

Shiitake SAP

Science-based hot-water mushroom extract for optimal health and immune support*

Shiitake SAP is a hot water-extracted medicinal mushroom. Shiitake, also known as *Lentinula edodes*, is an edible mushroom that grows predominantly in Asia. Shiitake is the second most commonly consumed type of mushroom, but it also has several medicinal functions. **Shiitake SAP** can be used to help support healthy immune function and cardiovascular health, and is an excellent source of antioxidants.* Further studies show that shiitake may help support the immune system in the management of various cancers, and may improve quality of life for patients undergoing chemotherapy.*

SUPPLEMENT FACTS

Serving Size: 1 Capsule	Amount Per Serving	Servings: 90 % Daily Value
Shiitake (<i>Lentinula edodes</i> fruiting body) 8:1 extract, equivalent to 4 g of dried mushroom, 40% polysaccharides providing 25% <i>beta</i> -glucans	300 mg	**

**Daily Value not established

Note: Polysaccharide and β -glucan content may vary from lot to lot.

This product is non-GMO.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

DIRECTIONS FOR USE

Adults: Take 1 capsule three times daily or as directed by your healthcare practitioner. To avoid digestive upset, take with food / a meal.

INDICATIONS

Shiitake SAP:

- Can be used to help support healthy immune function.*
- Is a source of antioxidants.*
- May help lower homocysteine levels and support healthy cholesterol levels.*
- May help quality of life and immune function for patients undergoing chemotherapy.*

SAFETY AND SIDE EFFECTS

There have been no reported side effects from consumption of shiitake mushroom. Consult a healthcare practitioner prior to use if you suffer from an immune system disorder (e.g. Crohn's disease, myasthenia gravis, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, HIV/AIDS, etc.), if you are taking immunosuppressants, anticoagulants or if you have diabetes.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Shiitake SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Scientific Advisory Panel (SAP):
adding nutraceutical research
to achieve optimum health



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Shiitake is a medicinal mushroom that helps regulate and support healthy immune function in conditions varying from bacterial infections to certain cancers. Shiitake may also be used to support the cardiovascular system by regulating homocysteine and cholesterol levels.

IMMUNE BENEFITS

In a study exploring the antibacterial effect of a bioprocessed polysaccharide (BPP) isolated from *Lentinus edodes* against murine salmonellosis, BPP did not demonstrate bactericidal properties in vitro, but did stimulate the uptake of the bacteria into RAW 264.7 murine macrophage cells. This was demonstrated by an increase in colony-forming unit counts of the contents of the macrophages incubated with salmonella.^[1] These results suggest that the activity of BPP functions by improving T_H1 immunity by activating macrophages to help fight bacterial infection.^[1]

In a human clinical trial, researchers explored the use of oral administration of the active substance (1-6,1-3)- β -glucan (Lentinex) from *Lentinus edodes* in healthy elderly patients.^[2] In the double-blind, crossover, placebo-controlled trial, 42 subjects were allocated to either control or treatment group receiving 2.5 mg/d Lentinex or placebo for 6 weeks.^[2] After a washout period of 4 weeks, groups were reversed. There was no difference noted between placebo and treatment groups in the safety blood variables, which included CBC, liver, and kidney function.^[2] The treatment group given Lentinex had a significant increase in the number of circulating B-cells compared to controls.^[2]

In a study of the specific polysaccharide L-II isolated and purified from the fruiting body of *Lentinus edodes* and its effects on the cellular immune response of sarcoma 180-bearing mice,^[3] researchers included four study arms and administered the mice one of three doses of the polysaccharide L-II (1, 5, and 10 mg/kg_{bw}), or control, for 10 days.^[3] Tumour weight, relative thymus and spleen weight, phagocytosis, and macrophage proliferation were studied.^[3] In all three treatment groups, a significant increase in spleen and thymus weight were noted, as well as a significant increase in phagocytosis and macrophage activity and a decrease in tumour formation.^[3] The control group saw an increase in the concentration of both TNF- α and IFN- γ , which was not observed in the treatment groups.^[3] Researchers concluded that the antitumour activity of the polysaccharide L-II on mice transplanted sarcoma 180 was mediated by immunomodulation inducing both the macrophage- and T-cell-dependent immune responses.^[3]

HOMOCYSTEINE AND CARDIOVASCULAR HEALTH

Elevated homocysteine has been associated with neuronal degenerative diseases and cardiovascular concerns.^[4] In a study exploring the effect of *Lentinus edodes* on hyperhomocysteinemia, hyperhomocysteinemia was induced in mice by the administration of a folate- and vitamin B₁₂-deficient diet (DFV).^[4] Mice were split into five groups and received either 5, 10 or 20% *L. edodes* flour or eritadine (10 mg/kg) or DFV (control group) for two weeks.^[4] The DFV group experienced a significant increase in homocysteine.^[4] The increased homocysteine serum levels were reduced in all the treatment groups in a dose-dependent manner.^[4] The mRNA expression of DNA methyl transferases DNMT1 and DNMT3a were both reduced in the DFV group, but those levels were recovered in all four treatment groups.^[4] The results of this study suggest that *L. edodes* components including eritenine may have beneficial effects on hyperhomocysteinemia by regulating DNA methylation-related genes in mice.^[4]

Eritenine has also been shown to reduce cholesterol levels.^[5] In a mouse study exploring this effect, researchers divided mice into six groups.^[5] One group was fed a normal diet, second group was fed a high-fat diet, and the third group a high-fat diet with eritadenine (10 mg/kg_{bw}) and the other three groups a high-fat diet with 5, 10 or 20% *L. edodes* for four weeks.^[5] Mice across all groups had similar weight gain.^[5] Levels of total serum cholesterol (T-CHO), low-density lipoprotein (LDL), and triglyceride (TG) were increased in the high-fat diet group compared to the normal controls; high-density lipoprotein (HDL) was unaffected.^[5] Mice in the treatment groups of *L. edodes* had reductions in a dose-dependent manner of the T-CHO, LDL and TG levels.^[5] The mRNA expression of cholesterol 7- α -hydroxylase 1 (CYP7A1) was reduced in the hypercholesterolemic mice, but was increased with supplementation of both *L. edodes* at each dose, and by eritadenine supplementation.^[5] It was also observed that the liver tissues showed reduced lipid accumulation in all four treatment groups, and there was

suppression of atherosclerotic plaque development due to the high-fat diet in the four treatment groups as well.^[5] Results of this study indicate that a high-fat diet may increase serum T-CHO, LDL, and TG levels by inhibiting the liver's expression of CYP7A1, and that *L. edodes* may help regulate lipid metabolism by regulating the expression of this gene in the liver.^[5]

SHIITAKE AND CHEMOTHERAPY

In a pilot study, researchers explored the safety and efficacy of *Lentinula edodes* mycelia (LEM) extract in patients undergoing postoperative adjuvant chemotherapy for breast cancer or gastrointestinal cancer.^[6] Study participants underwent their first round of chemotherapy with no supportive therapy, and their second round with the concomitant administration of LEM.^[6] Researchers monitored adverse events, quality of life (QOL) score, lymphocyte subpopulations, lymphocyte activity, and serum immune indices during the study.^[6] During the first course of chemotherapy, no changes in QOL or immune parameters were noted. Following the second course of combined therapy, there were improvements noted in QOL, NK-cell activity, and immune function, with no adverse effects noted.^[6] Researchers concluded that a large-scale investigation is important to confirm these results, but that the data suggests the concomitant use of LEM with chemotherapy is safe and improved that immune function and quality of life of patients undergoing chemotherapy.^[6]

SHIITAKE AND CANCER

Researchers examined the antitumour effect of oral supplementation of LEM extract on mice that had been inoculated subcutaneously with B16 melanoma.^[7] Ingestion of LEM extract significantly inhibited tumour growth, which was not observed in the nude mice, suggesting a T-cell-dependent mechanism.^[7] Ingestion of the LEM extract led to a significant restoration of H-2K^b-restricted and melanoma-reactive T cells in both the spleen and draining lymph nodes of melanoma-bearing mice.^[7] Analysis via flow cytometry showed that the percentage of Foxp3⁺ CD4⁺ T cells increased in the spleen and draining lymph nodes in the melanoma-bearing mice, but reduced significantly with the LEM extract treatment.^[7] Results of this study indicate that oral supplementation of LEM extract restores the immune responses of class I-restricted and melanoma-reactive CD8⁺ T cells in melanoma-bearing mice likely via mitigation of regulatory T cells-mediated immunosuppression.^[7]

In a second study, researchers tested the antitumour effect and mechanism of oral ingestion of LEM following inoculation of murine colon carcinoma colon-26 (C26) cells into the subserosal space (i.c.) of the cecum of mice.^[8] The primary site of the immune response in this model is the gut-associated lymphoid tissue (GALT).^[8] GALT is known to be a site for immunological tolerance-inducing for several dietary antigens.^[8] Supplementation with LEM extract suppressed the growth of i.c.-C26 inoculated cells in a T cell-dependent manner and restored the T cell response of the mesenteric lymph nodes and the spleen.^[8] Ingestion of LEM showed only a marginal effect on Tregs, but significantly reduced the plasma levels of TGF- β and IL-6, both of which were increased in the i.c.-C26 inoculated mice.^[8] Researchers summarized that oral supplementation with LEM extract can restore antitumour T-cell responses of mice, even when the antitumour immune response is initiated in the GALT. This may have relevant implications for the anticancer immunotherapy of human colon cancer.^[8]

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