Shiitake

Lentinula edodes **[Berk.] Pegler [1976]**

Omphalotaceae

Commonly: sawtooth oak mushroom, black forest mushroom, oakwood mushroom, xiang gu (fragrant mushroom)

Part Used: fruit body (basidiocarp, mushroom)

Dosage Range: 2-15 g/day d.w.

- Maintenance: 2 g/day
- Therapeutic (general): 3-10 g/day
- Therapeutic (extreme/acute): 10-15 g/day

Key Application

Key Actions:

Anti-hypercholesterolaemic
Anti-inflammatory
Antimicrobial (bacteria, fungi, protozoa, viruses)
Antioxidant
Cancer adjuvant
Immunomodulator
Intestinoprotective
Lipid modulatory
Orodentoprotective
Probiotic

Key Indications:

Cancer adjuvant therapy ★
Dysbiosis ★
Hypercholesterolaemia
Hyperlipidaemia
Immune prophylaxis ★
Lung conditions & chronic obstructive pulmonary disease (COPD) ★
Immunosuppression ★
Infections
Inflammatory conditions
Orodental disease (topical) ★

Safety Information

Shiitake is safe for general use.[1]

- Allergic skin reaction possible (rare) if consumed raw; always cook well to avoid this possibility[2]
- Spore inhalation allergy possible (rare)[2]

Contraindications: n/a

Interactions: (speculation-based if no reference)

- Anticoagulant medications[2]
- Antidiabetic medications (monitor)
- Immunosuppressive medications

Pregnancy & Lactation: unknown

Historical Perspective

The first documentation of medicinal use is attributed to Shennong in ancient China, 5,000 years ago, where it was revered as a symbol of youthfulness and virility[3]. Traditional uses for shiitake include:

- Immunological: tumours, influenza[4]
- Cardiovascular: heart disease, hypertension[4,5]
- Metabolic: obesity, diabetes[4]
- Liver ailments[4]
- Respiratory/lung diseases[4,5]
- Intestinal worms[5]
- Pain and fatigue associated with aging[5]
- Exhaustion and weakness generally
- Sexual dysfunction

Active Constituents

Key Active Constituents	
Polysaccharides	Many have been isolated, including water-soluble α- & β-glucans, galactates, manganates, and xyloglucans, and water-insoluble heteroglycans, polyuronids, and β-glucans[6], examples include: ▪ Lentinan: β-1,3-glucan with side chains at (1,3) and (1,6) positions, triple helix conformation[7] ▪ LE: polysaccharide-protein complex[6] ▪ MPSSS: β-(1,6)-glucan branched at C-4 by more β-D-(1,6)-glucans[7] ▪ SLSP: heteropolysaccharide with mixed glycosidic links and massive acetyl groups[7] ▪ LEP-1 & LEP-2: heteropolysaccharides with mixed glycosidic links[7] ▪ L-II: α-(1,3)-glucan[6]
Other Active Components	
Proteins & amino acids	Many bioactive proteins including enzymes and glycoproteins (lectins)[8] ▪ Lentin[6]
Sterols	Ergosterol and derivatives[5,6]
Sulphurous compounds	Lenthionine and many others[5,6,9]
Phenolics & flavonoids	Many, including catechin, quercetin[8], tocopherols and β-carotene[6]
Other Compounds	▪ Ergothionine[5] ▪ Eritadenine (lentysine, lentinacin; nucleic acid derivative)[5,6] ▪ Lovastatin[5]

Quality Awareness

Extracts: Water is the preferred solvent. Select extracts at ratios of 1:1 or 4:1-8:1 (1:1 whole fruiting body, 4:1 extracts more polysaccharides, 8:1 extracts more ergothioneine). Whole mushroom can be used effectively.

Lentinan is a β-glucan extract from the fruit body (as well as the mycelium) and it is approved for clinical adjuvant therapy in several Asian countries[4,10].

Mycelium: Mycelium-based products are novel, with no medicinal historical use (other than as fermented foods). *L. edodes* mycelium from liquid- and solid-substrate, and their extracts, are undergoing research. Currently, most mycelium-based products on the market are from solid-substrate cultivation where the "fermented" substrate is inseparable from the mycelium and constitutes an entirely different product (closer to a fermented grain food product) to a pure fungal medicine. Liquid cultivated mycelium is different again, with a different polysaccharide profile (high proportion of exopolysaccharides). While there are health benefits from these products, and indeed some of them make it appear that these products could be interchangeable with the fruit body, the research around them is in its infancy. Research suggests *L. edodes* mycelium and its extracts might be valuable in various conditions[11]. Liquid cultivation is preferred and, whenever possible, mycelium preparations should be combined with that of the fruit body for a more complete bioactive profile and improved synergy. Mycelium-based products are not suitably interchangeable with fruit body extracts.

Cultivation: Whole logs produce a superior mushroom The growing medium affects bioactive compound concentration, with saw dust producing higher primary metabolites (high growth rate) and logs producing higher bioactive compound content with antioxidant activity[12].

Ultraviolet light exposure is required for vitamin D biosynthesis[6].

Actions & Indications Summary

This summary table is designed to be a broad and comprehensive snapshot of the potential that can be explored. Actions and indications are roughly grouped into subcategories for ease of navigation and will be updated as new research unfolds.

●*Human-based evidence*; ⭘*Animal and* in vitro *studies*; ○*Historical use*

★*Human evidence [see* Summary of the Human Evidence*, below]*

The actions in this exhaustive list are not all equally valid however the evidence is presented for independent evaluation. It is up to the practitioner to decide how reliable an action will be when applied to their situation, based on the data as it stands. The indications presented are a rudimentary guide, based on the literature behind the actions.

Potential Actions	Suggested Indications
IMMUNE FUNCTION & LUNG HEALTH	
Anthelmintic ○	▪ Cancer (as adjuvant) ★
Anti-cancer & adjuvant therapy ●⭘[8,10,13–30], anti-tumour ⭘[7]	▪ Chronic obstructive pulmonary disease ★
Anti-inflammatory ●⭘[4,6,7,9,31–37]	▪ Immunity prophylaxis ★
Antimicrobial: antibacterial ⭘[4,6,11,38,39]; antifungal ⭘[4,6,9,25,40]; antiprotozoal ⭘[41]	▪ Infections (acute or chronic) ▪ Inflammatory conditions
Antiviral ⭘[4,6–8,42,43] (HSV-1, HBV, SARS-Cov-2)	▪ Lung injury (acute)
Immunomodulatory ●⭘○[4,6,13,36,37,44–50]	▪ Suppressed immune function ★
Pneumoprotective & anti-COPD: ●⭘○[35,51]	▪ Viral infections
CELLULAR & TISSUE PROTECTION	
Antiaging/geroprotective ⭘○[48]	▪ Heart disease
Antioxidant ●⭘[4,6–8,25,35,39,40,47,52–56]	▪ Oxidative stress conditions
Genoprotective/Antimutagenic ⭘[13]	
CARDIOMETABOLIC HEALTH	
Anti-atherosclerotic ⭘[57]	▪ Cardiovascular disease
Anti-diabetic ⭘○[4,6,7,25,54]	▪ Diabetes
Anti-fatigue ○	▪ Fatty liver diseases
Anti-hypercholesterolaemic ⭘[4,6,47,58,59]	▪ Hepatitis
Anti-hyperglycaemic ⭘[4,6,54]	▪ Hypercholesterolaemia
Anti-hypertensive ○	▪ Hyperglycaemia & insulin resistance
Anti-obesogenic ⭘[60]	▪ Hyperlipidaemia, particularly triglycerides ★
Cardioprotective ○⭘[4]	▪ Obesity
Hepatoprotective ⭘○[4,7,31,47]	
Lipid-modulatory ●⭘[4,6,52,53,58–60]	
Pancreatoprotective ⭘[61]	
GASTROINTESTINAL SYSTEM	
Gastrointestinoprotective & anti-colitis ⭘[32–34,36,41,62]	▪ Dysbiosis ★
Microbiota-modulatory & prebiotic ●⭘[23,33,48,59,63]	▪ Inflammatory bowel diseases
Orodentoprotective ●⭘[40,42,64,65] (anti-plaque, anti-caries, anti-gingivitis, anti-biofilm, anti-adhesion)	▪ Orodental disease ★
GENITOURINARY SYSTEM	
Aphrodesiac ○	▪ Kidney disease
Nephroprotective ⭘[7]	
MUSCULOSKELETAL & INTEGUMENTARY SYSTEMS	
Anti-arthritic ⭘[66]	▪ Arthritis
Osteoprotective ⭘[67,68]	▪ Osteoporosis/osteopenia
NERVOUS SYSTEM	
Antidepressant ⭘[69]	▪ Cognitive decline (associated with obesity)
Myelinorestorative ⭘[70]	▪ Depression
Neuroprotective⭘[33,70]	▪ Inflammatory demyelinating disease (CNS) ▪ Neurodegeneration

Summary of the Human Evidence

Pharmaceutical products in the research:

- **AHCC® (active hexose correlated compound)**: standardised mycelium extract primarily composed of β-glucans and containing unique α-glucan oligosaccharides, administered at 3 g/day
- **Lentinex®**: β-(1,3)(1,6)-glucan (lentinan), 1 mg/mL

Cancer

Kamiyama et al (2022)	**Preventing recurrence of hepatocellular carcinoma after curative hepatectomy with active hexose-correlated compound derived from *Lentinula edodes* mycelia[29]**
Journal	Integrative Cancer Therapies
Study Design	Open-label, uncontrolled trial
Population	29 hepatocellular carcinoma patients (stage A or B preoperatively)
Study Length	2 years
Study Groups	Intervention: 3 g/day AHCC® Control: placebo
Brief Results	The intervention appears to exert beneficial effects on reducing recurrence with the 2-year recurrence-free survival rate at 48%(better result than previously reported). Immunomodulatory activity that promoted stable lymphocyte percentages and maintenance of favourable inflammatory scores key to this result.

Zhang et al (2019)	**Mushroom polysaccharide lentinan for treating different types of cancers: a review of 12 years clinical studies in China[17]**
Journal	Progress in Molecular Biology and Translational Science
Study Design	Systematic review
Population	135 clinical trials of cancer patients in China (from previous 12 years), including total 9474 subjects, comparing i.v. lentinan adjuvant to chemotherapy alone: ▪ Lung cancer (3469 cases) ▪ Gastric cancer (3039 cases) ▪ Colorectal cancer (1646 cases) ▪ Ovarian cancer (183 cases) ▪ Cervical cancer (130 cases) ▪ Non-Hodgkin lymphoma (70 cases) ▪ Pancreatic cancer (15 cases) ▪ Cardiac cancer (15 cases) ▪ Nasopharyngeal cancer (14 cases) ▪ Duodenal cancer (1 case) ▪ Unclassified cancer (110 cases)
Brief Results	Strong support for lentinan improving quality of life and promoting efficacy of chemotherapy and radiation therapy.

Zhang et al (2017)	**Lentinan as an immunotherapeutic for treating lung cancer: a review of 12 years clinical studies in China[10]**
Journal	Journal of Cancer Research and Clinical Oncology
Study Design	Systematic review
Population	38 Chinese RCTs with 3,117 lung cancer patients with lentinan adjuvant therapy
Brief Results	Lentinan improves overall response rates compared to chemotherapy alone (p<0.001).

Nagashima et al (2017)	***Lentinula edodes* mycelia extract plus adjuvant chemotherapy for breast cancer patients: results of a randomized study on host quality of life and immune function improvement[18]**
Journal	Molecular and Clinical Oncology
Study Design	Randomised, double-blind, placebo-controlled trial
Population	47 female breast cancer patients scheduled postoperative chemotherapy
Study Length	6 weeks
Study Groups	Intervention: 1.8 g/day hot water extracted mycelium (sugar-cane & rice bran substrate) Control: placebo
Brief Results	Intervention may be a suitable adjuvant therapy compared to placebo: ▪ Protected against loss of quality of life score (p<0.05) ▪ Counteracted immunosuppression by reducing the proportion of regulatory T cells to other $CD4^+$ cells (p<0.01)

Tanigawa et al (2016)	**Improvement of QOL and immunological function with *Lentinula edodes* mycelia in patients undergoing cancer immunotherapy: an open pilot study[14]**
Journal	Asian Pacific Journal of Cancer Prevention
Study Design	Open-label pilot study
Population	10 cancer patients undergoing chemotherapy
Study Length	8 weeks (4 weeks chemotherapy alone, 4 weeks chemotherapy plus intervention)
Study Groups	Intervention: 1.8 g/day hot water extracted mycelium (sugar-cane & rice bran substrate) Control: chemotherapy alone
Brief Results	Intervention may be a suitable adjuvant therapy: ▪ Improved quality of life (p<0.05) ▪ Improved immune function with raised IFN-γ correlated with Treg cell modulation

Okuno et al (2011)	**Efficacy of orally administered *Lentinula edodes* mycelia extract for advanced gastrointestinal cancer patients undergoing cancer chemotherapy: a pilot study**[16]
Journal	Asian Pacific Journal of Cancer Prevention
Study Design	Open-label pilot study
Population	8 cancer patients undergoing chemotherapy for gastric (1) and colorectal (7) cancers with metastasis
Study Length	8 weeks (4 weeks chemotherapy alone, 4 weeks chemotherapy plus intervention)
Study Groups	Intervention: 1.8 g/day hot water extracted mycelium (sugar-cane & rice bran substrate) Control: chemotherapy alone
Brief Results	Intervention may be a suitable adjuvant therapy: ▪ Reduced adverse reactions from chemotherapy alone (6/8 patients) to no adverse effects ▪ Tendency toward improved IFN-γ production by $CD4^+$ and $CD8^+$ T cells, and $CD56^+$ NK T cells

Yamaguchi et al (2011)	**Efficacy and safety of orally administered *Lentinula edodes* mycelia extract for patients undergoing cancer chemotherapy: a pilot study**[15]
Journal	The American Journal of Chinese Medicine
Study Design	Open-label pilot study
Population	7 cancer patients undergoing chemotherapy for breast (3) and gastrointestinal (4) cancers
Study Length	8 weeks (4 weeks chemotherapy alone, 4 weeks chemotherapy plus intervention)
Study Groups	Intervention: 1.8 g/day hot water extract of mycelium in sugarcane & rice bran substrate Control: chemotherapy alone
Brief Results	Intervention provided significant adjuvant support in the following areas: ▪ Improved quality of life ($p<0.05$) ▪ Improved NK cell activity ($p<0.05$) ▪ Decreased immunosuppressive acidic protein (IAP) levels ($p<0.05$)

Cancer Quality of Life

Yanagimoto et al (2023)	**Efficacy of *Lentinula edodes* mycelia extract on chemotherapy-related tasted disorders in pancreatic cancer patients**[27]
Journal	Nutrition and Cancer
Study Design	Randomised, double-blind, placebo-controlled trial
Population	98 patients with pancreatic ductal adenocarcinoma undergoing chemotherapy
Study Groups	Intervention: AHCC® Control: placebo
Brief Results	Intervention improved quality of life during chemotherapy with significant prevention of taste disorders and subsequent loss of nutritional status compared to placebo ($p=0.0077$).

Aldwinckle et al (2020)	**A quality-of-life study in healthy adults supplemented with Lentinex® beta-glucan of shiitake culinary–medicinal mushroom, *Lentinus edodes* (Agaricomycetes)**[28]
Journal	International Journal of Medicinal Mushrooms
Study Design	Randomised, double-blind, placebo-controlled trial
Population	56 healthy adults
Study Length	4 weeks
Study Groups	Intervention: 1-2 mL/day Lentinex® Control: placebo
Brief Results	Intervention provided significant improvement in subjective wellbeing ($p=0.004$), particularly evident for subpopulation with lower baseline scores relative to placebo ($p=0.0004$).

D'Orta et al (2018)	**Management and treatment of sarcopenia in fifty patients receiving chemotherapy with AHCC (active hexose correlated compound)**
Journal	International Journal of Medicinal Mushrooms
Study Design	Randomised, double-blind, placebo-controlled trial
Population	50 adenocarcinoma patients with malnutrition undergoing radio-chemotherapy
Study Length	3-6 months
Study Groups	Intervention: 1.5 g/day AHCC® plus nutritional therapy Control: n/a
Brief Results	Intervention prevented progression of cachexia and improved body cell mass.

Cardiometabolic Health

Spim et al (2021)	**Effects of Shiitake Culinary-Medicinal Mushroom, Lentinus edodes (Agaricomycetes), Bars on Lipid and Antioxidant Profiles in Individuals with Borderline High Cholesterol: A Double-Blind Randomized Clinical Trial**[53]
Journal	International Journal of Medicinal Mushrooms
Study Design	Randomised, double-blind, placebo-controlled trial
Population	68 adults with mild hypercholesterolaemia
Study Length	66 days
Study Groups	Intervention: 3.5 g/day dry fruit body powder in a bar Control: placebo
Brief Results	Intervention modulated lipids and improved antioxidant defenses: ▪ Achieved a 10% reduction in plasma TG (p=0.0352) ▪ Improved reduced glutathione levels and lowered incidence of lipid peroxidation ▪ Dermatitis triggered in 10% of participants taking intervention

Chronic Obstructive Pulmonary Disease

Sun et al (2019)	**Clinical effects of lentinan combined with budesonide inhalation in treating acute exacerbation of chronic obstructive pulmonary disease under mechanical ventilation**[51]
Journal	Experimental and Therapeutic Medicine
Study Design	Double-blind RCT
Population	72 patients admitted to hospital with acute exacerbation of COPD
Study Length	4 days
Study Groups	Intervention: 1 g/day lentinan (two divided doses, orally), plus budesonide and antibiotic treatment Control: standard budesonide and antibiotic treatment only
Brief Results	Intervention significantly improved recovery from acute event as an adjuvant therapy compared to control: ▪ Reduced time on mechanical ventilation and time in intensive care unit (both p<0.001) ▪ Reduced airway pressure and pressure of CO_2, and increased partial O_2 pressure (all p<0.001) ▪ Reduced plasma inflammatory markers: adiponectin, D-dimer, IL-17, and hs-CRP (all p<0.001) ▪ Modulated levels of circulating lymphocytes: raised $CD3^+$ and $CD4^+$ T cells and lowered the proportion of $CD8^+$ T cells (non-significantly)

Exercise Performance

Zembron-Lacny et al (2013)	**Effect of shiitake (*Lentinus edodes*) extract on antioxidant and inflammatory response to prolonged eccentric exercise**[56]
Journal	Journal of Physiology and PHarmacology
Study Design	Double-blind, placebo-controlled, cross-over RCT
Population	14 healthy men exposed to exercise-induced skeletal muscle damage
Study Length	2 sets of 10 days intervention before an assigned exercise session (3 weeks wash-out period between)
Study Groups	Intervention: 1.4 g/day unknown shiitake extract Control: placebo
Brief Results	No observed effect upon inflammatory markers following prolonged eccentric exercise, however intervention demonstrated antioxidant activity via regulation of NO concentration and thiol redox status.

Immunological Function

Dai et al (2015)	**Consuming *Lentinula edodes* (shiitake) mushrooms daily improves human immunity: a randomized dietary intervention in healthy young adults**[37]
Journal	Journal of the American College of Nutrition
Study Design	Double-blind RCT
Population	52 healthy adults
Study Length	8 weeks
Study Groups	Intervention: 5 or 10 g/day dry fruit body (equivalent to 1 or 2 dietary servings of about 5 mushrooms) Control: n/a
Brief Results	Intervention promotes significant beneficial immunological and anti-inflammatory activity dose-dependently: ▪ Increased proliferation of NK-T cells (p<0.0001) and γδ-T cells (p<0.0001), and their effector function ▪ Increased salivary IgA (p=0.049) ▪ Modulated cytokine expression toward anti-inflammatory profile

	▪ Reduced CRP (p=0.008) even though participants were in normal range at baseline

Choi et al (2014)	**Dietary supplementation with rice bran fermented with *Lentinus edodes* increases interferon-γ activity without causing adverse effects: a randomized, double-blind, placebo-controlled, parallel-group study**[45]
Journal	Nutrition Journal
Study Design	Double-blind, randomised, placebo-controlled trial
Population	80 healthy adults
Study Length	8 weeks
Study Groups	Intervention: 18 g/day polysaccharide extract from mycelium with rice bran substrate Control: placebo
Brief Results	Intervention promotes significant beneficial immunological activity compared to placebo: ▪ Increased IFN-γ secretion (p=0.012) ▪ No effects on NK cell activity or cytokine levels

Gaullier et al (2011)	**Supplementation with a soluble β-glucan exported from shiitake medicinal mushroom, *Lentinus edodes* (Berk.) singer mycelium: a crossover, placebo-controlled study in healthy elderly**[46]
Journal	International Journal of Medicinal Mushrooms
Study Design	Double-blind, randomised, placebo-controlled, cross-over trial
Population	42 healthy, elderly adults
Study Length	6 weeks (6-weeks, 4 week wash-out, then 6 weeks cross-over)
Study Groups	Intervention: 2.5 mg/day Lentinex® Control: placebo
Brief Results	Intervention promotes significant beneficial immunological activity compared to placebo: ▪ Maintained stable levels of $CD4^+$ and $CD3^+$ T cells while the control had a significant reduction (p=0.038 and p=0.041) ▪ Maintained and improved declining count of $CD19^+$ B cells (p=0.037) ▪ No effects on cytotoxic T cells, NK cells, immunoglobulins, complement proteins, or cytokines

Gordon et al (1998)	**A placebo-controlled trial of the immune modulator, lentinan, in HIV-positive patients: a phase I/II trial**[49]
Journal	Journal of Medicine
Study Design	Double-blind, randomised, placebo-controlled trial
Population	Phase I: 10 patients with HIV infection Phase II: 50 patients with HIV infection
Study Length	Phase I: 8 weeks Phase II: 12 weeks
Study Groups	Intervention phase I: 2, 5, or 10 mg/week lentinan (i.v. once a week) Intervention phase II: 2 or 10 mg/week lentinan (i.v. divided into two weekly doses) Control: placebo
Brief Results	Intervention promotes beneficial immunological activity with improved counts of CD4+ T cells and, in some patients, neutrophils (non-statistically significant trends).

Microbiota-Modulation

Morales et al (2021)	**Modulation of human intestinal microbiota in a clinical trial by consumption of a β-D-glucan-enriched extract obtained from Lentinula edodes**[63]
Journal	European Journal of Nutrition
Study Design	Double-blind, randomised, placebo-controlled trial
Population	52 adults with untreated mild hypercholesterolaemia
Study Length	8 weeks
Study Groups	Intervention: 10.4 g/day fruit body special extract (3.5 g β-glucan) blended with a "vegetable cream" and taken as part of lunch Controls: placebo (cream without mushroom)
Brief Results	Colonic microbiota was significantly altered by intervention, with some of the population changes correlated to improved cholesterol metabolism. No significant changes occurred regarding the lipid or cholesterol profiles, immune function or to inflammatory markers.

Orodental Health

Lingstrom et al (2012)	**The anticaries effect of a food extract (shiitake) in a short-term clinical study**[65]

Journal	Journal of Biomedicine and Biotechnology
Study Design	Double-blind, randomised, placebo-controlled, cross-over trial
Population	65 healthy adults
Study Length	14 weeks (3 2-week periods of experiment with 2-week wash-outs before, between and after each)
Study Groups	Intervention: low molecular weight fraction, as a mouthwash, applied twice daily Controls: placebo and Meridol
Brief Results	Intervention reduced the metabolic activity of dental plaque compared to placebo (p>0.05), but did not affect plaque scores or production of organic acids in plaque; anticariogenic potential but not to the extent of positive control.

Signoretto et al (2011)	**Testing a low molecular mass fraction of a mushroom (Lentinus edodes) extract formulated as an oral rinse in a cohort of volunteers**[71]
Journal	Journal of Biomedicine and Biotechnology
Study Design	Double-blind, randomised, placebo-controlled trial
Population	90 young adults
Study Length	18 days (6 days ordinary oral hygiene, 12 days mouth wash protocol only)
Study Groups	Intervention: low molecular weight fraction, as a mouthwash, applied twice daily Controls: placebo (water) and Listerine
Brief Results	Mouthwash has positive effects on orodental health: ▪ Significant improvement in plaque index on day 12 against placebo (p>0.05) ▪ Significant improvement in gingival index on day 12 against placebo and Listerine (both p>0.05), ▪ Reduced bacterial counts of specific oral pathogens (non-significantly)

Abbreviations: COPD: chronic obstructive pulmonary disease; RCT: randomised controlled trial; hs-CRP: high sensitivity C-reactive protein; IL: interleukin; NK: natural killer.

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