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Review Article

TREATMENT OF CANCER BY MEDICINAL MUSHROOMS

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ABSTRACT

A term combining the words “nutrition” and “pharmaceutical,” is a food or food product that provides health and medical benefits, including the prevention and treatment of diseases. They have shown activities like antioxidant, effect on cholesterol, anti-hormone activity and in treatment of cancer. Different species like *trametes versicolor*, a cancer drug called polysaccharide-k, which counter-act the immune system depressing action of common chemotherapeutic drug. *Grifola frondosa* has anti-cancer activity. *Agaricus subrufescens* shows similar effect. *Agaricus bisporus* shows inhibition of breast cancer development. Similarly other species like *Lentinula edodes*, *Hericium erinaceus* *Flammulina velutipes* shows effect.

Key words: Nutraceuticals, Mushroom, Cancer, Anti-oxidant, Anti-hormonal, Hericium, Angiogenesis

INTRODUCTION

Nutraceutical, a term combining the words “nutrition” and “pharmaceutical,” is a food or food product that provides health and medical benefits, including the prevention and treatment of disease. Such products may range from isolated nutrients, dietary supplements and specific diets to genetically engineered foods, herbal products, and processed foods such as cereals, soups, and beverages. With recent breakthroughs in cellular-level nutraceuticals agents, researchers, and medical practitioners are

developing templates for integrating assessing and assessing information from clinical studies on complimentary and alternative therapies into responsible medical practice

Medicinal mushrooms are mushrooms used in the practice of medicine. Many species of mushrooms have been used in folk medicine for thousands of years. The use of mushrooms in folk medicine is best documented in the East. Medicinal mushrooms are now the subject of study for many ethnobotanists and medical researchers. The ability of some mushrooms to inhibit tumor growth and enhance aspects of the immune system has been a subject of research for approximately 50 years.^[1] Preclinical studies suggest that compounds from up to 200 species of mushrooms may inhibit tumor growth,^[2] but required dosage and effects on humans is mostly unknown.

Fungus research has led to the discovery of many pharmaceutical drugs, including penicillin, ciclosporin, griseofulvin, cephalosporin, ergometrine as well as the popular statin class of cholesterol drugs. Statins, like lovastatin and mevastatin were first isolated from different strains of fungi. Recent research has found lovastatin is present in the popular oyster mushroom,^[3] mushrooms produce vitamin D when exposed to UV light,^[4] and fungi are a potential source of taxol.^[5] Currently, researchers are focusing on mushrooms that appear to offer anti-cancer and immune system enhancing activity.



Clinical and animal studies suggest medicinal mushrooms may be able to increase certain aspects of the immune system. Compounds in medicinal mushrooms most responsible for up-regulating the immune response, are a specific type of polysaccharide known as beta-glucan. Beta-glucan compounds are made up of repeating units of D-glucose monomers and come in a large variety of shapes and molecular weights. Proteins can also be attached to these mushroom compounds.

Beta-glucans are currently known as "biological response modifiers", and their ability to activate the immune system is well documented. Specifically, beta-glucans stimulate the innate branch of the immune system. Research has shown beta-glucans have the ability to stimulate macrophage,^[13] NK cells,^[14] T cells,^[15] and the production of immune system cytokines.

Antioxidant activity

Mushrooms are known to contain antioxidants such as ascorbic acid, tocopherols, phenolic compounds, and carotenoids.^[19] Examples of mushrooms with documented antioxidant activity include Maitake,^[20] *Agrocybe aegerita*^[21], Reishi,^{[22][23]} *Agaricus blazei*^[24], Oyster mushrooms,^[25] *Agaricus bisporus*, Chaga, and Shiitake. Chemical analysis has shown that a specific antioxidant found in some mushrooms like *Flammulina velutipes* and *Agaricus bisporus* is ergothioneine.

Effect on blood sugar

Research has shown that some medicinal mushrooms may be able to lower elevated blood sugar levels. Mushrooms noted for this ability include Reishi,^[14] *Agaricus blazei*, Chaga, *Agrocybe aegerita*, and Cordyceps.^[24] Explanation for this effect is limited, with the exception of the Maitake mushroom. The Maitake mushroom's ability to lower blood sugar levels has been explained by the fact that the mushroom naturally contains a compound known as an alpha-glucosidase inhibitor.^[4]

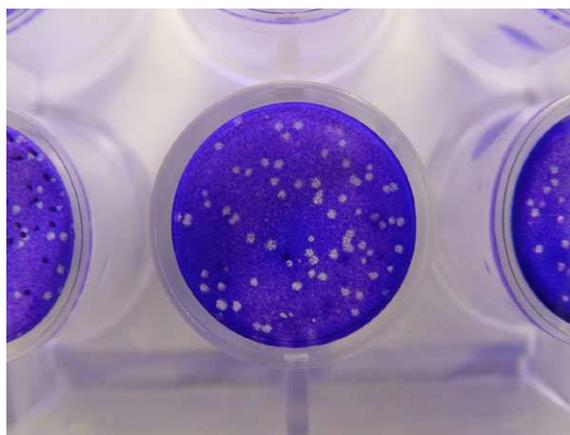
Effect on cholesterol

Some mushrooms like *Agaricus blazei*^{[3][7]} and Reishi^{[5][6]} have been shown to be able to have an inhibitory effect on cholesterol levels. Shiitake mushrooms have been found to contain a specific anti-cholesterol compound known as eritadenine.^[7] Oyster mushrooms have been found to naturally contain a statin drug known as lovastatin (brand name: Mevacor, Altoprev)^[3] a drug used to lower cholesterol. Tests have shown the oyster mushroom contains up to 2.8% Lovastatin on a dry weight basis.^[8] Animal research has shown that Oyster mushroom consumption lowers cholesterol levels.

Direct anti-hormone activity

Mushrooms may be able to influence the production of certain human hormones, due to evidence from enzyme assay analysis. Mushrooms like *Agaricus bisporus* may be able to partially inhibit the activity of aromatase, the enzyme responsible for producing estrogen. Some researchers have proposed that this anti-aromatase activity may be responsible for studies that have linked an inverse relationship between dietary intake of mushrooms and risk of breast cancer. Mushrooms like Reishi may be able to partially inhibit the activity of 5-alpha reductase, the enzyme responsible for producing dihydrotestosterone.

Research on direct anti-viral and anti-microbial properties



HSV-1 cultured *in vitro*.

Research has shown that some mushrooms exhibit direct (*in vitro*) anti-viral, anti-bacterial, and anti-fungal properties.^[8] The fact that studies have not been published showing this effect in humans or animals, suggests these properties are limited to direct contact. These properties are due to compounds mushrooms create to protect against infection. Fungi also create and secrete other compounds, like digestive enzymes, to process food.

- *Agaricus blazei* - Polio,^[8] Western equine encephalitis,^[2] *escherichia coli*
- *Cordyceps sinensis* - Hepatitis B
- *Kuehneromyces mutabilis* - Influenza virus^[8]
- *Lentinula edodes* (Shiitake) - HSV-1,^[8] HIV, Influenza virus, *Vesicular stomatitis, candida albicans, listeria monocytogenes, mycobacterium tuberculosis, staphylococcus aureus, streptococcus pneumoniae, streptococcus pyogenes*. Shiitake mushrooms naturally contain anti-viral agents known as proteinase inhibitors.^[9]
- *Piptoporus betulinus* - Vaccinia virus. Contains an antibiotic compound
- *Pleurotus ostreatus* (Oyster mushroom) - HIV,^[9] *aspergillus niger, Bacillus cereus, escherichia coli, plasmodium falciparum, pseudomonas aeruginosa, pseudomonas fluorescens*
- *Trametes versicolor* (Turkey tail mushroom) - HIV,^[6] *aspergillus niger, candida albicans, escherichia coli, streptococcus pneumoniae*
- *Tuber* mushrooms (Truffles) - Contains antibiotic activity.^[7]

Species

Trametes versicolor (Coriolus versicolor)



Trametes versicolor

Main article: Polysaccharide-K

Trametes versicolor (*Coriolus versicolor*, Turkey tail, Kawaratake, Yun-Zhi, is probably the best documented medicinal mushroom. It is a mushroom which has provided the world with a leading cancer drug. The drug is known as Polysaccharide-K (Kresin, PSK, PSP) and its use is intended to counter-act the immune system depressing actions of common chemotherapeutic drugs.

Used in conjunction with chemotherapy, PSK has increased the survival time of cancer patients in randomized, control studies.^[12] Large clinical trials have indicated it is useful in the treatment of stomach cancer (meta-analysis of 8,009 patients from eight randomized controlled trials),^[14] colorectal cancer (randomized, controlled study of 448 patients), small cell carcinoma of the lungs,^[12] and non-small cell lung carcinoma

Grifola frondosa (Maitake)



Grifola frondosa

Maitake (Hen of the Woods) is an edible mushroom commonly found on oak trees. Maitake has been researched for possible anti-cancer activity. Researched polysaccharide compounds isolated from Maitake, include "MD-fraction" and "Grifron-D". Published research conducted with Maitake, MD-fraction, and Grifron-D has demonstrated the following:

Experimental Model	Experimental Effect (<i>in vitro</i>)	Experimental Effect (<i>in vivo</i>)	Experimental Effect (Clinical)
<u>Breast cancer</u> , <u>Liver cancer</u> , <u>Lung cancer</u>			Inhibited cancer development (non-randomized studies) ^{[122][123][124][125]}
<u>Lung cancer</u>	<u>Inhibited metastasis</u> ^[16]		
Murine cancer		Inhibited tumors and up-regulated immune system ^[12]	
Various cancer <u>cell lines</u> (including human and animal)	Inhibited growth		

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.^[11] *In vitro* research has also shown Maitake can stimulate immune system cells.^[13] An *in vivo* experiment showed that Maitake could stimulate both the innate immune system and adaptive immune system.^[16] In 1997, the U.S. Food and Drug Administration (FDA) approved an Investigational New Drug Application for a portion of the mushroom. Maitake may partially inhibit the enzyme cyclooxygenase (the same enzyme which is the target of Advil, Tylenol, and other NSAIDs).^[20] An experiment showed that an extract of Maitake inhibited angiogenesis.^[18]

Agaricus subrufescens (Agaricus blazei)



Agaricus blazei

Agaricus blazei (*Agaricus brasiliensis*, *Agaricus sylvaticus*, Agarikusutake, Kawarihiratake, Himematsutake, is a species of mushroom, that research has shown may stimulate the immune system and exhibit anti-cancer activity.^[19] Unlike some other medicinal mushrooms, *Agaricus blazei* was not cultivated in the East until fairly recently. In Japan, *Agaricus blazei* is a highly popular alternative medicine, which is used by close to 500,000 people.^[10] In Japan, *Agaricus blazei* is also the most popular complementary and alternative medicine used by cancer patients.^[11]

Additional research suggests, *Agaricus blazei* can partially inhibit aspects of angiogenesis and may inhibit the activity of pathogenic factors. Most published research concerning *Agaricus blazei* is focused on its potential as an anti-cancer agent as shown in the table below.

Experimental Model	Experimental Effect (<i>in vitro</i>)	Experimental Effect (<i>in vivo</i>)	Experimental Effect (Clinical)
<u>Colorectal cancer</u>			Benefited hematological and immunological parameters (randomized, placebo-controlled) ^[9]
<u>Fibrosarcoma</u>	Inhibited growth via <u>apoptosis</u> ^[19]	Inhibited growth ^[14]	
<u>Sarcoma</u>		Inhibited <u>angiogenesis</u> . Inhibited growth	
<u>Gynaecological cancer</u>			Increased <u>NK cell activity</u> , quality of life (randomized, placebo-controlled) ^[15]
<u>Ovarian cancer</u>	Inhibited growth and <u>metastasis via apoptosis induction</u> ^[15]	Inhibited <u>metastasis, growth</u> ^[12]	
<u>Lung cancer</u>	Inhibited growth via <u>apoptosis</u> ^[13]	Inhibited <u>metastasis, growth</u> ^[11]	
<u>Leukaemia</u>	Inhibited growth via <u>apoptosis</u>	Inhibited growth	

<u>Myeloma</u>		Inhibited growth ^L	
<u>Hepatocarcinoma</u>	Inhibited abnormal collagen formation ^[19]	Inhibited growth	
<u>Stomach cancer</u>	Inhibited growth via <u>apoptosis</u> ^{[15][12]}		
<u>Prostate cancer</u>	Inhibited growth via <u>apoptosis</u>	Inhibited growth ^[13]	
<u>Skin cancer</u>		Inhibited growth ^[11]	

***Agaricus bisporus* (Common mushroom, Portobello, Champignon mushroom)**



Agaricus bisporus

The White Button, Crimini, and Portobello (Common mushroom, Champignon mushroom) is the world's most popular edible mushroom, and is known by many names. The French, play a role in this mushroom's popularity, having cultivated the mushroom since the 1600s.^[16] Researchers at the City of Hope National Medical Center are studying whether this mushroom may inhibit breast cancer development.^[9] Agaricus bisporus mushrooms may reduce the risk of breast cancer, because white button mushrooms have been shown *in vitro* to inhibit the enzyme aromatase, which is used by the body to create estrogen.^{[7][4].}

A case-control study in southeast China compared the diets of 1009 women had been diagnosed with breast cancer with 1009 healthy women. Compared to non-consumers of mushrooms, women who consumed at least 10 grams of fresh mushrooms per day had a breast cancer risk of only 36% (95% confidence interval, 25%-51%). The risk for those who consumed at least 4 grams of dried mushrooms per day was 53% (95% CI, 38%-73%). A similar case-control study involving 362 Korean women with breast cancer also found a strong association between mushroom consumption and decreased risk of breast cancer in postmenopausal, but not premenopausal, women.

***Lentinula edodes* (Shiitake)**



Lentinula edodes

Shiitake is a popular culinary mushroom used in dishes around the world. The mushroom also has a extensive history as a folk remedy. During the Ming Dynasty (AD 1368–1644), physician Wu Juei wrote that Shiitake was a remedy for upper respiratory diseases, poor blood circulation, liver trouble, exhaustion, and weakness. Modern research has indicated that Shiitake mushroom may stimulate the

immune system,^[6] possess anti-bacterial properties reduce platelet aggregation,^[18] and possess anti-viral properties, possibly through anti-viral agents known as proteinase inhibitors.

Hericium erinaceus



Hericium erinaceus

Hericium erinaceus (Lion's Mane Mushroom, Yamabushitake, has been researched for possible anti-dementia activity. *In vitro* experiments with *hericium* have demonstrated its ability to stimulate rat nerve cells,^[23] stimulate nerve growth factor in human astrocytoma cells,^[24] and stimulate myelination.^[20] Additionally, a double-blind, parallel-group, placebo-controlled trial showed that supplementation with *hericium* improved cognitive ability.^[25]

***Flammulina velutipes* (Enokitake)**



Flammulina velutipes

Enokitake are long, thin white mushrooms commonly used in Asian cuisines. Enokitake mushrooms contain compounds with anti-tumor activity and epidemiological studies in Japan have associated the

mushroom with lower cancer rates.^[20] *In vivo* research showed that Proflamin, a compound isolated from Enokitake provided an 85% longer survival time in mice with cancer.^[21] Another *in vivo* study showed that Enokitake demonstrated anti-cancer activity in Swiss albino mice with Sarcoma 180.^[22]

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References

1. Borchers AT, Krishnamurthy A, Keen CL, Meyers FJ, Gershwin ME (March 2008). "The immunobiology of mushrooms". *Experimental Biology and Medicine* **233** (3): 259–76. doi:10.3181/0708-MR-227. PMID 18296732.
2. Wasser SP, Weis AL (1999). "Therapeutic effects of substances occurring in higher Basidiomycetes mushrooms: a modern perspective". *Critical Reviews in Immunology* **19** (1): 65–96. PMID 9987601.
3. Gunde-Cimerman N, Cimerman A (March 1995). "Pleurotus fruiting bodies contain the inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A reductase-lovastatin". *Experimental Mycology* **19** (1): 1–6. doi:10.1006/emyc.1995.1001. PMID 7614366. (Primary source)
4. Bowerman S (31 March 2008). "If mushrooms see the light". Los Angeles Times. <http://articles.latimes.com/2008/mar/31/health/he-eat31>.
5. Ji Y, Bi JN, Yan B, Zhu XD (January 2006). "[Taxol-producing fungi: a new approach to industrial production of taxol]" (in Chinese). *Sheng Wu Gong Cheng Xue Bao* **22** (1): 1–6. PMID 16572833.
6. Smith JE, Rowan NJ, Sullivan R (May 2002). [http://sci.cancerresearchuk.org/labs/med_mush/med_mush.html] "Medicinal Mushrooms:

Their therapeutic properties and current medical usage with special emphasis on cancer treatments"].
Cancer Research UK. p. 5. http://sci.cancerresearchuk.org/labs/med_mush/med_mush.html.

7. Sarfaraz Khan Marwat, Mir Ajab Khan, Muhammad Aslam Khan, Mushtaq Ahmad, Muhammad Zafar, Fazal-ur-Rehman and Shazia Sultana (2009). "Vegetables mentioned in the Holy Qura'n and Ahadith and their ethnomedicinal studies in Dera Ismail Khan, N.W.F.P., Pakistan". *Pakistan Journal of Nutrition* **8** (5): 530-538. <http://scialert.net/fulltext/?doi=pjn.2009.530.538>. Sahih Muslim, Book 23, Chapter 27, Hadiths
8. Shashkina MIa, Shashkin PN, Sergeev AV (October 2006). "[Chemical and medicobiological properties of Chaga (review)]". *Farmatsevtichnyĭ zhurnal* **40** (10). doi:10.1007/s11094-006-0194-4.
9. Di Rado, Alicia (July 2008). "A salad fixin' with medical benefits?". *EHope* (City of Hope National Medical Center) **7** (7). <http://www.cityofhope.org/about/publications/eHope/2008-vol-7-num-7-july-29/Pages/a-salad-fixin-with-medical-benefits.aspx>.
10. Di Rado, Alicia (November 2008). "Can a mushroom help fight lung cancer?". *EHope* (City of Hope National Medical Center) **7** (11). <http://www.cityofhope.org/about/publications/eHope/2008-vol-7-num-11-november-26/Pages/can-a-mushroom-help-fight-lung-cancer.aspx>.
11. Deng G, Lin H, Seidman A (September 2009). "A phase I/II trial of a polysaccharide extract from *Grifola frondosa* (Maitake mushroom) in breast cancer patients: immunological effects". *Journal of Cancer Research and Clinical Oncology* **135** (9): 1215–21. doi:10.1007/s00432-009-0562-z. PMID 19253021.
12. Kobayashi H, Matsunaga K, Oguchi Y (1995). "Antimetastatic effects of PSK (Krestin), a protein-bound polysaccharide obtained from basidiomycetes: an overview". *Cancer Epidemiology, Biomarkers&Prevention* **4**(3):275–81. PMID 7606203.
<http://cebp.aacrjournals.org/cgi/pmidlookup?view=long&pmid=7606203>.

13. Hetland G, Sandven P (March 2002). "beta-1,3-Glucan reduces growth of Mycobacterium tuberculosis in macrophage cultures". *FEMS Immunology and Medical Microbiology* **33** (1): 41–5. PMID 11985967. (primary source).
14. Amino M, Noguchi R, Yata J (September 1983). "[Studies on the effect of lentinan on human immune system. II. In vivo effect on NK activity, MLR induced killer activity and PHA induced blastic response of lymphocytes in cancer patients]" (in Japanese). *Gan to Kagaku Ryoho* **10** (9): 2000–6. PMID 6225393. (primary source)
15. Chan Y, Chang T, Chan CH (June 2007). "Immunomodulatory effects of Agaricus blazei Murill in Balb/cByJ mice". *Journal of Microbiology, Immunology, and Infection* **40** (3): 201–8. PMID 17639159. <http://www.jmii.org/content/abstracts/v40n3p201.php>. (primary source)
16. Masuoka, J (Apr 2004). "Surface glycans of Candida albicans and other pathogenic fungi: physiological roles, clinical uses, and experimental challenges" (Free full text). *Clinical microbiology reviews* **17** (2): 281–310. doi:10.1128/CMR.17.2.281-310.2004. ISSN 0893-8512. PMID 15084502.PMC 387410. <http://cmr.asm.org/cgi/pmidlookup?view=long&pmid=15084502>.
17. Roeder A, Kirschning CJ, Rupec RA, Schaller M, Weindl G, Korting HC (December 2004). "Toll-like receptors as key mediators in innate antifungal immunity". *Medical Mycology* **42** (6): 485–98. doi:10.1080/13693780400011112. PMID 15682636.
18. Firenzuoli F, Gori L, Lombardo G (March 2008). "The Medicinal Mushroom Agaricus blazei Murrill: Review of Literature and Pharmaco-Toxicological Problems". *Evidence-based Complementary and Alternative Medicine* **5** (1): 3–15. doi:10.1093/ecam/nem007. PMID 18317543.
19. Ferreira IC, Barros L, Abreu RM (2009). "Antioxidants in wild mushrooms". *Curr Med Chem* **16** (12): 1543-60. PMID 19355906.

20. Zhang Y, Mills GL, Nair MG (December 2002). "Cyclooxygenase inhibitory and antioxidant compounds from the mycelia of the edible mushroom *Grifola frondosa*". *Journal of Agricultural and Food Chemistry* **50** (26): 7581–5. doi:10.1021/jf0257648. PMID 12475274. (primary source).
21. Kim WG, Lee IK, Kim JP, Ryoo IJ, Koshino H, Yoo ID (July 1997). "New indole derivatives with free radical scavenging activity from *Agrocybe cylindracea*". *Journal of Natural Products* **60** (7): 721–3. doi:10.1021/np970150w. PMID 9249978. (primary source)
22. Kim MY, Seguin P, Ahn JK (August 2008). "Phenolic compound concentration and antioxidant activities of edible and medicinal mushrooms from Korea". *Journal of Agricultural and Food Chemistry* **56** (16): 7265–70. doi:10.1021/jf8008553. PMID 18616260. (primary source)
23. Wu Y, Wang D (February 2009). "A new class of natural glycopeptides with sugar moiety-dependent antioxidant activities derived from *Ganoderma lucidum* fruiting bodies". *Journal of Proteome Research* **8** (2): 436–42. doi:10.1021/pr800554w. PMID 18989955. (primary source)
24. Ker YB, Chen KC, Chyau CC (September 2005). "Antioxidant capability of polysaccharides fractionated from submerge-cultured *Agaricus blazei* mycelia". *Journal of Agricultural and Food Chemistry* **53** (18): 7052–8. doi:10.1021/jf0510034. PMID 16131110.
25. Bobek P, Galbavy S (2001). "Effect of pleuran (beta-glucan from *Pleurotus ostreatus*) on the antioxidant status of the organism and on dimethylhydrazine-induced precancerous lesions in rat colon". *British Journal of Biomedical Science* **58** (3): 164–8. PMID 11575739. (primary source)
26. Shi YL, James AE, Benzie IF, Buswell JA (2002). "Mushroom-derived preparations in the prevention of H₂O₂-induced oxidative damage to cellular DNA". *Teratogenesis, Carcinogenesis, and Mutagenesis* **22** (2): 103–11. doi:10.1002/tcm.10008. PMID 11835288. primary source.

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