergy on the different components of immunity. Among its active substances are polysaccharides, and specifically, beta-glucans, which are responsible for its inestimable therapeutic value focused on activating immune response, anti-tumour activity and antibacterial and antiviral response. Our product is an extract providing the highest concentration of polysaccharides (40%).

In addition to its activity on the immune system, other constituents such as betulinic acid (chaga); 3-deoxyadenosine or cordycepin (cordyceps); hericenones and erinacines (lion's mane); triterpenes (reishi); and lentinan (shiitake) exert further activities unique to each mushroom. Each of these mushrooms offers its own unique health benefits.

The method of polysaccharide extraction is a critical point that determines the concentration and efficacy of the product. Our extract is obtained through a validated extraction process in hot water which concentrates, guarantees and preserves the active compounds, leading to a higher final concentration of polysaccharides. Mycelium contains polysaccharides that are bound to the cell walls of chitin, which is indigestible in the gastrointestinal tract. Chitin must be dissolved in hot water in order to release the polysaccharides and guarantee a high polysaccharide content as well as greater bioavailability. The extract is standardized to 40% polysaccharide content.

The mushrooms used for our formulation have been cultivated in greenhouses under climate controlled conditions and are free of heavy metals, herbicides and pesticides in order to guarantee the purity and strength of the extract.

Ingredients: Reishi extract (Ganoderma lucidum), Maitake extract (Grifola frondosa), Shiitake extract (Lentinula edodes), Chaga extract (Inonotus obliquus), Cordyceps extract (Paecilomyces hepiali), Lion's mane extract (Hericium erinaceus), anticaking agent (magnesium salts of fatty acids), vegetable capsule (glacing agent: hydroxypropylmethylcellulose; purified water).

Nutritional Information:	3 capsules (1 566 mg)
Reishi (<i>Ganoderma lucidum</i>) (8:1)*	238,5 mg
Maitake (Grifola frondosa) (8:1)*	238,5 mg
Shiitake (Lentinula edodes) (8:1)*	238,5 mg
Chaga (Inonotus obliquus) (8:1)*	238,5 mg
Cordyceps (Paecilomyces hepiali) (8:1)*	123 mg
Lion's mane (Hericium erinaceus) (8:1)*	123 mg

^{*}Standardized extract, 40% polysaccharides.

Hot-water extraction.

Size and format:

90 vegetabe capsules

Recommended daily dose:

1 capsule three times daily.

Do not exceed the stated recommended daily dose.

Indications and uses:

- Increasing immune response in a variety of imbalances related to viral and bacterial infections (hepatitis, herpes, candidiasis...), repeated infection, autoimmune diseases (rheumatoid arthritis, systemic lupus, polymyalgia), immune-deficiency and inflammatory diseases. It also offers cardiovascular protection and acts as an antioxidant (high cholesterol, diabetes, hypertension, coronary disease).
- It is helpful for respiratory health (asthma, bronchitis, allergies...), liver protection, benign prostatic hyperplasia, neuroprotection (Parkinson's disease), antiaging therapies, states of convalescence and feeling run-down, and in situations requiring greater resistance to several types of stress (anxiety, depression, insomnia).
- Additionally, it has anti-tumour properties and is recognized as a co-adjuvant for chemotherapy and radiotherapy.

Cautions:

Consult a health-care practitioner before use if you are pregnant or breast-feeding, if you are treated with medication (immunosuppressors or anticoagulants), or if you have a special medical condition (immune system disorder or diabetes).

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<u>REISHI</u>: Used and known as Lingzhi in Traditional Chinese Medicine for thousands of years, today it is still one of the most widely used medicinal fungi because of its great variety of properties. Reishi is its name in Japanese, which translates as "the mushroom of immortality" and "the elixir of life", as it is known for increasing longevity and as an adaptogen, improving the body's ability to adapt to changes and diverse stressors (physical, mental or emotional).

The use of its extract allows for a synergic effect between the different active principles that make it up; the triterpenes suppress the growth and invasive behaviour of cancer cells, while the polysaccharides stimulate the immune system, increasing the cytokine production and anti-tumour activity of the immune cells, as well as exerting an antioxidant action. This fungus also exerts antiangiogenic activity, suppressing the creation of new blood vessels which supply nutrients to tumour cells and allow for their invasion.

This fungus has been used in different clinical trials for its benefits on strengthening the defences of cancer patients (lung, breast, colon and prostate cancer), above all in combination with chemotherapy and/or radiotherapy. It significantly increases immune response in patients with advanced stages of cancer ⁽¹⁻³⁾. In several studies, G. lucidum interferes with different points of the cell cycle, detaining the growth of tumour cells and reducing fatigue related to breast cancer ⁽⁴⁾.

Its activity against allergies and asthma is due to its immune-modulating and anti-inflammatory properties, which inhibit the release of histamine and other chemical mediators of mastocytes, neutrophils and macrophages (5-7).

Triterpenes are attributed other properties as well, such as their hepatoprotective effect, for which they have been used in the treatment of hepatic diseases $^{(8-10)}$. Clinical studies show that its extracts are effective in patients with chronic hepatitis B $^{(11-12)}$.

Some of the triterpenes in G. lucidum have been studied in cardiovascular disease with very good results, showing beneficial effects on blood pressure and serum lipids in patients with coronary disease (13-14).

It is also highly considered for certain states such as anxiety, insomnia and stress because of its hypnotic and calming effect on the nervous system, significantly decreasing time to sleep onset and increasing total sleep time (15-16).

Its anti-inflammatory properties explain its effect on chronic pathologies such as arthritis, or its modulating effect on chronic inflammatory response. "In vitro", it inhibits the production of synovial fibroblasts of rheumatoid arthritis, suggesting its possible application in treating autoimmune conditions such as rheumatoid arthritis (17).

It inhibits the toxicity of synaptic beta-amyloid, making it a potential treatment for Alzheimer's disease (18).

It also affects cardiovascular health ⁽¹³⁻¹⁴⁾, the immune system (1) and the control of glucose ⁽¹⁹⁾ and cholesterol levels ⁽²⁰⁾. It improves the symptoms of neurasthenia ⁽²¹⁾.

It also has an effect on glucose control in patients with diabetes mellitus type II (22).

The synergy between polysaccharides and triterpenes has also been seen in benign prostatic hyperplasia upon inhibiting the activity of 5-alpha-reductase (23) and improving its related symptoms (24).

Many studies have been carried out in order to quantify this antioxidant action using biomarkers, the assessment of antioxidant enzymes and the activity of the mitochondrial complex in cardiac cells. The results indicate a potent antioxidant action in G. lucidum that has been linked to a lower risk of coronary disease and a decrease in cell energy loss associated with age ⁽²⁵⁾.

It also exerts an antiviral effect by inhibiting replication, which has been shown in herpes simplex I and II, HIV and Hepatitis B ^(11, 26, 27). As an antibacterial agent, it has shown efficacy against Gram + bacteria (B. subtilis, Staphylococcus aureus, E. faecalis) and Gram – bacteria (E.coli, Pseudomonas aeruginosa) ⁽²⁸⁾.

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MAITAKE: This mushroom with a Japanese name ("king of mushrooms") has long been highly regarded in Japan for its delicious flavour and great health benefits. It grows in a fan-like shape in shades of greyish-brown on trees and fallen wood, and can reach over 45 kg in weight. A Japanese mycologist identified a fraction present in the mushroom with excellent anti-tumour activity, consisting of a mix of proteins and polysaccharides called the D-fraction. This important activity has an antimetastatic effect, slowing the progression of malignant cells and increasing the activity of NK cells and Th lymphocytes. The D-Fraction has been widely studied for diseases such as hypertension, type II diabetes, hepatitis B and HIV, among others, and has been shown to activate macrophages, Th lymphocytes, interleukins 1 and 2 and lymphokines.

Maitake is a good preventive and coadjuvant treatment for therapies such as chemotherapy, since it induces apoptosis in tumour cells ⁽¹⁾. There are many mechanisms that modify the expression of certain genes involved in the stimulation of apoptosis, the inhibition of cell growth and proliferation, detaining the cell cycle and tumour cell metastasis and inducing sensitivity to multiple drugs. Specifically, the concomitant use of maitake with chemotherapy decreased the incidence of adverse effects caused by anti-neoplastic agents for breast, lung and prostate cancer ⁽²⁻⁴⁾. In mice, it increases the efficacy of chemotherapy with cisplatin and reduces the nephrotoxicity⁽⁵⁾. The maitake D-fraction (beta-glucans) has great potential for treating cancer, stimulating the immune system and reducing the adverse effects of chemotherapy ^(4,6-8). It has also shown beneficial and preventive effects in bladder cancer ⁽⁹⁻¹⁰⁾.

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Maitake is specifically recognized for its action on metabolic syndrome since it very effectively controls hyperglycaemia by improving insulin sensitivity and by protecting pancreatic beta cells from oxidative stress and from nitric oxide synthesis. (11-12) Other studies have shown that it contains an alpha-glucosidase inhibitor that decreases blood sugar levels naturally (13).

Its cholesterol-lowering activity is associated with its possible role in lipid metabolism by regulating gene expression in the liver. In animals fed a high-fat diet, it helps lipid metabolism by inhibiting hepatic and serum lipids ⁽¹⁴⁾. It also has the short-term effect of reducing blood pressure in animals ⁽¹⁵⁾.

Some studies have shown that maitake, alone or combined with drug therapy, can induce ovulation in patients with polycystic ovary syndrome ⁽¹⁶⁾.

Certain isolated beta-glucans in maitake participate actively in the collagen biosynthesis of fibroblasts and as cicatrizing agents in cosmetic and skincare products ⁽¹⁷⁾.

It increases antibody production in response to flu vaccination, and also reduces cold symptoms (18).

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<u>SHIITAKE (Lentinula edodes)</u>: This mushroom with a Japanese name (Shii=brown; Take=mushroom) has been used since antiquity both in China and Japan. A famous doctor from the Ming dynasty said that Shiitake was a good remedy for liver problems, diseases of the upper respiratory tract, venous insufficiency and weakness, preventive of premature ageing and revitalizing of the Chi (life force). Today, these benefits have been proven through modern medicine.

It supplies a great amount of lentinan, a beta-glucan which is responsible for its anti-tumour action, which, according to experimental studies, works by inhibiting tumour growth through the induction of T cell and macrophage-dependent immune response. Study data confirm that the administration of Shiitake improves immune function, quality of life and survival in patients undergoing chemotherapy.

One study has shown that the combination of shiitake and monoclonal antibodies could act synergically to activate the complementary system, making it one of the most efficient treatments for gastric cancer ⁽¹⁾. A meta-analysis of 5 clinical trials showed a significant increase in survival in advanced gastric cancer patients treated with chemotherapy and lentinan,

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the beta-glucan found in shiitake ⁽²⁾. One study showed that the administration of tegafur with lentinan increased survival in metastatic prostate cancer ⁽³⁾. Other studies confirm an increase in survival, a decrease in side effects from chemotherapy and improvement in quality of life for colorectal, hepatic, prostate, breast and oesophageal cancer patients ⁽⁴⁻⁷⁾

Eritadenine, an active compound of this mushroom, is responsible for its ability to reduce cholesterol and blood lipids. It exerts a very beneficial effect on patients with hyperhomocysteinemia, a pathological situation associated with cardiovascular and neurodegenerative disorders, and it has a pronounced anti-atherosclerotic action. In one study, it was shown that Shiitake inhibits the expression of adhesion molecules on vascular endothelia in pro-inflammatory conditions. Its cholesterol-lowering activity is associated with its possible role in lipid metabolism by regulating gene expression in the liver ⁽⁸⁾.

Shiitake has been extensively studied for viral diseases such as hepatitis B, HIV, herpes simplex I and II, polio, measles and mumps, among others, with good results as it activates T cells and macrophages and stimulates interleukin-1. ⁽⁹⁾ The lignin derivatives in this mushroom are partially responsible for its antiviral action ⁽¹⁰⁾.

The increased immunity provided by this mushroom is from an increase in antiviral activity shown in vivo and in vitro for HIV (11-12), and clinical studies have shown its immune-modulating effect in HIV patients. (13-14)

It has been proven to exert powerful anti-candida activity in-vitro. (15-18)

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<u>CHAGA:</u> The active components of chaga are polysaccharides (β -glucans) and the triterpene betulinic acid and its derivatives. Chaga that grows on birch trees has been shown to be rich in betulinic acid since it is absorbed from the tree's bark. It has traditionally been used in Russia and Poland as a cancer remedy ⁽¹⁾.

Betulinic acid induces mitochondrial apoptosis in cancer cells ⁽²⁾ and chaga extract and/or betulinic acid has been shown to inhibit the growth of several types of cancer cells, including those of the colon, breast, lung and brain ⁽³⁻⁷⁾. The polysaccharide fraction of the chaga mushroom has also shown anti-tumour effects ⁽⁸⁾.

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Other in vitro studies show that the betulinic acid present in chaga exerts activity against different types of cancer cells (human melanoma, neuroblastoma, brain tumour, ovarian cancer, leukaemia, etc.) ⁽⁹⁻¹⁰⁾. It shows a promising effect when combined with radiotherapy on human melanoma cells ⁽¹¹⁾. In rodents it exerts cancer-fighting activity with no systemic toxicity (9). Its polysaccharides have an immune-stimulating effect ⁽¹²⁾.

Betulinic acid has been proven effective against the HIV-1 virus by inhibiting replication ⁽¹³⁻¹⁵⁾. In a preliminary study, activity was detected against flu virus A and B ⁽¹⁶⁾, as well as herpes simplex ⁽¹⁷⁾ and human papilloma virus ⁽¹⁸⁾.

It shows an anti-inflammatory effect in vitro (19) and in vivo (20).

In animal models, a blood sugar-lowering effect has been seen (21).

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<u>CORDYCEPS</u>: Used in Traditional Chinese Medicine as an aphrodisiac and diuretic, it favours kidney function because of its mannitol content. The antioxidants supplied by this fungus neutralize the free radicals responsible for cell mutation, the cause of the ageing process. By reducing cell damage and acting on collagen, antioxidants help prevent expression lines and wrinkles and preserve a youthful appearance in the skin ^(2,3).

Cordyceps causes an increase in ATP levels in cells and increases aerobic capacity and oxygen use, as well as offering a greater resistance to fatigue. In athletes it improves sports performance upon increasing muscle tissue metabolism. In healthy individuals between 50 and 75 it improves exercise capacity and resistance to fatigue ⁽⁴⁾.

In sedentary people, aerobic capacity is increased ⁽⁵⁾ while in athletes this effect is not noticed since maximum aerobic capacity has already been reached ⁽⁶⁾. It increases the antioxidant capacity of enzymes such as superoxide dismutase, glutathione peroxidase and catalase, providing additional benefits for cardiovascular health in older patients, while its antifatigue and anti-stress effect allows for its use in cases of asthenia and depression ⁽²⁾.

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This fungus treats hyposexuality, driving sexual desire. It increases libido in both men and women, and increases steroid hormones in urine. One study has shown that cordyceps acts through the sex hormone system by exerting a regulatory effect on reproductive organs, indicating its use for infertility and irregular menstruation by stimulating the production of 17β -estradiol (oestrogen) ⁽⁸⁾. This effect could be beneficial for the treatment of post-menopausal osteoporosis ⁽⁹⁾. Other studies in animals have shown that it increases male hormone levels and improves the quality and quantity of sperm ⁽⁷⁾.

Cordyceps can also increase insulin release and cellular insulin sensitivity ^(10,11). Cordycepin and its derivatives have an active role in its anti-diabetic action ⁽¹²⁾. Additionally, in animals it has been proven capable of inhibiting hepatic fibrosis and of helping re-establish and improve hepatic function in patients with renal failure ⁽¹³⁾. It protects the kidneys from nephrotoxicity caused by cyclosporine ⁽¹⁴⁾ and gentamicin ⁽¹⁵⁾.

Its nucleosides inhibit viral replication (19) and its polysaccharides modulate immune response to viral infections (20).

The fungus strengthens the respiratory system and has a mucolytic and cough suppressing function. This makes it valid as a treatment for asthma, chronic bronchitis, respiratory insufficiency, emphysema, tuberculosis and cystic fibrosis (16,17).

Research has revealed that it has a regulating effect on blood lipid metabolism, helps control hyperlipidaemia and acts against the formation of atherosclerosis, decreasing triglycerides and increasing HDL cholesterol ⁽¹⁸⁾.

Cordyceps modulates the immune system, preventing organ transplant rejection and protecting against the effects of radiotherapy, particularly on bone marrow and the gastrointestinal system. It carries out an important role in immune modulation by stimulating Th cells, prolonging lymphocyte survival and increasing the production of tumour necrosis factor and interleukin. In vitro evidence shows promising activity for cancer treatment (21-24). It aids recovery from Taxol-induced leukopenia in mice. (25) It also offers protection against radiotherapy-induced damage to bone marrow and intestinal tissue in mice (26).

The effective dose was 3-6 g/day for most conditions. Doses of up to 50 g/day have been used with good results in cancer (27). It improves survival in patients with hepatocellular carcinoma (28).

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<u>LION'S MANE</u>: Lion's mane is a mushroom with a unique aspect that grows in dead trees. Unlike common varieties of mushrooms, lion's mane has long white threads that give it the look of a mane or beard.

Lion's mane is well known in the Orient for its regenerative and restorative effects on cognition and the nervous system, as well as its immune-modulating function. This mushroom has great therapeutic potential, as it protects and regenerates both the gastrointestinal mucosa and the myelin sheaths that line nerve cells.

It is mainly composed of cyanthane derivatives, polysaccharides, beta-glucans, ergosterol (pro-vitamin D), erinacine and hericenone. Like many medicinal mushrooms, it's a natural source of beta-glucans which are responsible for its anti-tumour potential, and have immune-modulating, lipid-lowering, antioxidant and neuroprotective activity.

Erinacines and hericenones have the ability to cross the blood-brain barrier and stimulate the production of nerve growth factor (NFG), a soluble protein that promotes the growth of nerve cells and neuron survival, necessary for the development and function of the nervous system. These compounds stimulate the production of new neurons and protect against neuron death, useful for treating different types of dementia such as Alzheimer's or cognitive decline, multiple sclerosis, Parkinson's and neuropathy (1-2).

In patients with multiple sclerosis, lion's mane helps with myelin regeneration (myelinisation), the insulation that protects neurons and allows for intact nerve transmission in "in vitro" studies (3-4).

It stimulates nerve growth factor (NGF) which plays an important role in neuropathy ⁽⁵⁾. In animals, it has a protective effect for diabetic neuropathy ⁽⁶⁾. It also improves recovery in rodents with damaged peroneal nerve ⁽⁷⁾.

Lion's mane has shown activity against methicillin-resistant Staphylococcus aureus (MRSA), responsible for many nosocomial infections (contracted at hospital) (8).

Hericium erinaceus has been extensively studied in China for digestion and gastric ulcers because of its excellent regenerative capacity in the gastrointestinal mucosa, making it valuable for all disorders related to intestinal hyperpermeability such as gastritis, gastroesophageal reflux and gastric ulcers. It also inhibits the activity of Helicobacter pylori (9-10). Studies carried out also show the mushroom's positive effect on ulcerative colitis, Crohn's disease and cancers of the stomach, colon and pancreas (11-12) Its fibre is only metabolized by bacteria living in the intestine, so it stimulates proper development of intestinal flora, exerting a prebiotic effect, important for good intestinal function. It also stimulates macrophage production, the cells that reduce the invasion of pathogens through their antibacterial activity (11).

It strengthens apoptosis induced by doxorubicin in hepatocarcinoma cells ⁽¹³⁾. Its extracts have been shown to decrease the growth of several types of tumours both "in vitro" and "in vivo", due to its anti-tumour and immune-stimulating properties. ⁽¹⁴⁻¹⁶⁾

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