

Mycomedicinals (Mushrooms) for Cancer

Medicinal mushrooms, also known as "mycomedicinals," and mushroom-derived polysaccharide preparations have been studied as immune modulators and adjuvant agents in cancer treatment. Mycomedicinals have been found to modify tumor response and improve immune function, primarily in patients with solid tumors. Mushrooms contain biologically active polysaccharides in their fruit bodies, or mycelia. The β -glucans of mushrooms resemble bacterial cell walls and complex with complement on macrophages to activate an immune response triggering the release of various cytokines that are active in tumor inhibition. The following describes several mycomedicinals and the research related to their use.

Mushrooms have a cell wall made of chitin, which is the same fiber contained in the shell of a lobster. Chitin is indigestible by humans but contains bioactive β -glucans and polysaccharides. Different extraction methods result in varied antitumor properties exhibited by the mushroom. Hot water extraction breaks down the chitinous cell walls and releases the bioactive polysaccharide structurally intact and undamaged. This is performed by simmering or boiling the mushroom in water for 20 to 120 minutes. Alcohol extraction is another common method that is used.

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Coriolus (Trametes) versicolor (Turkey Tail)

Over 400 in vitro and animal studies of *Coriolus versicolor* extract have demonstrated that it stimulates the immune system, inhibits the growth of cancer cells, and acts as a strong antioxidant. Polysaccharide krestin (PSK) and polysaccharide peptide (PSP) are bioactive extracts of *C. versicolor*. In Japan, PSK is an anticancer drug currently used as an adjuvant treatment with surgery, chemotherapy, and radiation for esophageal, lung, stomach, breast, and colon cancer. PSP was discovered more recently and has been studied mainly in China. PSP activates the immune system by increasing production of cytokines and chemokines, stimulating dendritic and T-cell infiltration into tumors, and reducing chemotherapy side effects. Studies of PSK have found increased activity against trastuzumab-mediated breast cancer and docetaxel-induced prostate cancer suppression in mice.¹

A systematic review and meta-analysis of 13 clinical trials analyzing survival in cancer patients taking 1 to 3.6 gm of PSK or PSP per day for 1 to 36 months found that those taking *C. versicolor* had a 9% absolute reduction in 5-year mortality, resulting in one additional patient alive for every 11 patients treated. The effects were more evident in patients with breast, gastric, or colorectal cancer.²

A study found that stage II and III colorectal cancer patients who received conventional therapy along with 3 gm of PSK per day had a greater percentage of 5-year disease-free survival and a

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decreased relative risk of regional metastases.³ A meta-analysis of three trials involving 1,094 subjects with colorectal cancer confirmed that those who took PSK showed a significant improvement in overall survival and disease-free survival.⁴ In a meta-analysis of 8,009 gastric cancer patients from eight randomized controlled trials (RCTs), those taking PSK had increased survival.⁵

A review of PSK used in human trials demonstrated improved immune function, tumor-related symptoms, and survival in patients with lung cancer when used as an adjunctive therapy. It improves survival in patients with Stage I, II, or III lung cancer and reduces bone marrow suppression.⁶

Grifola frondosa (Maitake)

Grifola frondosa is an edible mushroom extensively used in traditional Asian medicine for numerous health-promoting purposes. Maitake means "dancing mushroom." The maitake D-fraction is the bioactive extract that has been widely studied as an adjuvant therapy. It acts as a biologic response modifier, providing T-cell dependent immune enhancement and activation that enhanced antitumor effect. Maitake is often used to reduce the side effects of chemotherapy and make it more effective. It is most effective against breast, prostate, and liver cancer.

When maitake D-fraction was given to patients receiving chemotherapy for several different cancers, response rates increased from 12% to 28%, and chemotherapy side effects were reduced.⁷ Another study, among numerous others, suggests a direct antitumor effect of maitake D-fraction with induction of apoptosis observed in breast cancer cell lines.⁸

Ganoderma lucidum (Reishi)

Reishi is often referred to as the "mushroom of immortality." The mushroom itself is not edible due to its strong bitterness, but *Ganoderma lucidum* products are commercially available in many forms. Polysaccharides GL-PS and GL-T have the strongest anticancer activity. They can inhibit the cell cycle, are cytotoxic, and have antimetastatic, immunomodulatory, antioxidant, antimicrobial, and anti-inflammatory effects. GL-T is synergistic with doxorubicin *in vitro* and extracts reduce cardiotoxicity in rats. When GL-PS is combined with bleomycin, it reduces druginduced pulmonary fibrosis in rats. *G. lucidum* extracts given in conjunction with cisplatin reduce nausea and vomiting, decrease nephrotoxicity, and enhance chemosensitivity in rats. ⁹

A Cochrane review of five RCTs concluded that *G. lucidum* could be administered as an adjuvant to conventional treatment, given its potential to enhance tumor response and stimulate host immunity. Patients who had been given *G. lucidum* with chemotherapy and/or radiation were 1.27 times more likely to respond versus those given conventional treatment alone. *G. lucidum* treatment alone did not demonstrate the same regression rate as that seen in combined therapy. Four of the studies found that patients in the *G. lucidum* group had improved quality of life.^{10,11}

Lentinula edodes (Shiitake)

Shiitake is the second largest cultivated—and the most popular—edible mushroom in the world. The polysaccharide extract active hexose correlated compound (AHCC) of the *Lentinula edodes* mushroom has been tested in several human trials. Eleven advanced cancer patients who were

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given 3 gm per day of AHCC for 1 month in an uncontrolled trial showed a 2.5 times increase in natural killer cell activity, and over half had a tumor response. Statistically significant increases in lymphocyte percentage, albumin levels, general physical health status, and maintenance of activities of daily living were reported in advanced liver cancer patients who were given AHCC instead of placebo. A cohort of 269 hepatocellular cancer patients who received curative resection was assigned to receive either 3 gm of AHCC daily or control after surgery. The treated group had a significantly longer disease-free interval, and increased overall survival. Lentinan is another polysaccharide extract of *L. edodes*. Long-term use in China has found it improves of quality of life and increases the efficacy of chemotherapy and radiation.

Hericium erinaceus (Lion's Mane)

Hericium erinaceus is commonly used for its neuroprotective effects. Water and ethanol extracts have shown growth inhibitory effects on gastric, liver, and colon cancer cells. Oral administration to mice shows tumor suppressing activity similar to 5-fluorouracil. It also has antimetastatic activity and has shown a 50% reduction in lung metastases of colorectal cancer in mouse models. H. erinaceus extracts demonstrate numerous anticancer activities that are immunostimulatory, antimetastatic, pro-apoptotic, antioxidant, gastrointestinal protective, and inhibitory of angiogenesis.¹

Summary

While more research is still needed, mycomedicinals are showing promise for many cancer-related indications. Mycomedicinals are best absorbed when taken on an empty stomach. The typical dose of mycomedicinals varies from 800 mg to 3,000 mg of the active polysaccharide per day. Mycomedicinals rarely cause side effects, but they should be used with caution in patients with leukemia and lymphoma, those who have recently had a bone marrow transplant, and people on immunosuppressants (due to mushrooms' effects on immune modulation).

Resource Links

 <u>Passport to Whole Health</u>: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020 508.pdf

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"Mycomedicinals for Cancer" was adapted for the University of Wisconsin Integrative Health Program from the original written by Srivani Sridhar, MD (2014, updated 2020). Modified for UW Integrative Health in 2021.

This Integrative Health tool was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

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